ISSN NO. 2320-5407

Journal homepage: http://www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

Color Doppler evaluation of thyroid nodules : Validation of quantitative & qualitative analysis in predicting malignancy

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Manuscript Info

Manuscript History:

Received: 14 May 2015
Final Accepted: 19 June 2015
Published Online: July 2015

Key words:

Thyroid Doppler , Thyroid nodules, Thyroid Malignancy

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Abstract

INTRODUCTION: Changes in vasculature pattern and doppler parameters is well established with cellular proliferation in malignant lesions. We have evaluated the quantitative and qualitative differences in vascularity in pathologically confirmed malignant and benign thyroid nodules. MATERIALS AND METHODS: Pattern of vascularity and color doppler spectral parameters were evaluated in 40 patients with thyroid nodules and correlated with pathological findings. RESULTS: Pattern of vascularity as well as doppler spectral parameters showed differences of high statistical significance in benign versus malignant thyroid nodules. CONCLUSION: Qualitative as well as quantitative analysis of vascularity of thyroid nodules show highly significant clinical importance proven statistically.

INTRODUCTION

There is high prevalence of palpable as well as non palpable thyroid nodules world wide as well as in Indian population especially in iodine deficient areas. However very low rate of malignancy in these nodules makes it essential to have accurate, easily accessible measures to rule out malignancy in these nodules pre operatively.

Ultrasound is easily available, non invasive, inexpensive means without any radiation exposure. Even present guidelines of American Thyroid Association state that ultrasound be performed in all thyroid nodules and Fine Needle Aspiration Cytology (FNAC) only in potentially malignant ones. [1] In a previous study we found grey scale ultrasound parameters especially poorly defined margins and thick incomplete halo to be accurate predictors of malignancy in thyroid nodules. [2]

In present study we have extrapolated the well established association of vascularity with cellular proliferation to thyroid nodules. The present study evaluates qualitative (pattern of vascularity) and quantitative (spectral parameters) analysis of color doppler in thyroid nodules and their effectiveness in differentiating benign form malignant nodules keeping histopathological findings as reference standard .

MATERIALS & METHODS

Necessary approvals were taken from institutional ethical committee. This is a prospective descriptive analytical study carried out on 40 patients with suspected non palpable thyroid nodules that included indoor & outdoor patients visiting the ultrasound section of the department of Radio-diagnosis, Rajindra Hospital, Patiala.

Color doppler Examination :

Color doppler examinations were conducted using 5-12 Hz linear probe on Philips Envisor (Andover MA , USA) . Vascularity pattern was evaluated using sagittal and transverse scans performed along the maximum

diameter of the nodule. For analyzing pattern of vascularity distribution, we have followed classification proposed by Chammas et al [3] as follows:

I Absent Signal Blood Flow
II Exclusively Perinodular Blood Flow
III Perinodular Blood flow equal to or greater then intranodular blood flow
IV Marked intranodular blood flow and less significant perinodular blood Flow
V Exclusively Intranodular Blood Flow

The amplifier gain settings were set in each case just below the point of appearance of random color noise. Necessary adjustments were made to pulse repetition frequency, wall filter and sample volume size to optimize flow imaging and minimize artifacts (PRF:900Hz , wall filter : 50)

The duplex parameters thereafter obtained included pulsatility index [PI] and resistivity index [RI] .The final value for these parameters was obtained as a mean of three parameters form different arteries. In nodules with intranodular flow, two of three values were obtained from intranodular vessels.

Values of PI > 1.5 and RI > 0.75 were presumed to be suggestive of malignancy following results of Chammas et al [3], Holden et al [4]and Cerbone et al [5].

Statistical Examination :

Calculations of accuracy, sensitivity, specificity, and negative and positive predictive values were performed with the use of a 2 × 2 contingency table. Statistical evaluation was performed using the chi square test, and the predictivity test of Galen and Gambino. The significance level was always set at a value of $p \leq .05$ (5%).

OBSERVATIONS AND RESULTS :

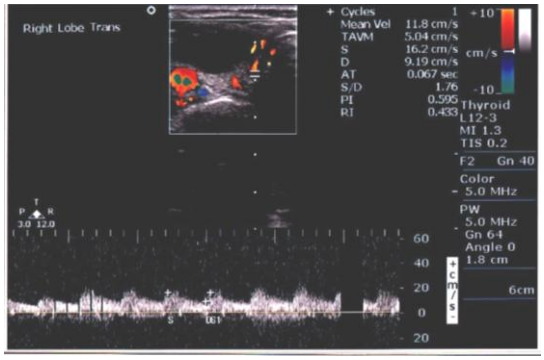

Figure 1: showing type II pattern of vascularity and spectral parameters in a cystic nodule

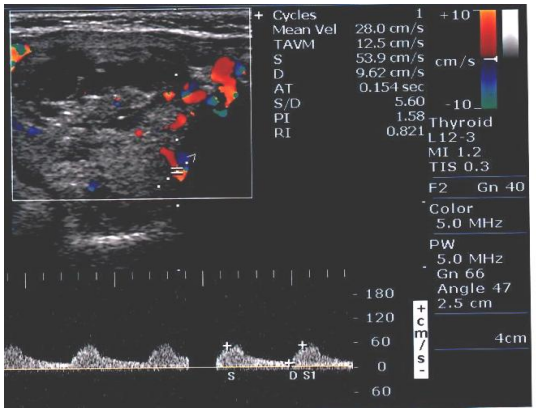

Figure 2

Figure 2: showing spectