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Original Article

A 'cut off' value of 'AP measurement to Transverse measurement Ratio (A/T Ratio)' for a provisional diagnosis of malignancy in sonologically confirmed solitary nodules of the thyroid

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Abstract
Introduction: *The low accuracy of ultrasound features for diagnosing malignancyin the thyroid justifies the widespread use of FNAC on sonologically selected nodules. The sonographic feature, 'height more than width'or in other words' anteroposterior measurement by transverse measurement ratio ≥1' has been studied earlier. No study has attempted to define the 'cut off' value of 'A/T ratio' that will give the best diagnostic yield in sonography and FNAC of solitary nodules of the thyroid gland and this study is an attempt to define the same.*
Aim of the work: *(1) To estimate the statistical measures of performance of positivity of the test criterion 'height (AP diameter) equal to or greater than the width (transverse diameter) to provisionally diagnose malignancy in solitary thyroid nodules. (2) To estimate the 'cut off' value of 'A/T ratio' that will give the best set of statistical measures of performance.*
Patients and Methods: *40 cases of sonologically confirmed solitary nodules were selected. The gray scale sonographic features of the solitary nodules and their three dimensions were noted. The 'A/T ratio', i.e., the ratio between anteroposterior measurement and transverse measurement of the nodules was calculated. The A/T ratio was correlated with presence of malignancy on FNAC/Histopathology.*
Results: *An A/T ratio greater than 0.79 has a sensitivity of 100% and specificity of 70.6% for a presumptive diagnosis of malignancy in sonologically confirmed solitary nodules of the thyroid gland. An 'A/T ratio equal to or greater than one' has a sensitivity of 66.67% only and specificity of 85.3%,for a presumptive diagnosis of malignancy in solitary nodules.*
Conclusion: *The test criterion of A/T ratio equal to or more than 0.79 is much superior to the test criterion, 'A/T ratio equal to or greater than one'for a sonologic presumptive diagnosis of malignancy in solitary nodules of the thyroid.*
Keywords: *Solitary thyroid nodule, recruitment for FNAC, A/T ratio, height more than width.*

Introduction

Malignancy is seen more frequently among solitary nodules of the thyroid than among cases of multinodular disease. But differentiation between malignant and benign nodules is not error-free on ultrasonography. The sonographic features which are associated with the malignant nodules (microcalcification, hypoechogenicity, irregular margin) have been used as morphologic features to diagnose malignancy with variable accuracy[1-5]. The low accuracy of ultrasound features for diagnosing malignancy has led to widespread use of FNAC for further evaluation of the nodules and ultrasound serves as a tool to select nodules for FNAC. A sonographic feature, 'height more than width' was added to the morphologic features suggestive of malignancy, by Kim et al[1]. The same feature was studied by Cappelli et al[6] and expressed as 'A/T ratio, i.e., anteroposterior measurement by transverse measurement ratio ≥1'. This feature used in thyroid sonography is analogous to the same feature used in solid lesions of the breast to diagnose malignanacy. The possible reason behind the higher association between nodules with anteroposterior measurement more than the transverse measurement ratio is that the benign nodules tend to 'respect' the longitudinal direction of the organ, during growth and tend to have a larger dimension along the longitudinal axis than in AP direction whereas the malignant nodules do not often 'respect' the longitudinal axis of the organ and are more often associated with the feature of 'anteroposterior measurement more than the transverse measurement' than benign nodules. No study has attempted to identify the 'cut off' value of 'A/T ratio' that will give the best diagnostic yield of malignant nodules in the sonography of the solitary nodules of the thyroid gland. This study is an attempt to define the same.

Methodology

Objectives

- To estimate the statistical measures of the performance of positivity of the test criterion 'height (AP diameter) more than the width (transverse diameter) to provisionally diagnose malignancyin solitary thyroid nodules.
- To estimate the 'cut off' value of 'A/T ratio' that will give the best set of statistical measures of the performance, as a screening test to provisionally diagnose malignancy in solitary thyroid nodules.

Sample Size: 40 cases of sonologically confirmed solitary nodules from patients referred as solitary nodule of thyroid.

Materials and Methods: The study was conducted at Department of Radiodiagnosis, Government Medical College Hospital, Thiruvananthapuram during the period from Jan 2012 to July 2013.

Inclusion criteria

1. palpatory impression of solitary thyroid noduleand
2. sonological confirmation of solitary nature of the nodule.

Exclusion criteria

1. Unwilling patients
2. Consent not obtained from patients
3. Presence of multiple nodules on ultrasound scanning
4. All the cases in which cytopathological diagnosis was not obtained
5. Patients with history of previous surgery or radiotherapy

Scanning protocol

Ultrasonography was performed using the machine GE-Logiq 200 PRO with 7.5 MHz linear probe and if necessary also with 5 MHz sector probe.

The sonographic features of the solitary nodules, particularly echotexture, margin & presence of microcalcifications, three dimensions and presence of lymph nodes were noted. The nodules with 'height (AP diameter) more than the width (transverse diameter) were specifically noted. The 'A/T rato', i.e., the ratio between anteroposterior measurement and transverse measurement of the

nodules was calculated and noted.

Data management

The statistical measures of performance of each individual ultrasound feature including 'A/T ratio equal to or greater than one,' were calculated, taking fine needle aspiration cytology as a confirmatory test; whenever available/possible, histopathology of the resected specimen was used as the confirmatory test. A Receiver Operating Characteristic Curve was plotted for various values of A/T ratio serving as test criteria to diagnose malignancy in a solitary nodule and the value of A/T ratio providing the bestpair of sensitivity and specificity is obtained and verified by 2 X 2 tables. The statistical measures of performance of this value of A/T ratio as a test criterion are compared with those of the test criterion 'A/T ratio equal to or greater than one'.

Observations and Results

More than two hundred cases of thyroid nodules which were considered to be solitary, on clinical palpation underwent ultrasound and a total number of 40 patients confirmed to have solitary nodules on ultrasound scan were included in the study.

The age of the patients varied between 16 years 66 years. Majority of patients (36 out of 40) (90%) were females.

Table 1 Distribution of study population according to age

Age Group	Frequency	Percentage
15-19	3	7.5
20-24	5	12.5
25-29	1	2.5
30-34	5	12.5
35-39	8	20
40-44	3	7.5
45-49	2	5
50-54	5	12.5
55-59	7	17.5
60 and above	1	2.5
Total	**40**	**100**

FNAC+/- histopathology showed benign nodule in 33 patients (82.5%) and malignant disease in 6 patients (15%) and thyroiditis with nodules in one (2.5%), thus making the benign processes 34 in number.

Table 2 Distribution of study population according to final diagnosis

		Frequency	Percentage
Final diagnosis	Malignant	6	15
	Benign	34	85
Total		**40**	**100**

Sonographically, these patients were assessed for size of the nodule, echotexture, margins, peripheral halo, calcification in nodule and lymph node enlargement.

Table No: 3 Distribution of study population according to presence of an 'AP diameter equal to or more than transverse diameter'

	Malignant	Benign	Total
AP≥ Tr	4	5	9
AP<Tr	2	29	31
Total	**6**	**34**	**40**

Statistical indices of the test criterion of presence of an 'AP diameter equal to or more than transverse diameter' for diagnosing malignancy

Sensitivity: 66.67%
Specificity: 85.29%
Positive Predictive value: 44.44%
Negative Predictive Value: 93.55%
LR+ : 4.53
LR-: 0.391
Accuracy: 82.50%
False Positive Rate: 14.71%

A nodule which is 'taller than wide' was defined as being greater in its anteroposterior dimension than its transverse dimension[1] and the feature was considered as a positive indicator of malignancy. If the criterion of being 'taller than wide', i.e., A/T ratio more than one (AP>Tr) is adopted as the test criterion, the sensitivity is less than that obtained for the criterion 'AP diameter equal to or more than transverse diameter' (AP≥Tr).

The Receiver Operating Characteristic curve for various cut-off values of A/T ratio was plotted (Fig. 1).

Fig. No: 1 The Receiver Operating Characteristic curve for various cut-off values of A/T ratio

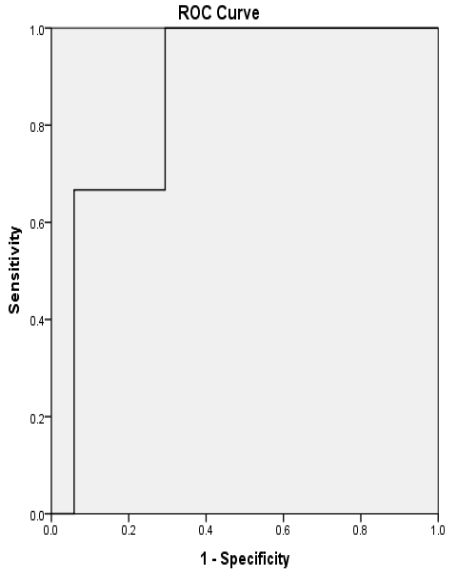

Table No: 4 Coordinates of the ROC curve

	Coordinates of the Curve			
	Test Result Variable(s):			
	Positive if Greater Than or Equal To[a]	Sensitivity	1 - Specificity	Specificity
1	-0.667	1.000	1.000	0.000
2	0.375	1.000	0.941	0.059
3	0.442	1.000	0.912	0.088
4	0.500	1.000	0.882	0.118
5	0.554	1.000	0.824	0.176
6	0.579	1.000	0.794	0.206
7	0.586	1.000	0.735	0.265
8	0.595	1.000	0.706	0.294
9	0.610	1.000	0.647	0.353
10	0.643	1.000	0.618	0.382
11	0.709	1.000	0.471	0.529
12	0.760	1.000	0.382	0.618
13	0.778	1.000	0.324	0.676
14	0.793	1.000	0.294	0.706
15	0.823	0.833	0.294	0.706
16	0.868	0.667	0.294	0.706
17	0.895	0.667	0.265	0.735
18	0.905	0.667	0.235	0.765
19	0.919	0.667	0.176	0.824
20	0.965	0.667	0.147	0.853
21	1.100	0.667	0.059	0.941
22	1.234	0.500	0.059	0.941
23	1.590	0.167	0.059	0.941
24	2.457	0.000	0.059	0.941
25	3.700	0.000	0.029	0.971
26	5.400	0.000	0.000	1.000

The ROC curve has an 'area under the curve' of 0.863. It can be seenthat a good'cut off' value is very close to 0.793 and in such a situation, the test criterion is fixed as presence of A/T ratio greater than the 'cut off value'. With this information at hand, '2 X 2' tables were prepared for each of the situation in which the test is considered positive, A/T ratio being greater than 0.78, 0.79 or 0.80.

Table No: 5 Distribution of study population according to the criterion 'A/T ratio more than 0.78'

	Malignant	Benign	Total
A/T>0.78	6	11	17
A/T≤ 0.78	0	23	23
Total	**6**	**34**	**40**

Statistical indices of the test criterion of presence of an 'A/T ratio more than 0.78'for diagnosing malignancy

Sensitivity: 100%
Specificity: 67.65%
Positive Predictive value: 35.29%
Negative Predictive Value: 100%
LR+: 3.09
LR- : 0.00
Accuracy: 72.50%
False Positive Rate: 32.35%

Table No: 6 Distribution of study population according to the criterion 'A/T ratio more than 0.79'

	Malignant	Benign	Total
A/T> 0.79	6	10	16
A/T ≤ 0.79	0	24	24
Total	**6**	**34**	**40**

Statistical indices of the test criterion of presence of an 'AP diameter more than 0.79' for diagnosing malignancy

Sensitivity: 100%
Specificity: 70.59%
Positive Predictive value: 37.50%
Negative Predictive Value: 100%
LR+ : 3.4
LR- : 0.00
Accuracy: 75.0%
False Positive Rate : 29.41%

Table No: 7 Distribution of study population according to the criterion 'A/T ratio more than 0.80'

	Malignant	Benign	Total
A/T> 0.80	5	10	15
A/T≤ 0.80	1	24	25
Total	**6**	**34**	**40**

Statistical indices of the test criterion of presence of an 'AP diameter more than 0.80' for diagnosing malignancy

Sensitivity: 83.3%
Specificity: 70.6%
Positive Predictive value: 33.3%
Negative Predictive Value: 96.0%
LR+: 2.83
LR-: 0.236
Accuracy: 72.50%
False Positive Rate: 29.41%

It can be seen that the diagnostic test criterion, 'A/T ratio > 0.79' gives the best pair of sensitivity (100%) and specificity (70.59) with a relatively low False Positive Rate (29.41%).

Statistical indices of test criterion of the presence of each of the grey scale features for a sonologic presumptive diagnosis of malignancy in a solitary nodule were calculated for the sake of completion, in this study. They were as follows. For hypoechogenicity of non-cystic nodules: Sensitivity 50%, Specificity 58.8%, PPV 17.6%, NPV 86.96%, LR+ 1.21 , LR- 0.85; For ill-defined/irregular margin: Sensitivity 83.3%, Specificity 91.17%, PPV 62.5%, NPV 96.9%, LR+ 9.44, LR- 0.18; For microcalcifications in the nodule: Sensitivity 66.67%, Specificity 100%, PPV 100%, NPV 94.4%, LR+ ∞, LR- 0.33.

Table No: 8 Distribution of Study Population According to Final Diagnosis

Malignant nodule	
Follicular carcinoma	1
Medullary carcinoma	1
Papillary carcinoma	4
	6
Benign nodule	
Follicular Adenoma thyroid	3
Colloid nodule	17
Degenerating colloid nodule	13
	33
Thyroiditis with nodule	
Nodular goitre with lympocytic thyroiditis	1

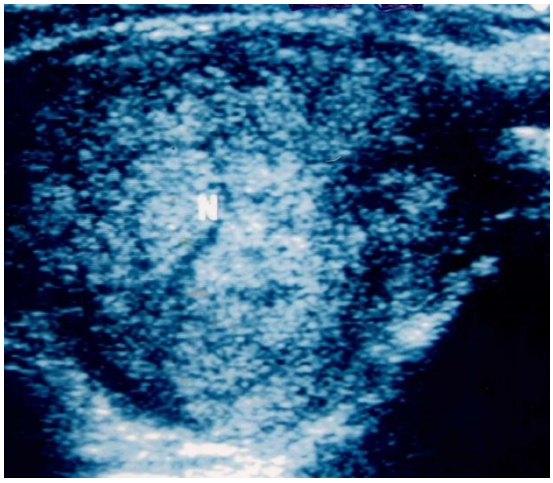

Fig. 2.A case of papillary carcinoma of the thyoid with ill-dfined margin and microcalcifications. Its anteroposterior diameter was more than its transverse diameter. Its A/T rato was 1.2, which is more than the 'cut off' value.

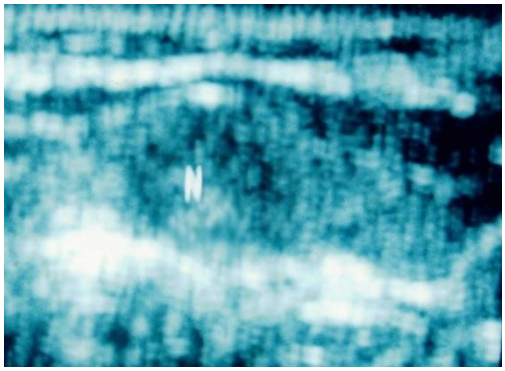

Fig.3 A case of papillary carcinoma of the thyroid. Its AP measurement is less than transverse measurement; however its A/T ratio was 0.8 which is more than the 'cut off' value of 0.79.

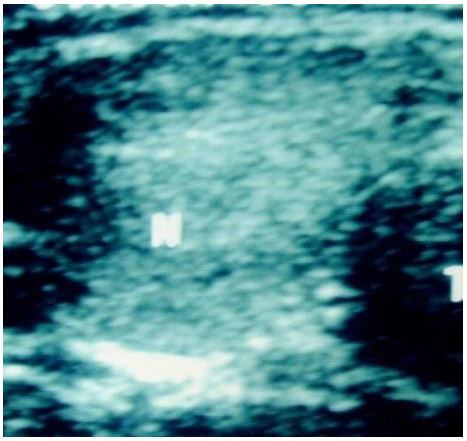

Fig. 4.A nodule with colloid degeneration on FNAC, which has an A/T ratio of 0.6, which is less than the 'cut off' value of 0.79.

Discussion

A screening test is a simple, non-invasive test that indicates suspicion of a disease, is often used in combination with other risk factors/indicators of the disease and needs confirmation. A confirmatory test is the one that establishes presence or absence of the disease, has high specificity, provides a definite diagnosis, can be invasive and gives importance to accuracy and precision than to patient acceptability. In thyroid nodules, particularly solitary nodules of the thyroid gland, FNAC is being used as a confirmatory test, particularly prior to surgery. Ultrasound features of the thyroid nodules lack high specificity and cannot alone effectively differentiate the malignant nodule from the benign ones. Thus ultrasound has been utilized more like a screening test and less like a confirmatory test.

Screening tests are devised in such a way that they have high sensitivity so that true positive cases should not be missed, even at the cost of low specificity; they may be allowed to have a lower specificity and they may miss out on true negatives and this problem can be corrected by confirmatory tests done afterwards which have high specificity. FNAC of solitary nodules of the thyroid serves as a confirmatory test with high specificity.

All the conventional gray scale ultrasound features of potentially malignant solitary nodules, namely microcalcifications, hypoechogenicity and irregular marginshave low sensitivity for a presumptive diagnosis of malignancy. All of them are nominal and dichotomous variables, which can be categorized as either of the two of presence and absence of an ultrasound feature. A novel gray scale feature, 'height more than width' (anteroposterior diameter more than transverse diameter) was added to the gray scale ultrasound features suggestive of malignancy, by Kim et al[1]. This ultrasound feature possesses the potential to be expressed as a continuous variable in the form of A/T ratio; 'height more than width' can be expressed as 'AP diameter divided by Transverse diameter, greater than one' (A/T ratio> 1).

The criterion, 'height more than width' or 'A/T ratio >1' is found to possess high specificity by Cappelli et al[6]. Since the role of ultrasound in the clinical practice is that of a screening test to recruit cases for another highly specific test, i.e., FNAC, a lower 'cut off' value of A/T ratio is more acceptable as it will yield a higher sensitivity, though it is at the cost of some decrease in specificity. Such a 'cut off value' is not yet described in the literature and this study is an attempt to define the same.

On an analysis of the ROC curve plotted with various A/T ratiosas cut off values, we can infer that the criterion, A/T ratio A/T>0.79 gives a very high sensitivity (which is 100% in this study, but can potentially be a little lower, in a study with a very large population) and an acceptable level of specificity for a screening test (70.59% in this study). The statistical measures of performance of these two test criteria are compared in the table given below.

Table No: 9 Comparison of the test criterion of 'A/T≥1' with that of 'A/T>0.79'

Test criterion	Sensitivity	Specificity	PPV	NPV	LR+	LR-	Accuracy	False Positive Rate
A/T≥1	66.67%	85.29%	44.44%	93.55%	4.53	0.391	82.50%	14.71%
A/T>0.79	100%	70.59%	37.50%	100%	3.40	0	75.0%	29.41%

The test criterion 'A/T ratio > 0.79for a presumptive diagnosis of malignancy can be seen to be positive in all malignant solitary nodules of thyroid in the present study, thus recruiting all such cases for the highly specific confirmatory test, namely FNAC. The false positive rate of the test criterion,'A/T > 0.79' is 29.41% which is acceptable considering that such a test criterion hardly misses any true positive cases, i.e., malignant nodules, and the false positive cases can be recognized at the next step by FNAC, which is not too 'invasive ' in nature.

Combining this newly proposed test criterion (A/T > 0.79) with other positive grey scale test criteria can yield a better diagnostic performance.

As the diagnostic features identified on solitary nodules are applicable to individual nodules of multinodular disease, to a good extent, the nodules exhibiting A/T ratio greater than 0.79 in multinodular disease may be viewed with suspicion.

Conclusions

1) An A/T ratio, i.e., a ratio between the anteroposterior diameter and transverse diameter greater than 0.79 has a sensitivity of 100% and specificity of 70.59% for a presumptive diagnosis of malignancy in sonologically confirmed solitary nodules of the thyroid gland.
2) An A/T ratio equal to or greater than one has a sensitivity of 66.67% and specificity of 85.29%only for a presumptive diagnosis of malignancy in sonologically confirmed solitary nodules of the thyroid gland.
3) As a screening test (preliminary test) to recruit cases for FNAC (FNAC being more specific and invasive), the test criterion of 'A/T ratio greater than 0.79 is much superior to the test criteria, 'A/T ratio equal to or greater than 1' and 'height more than width'.

The present authors recommend that all sonologically confirmed solitary nodules of the thyroid gland with A/T ratio greater than 0.79 should undergo FNAC/histopathology to rule out malignancy.

Conflict of interest: None

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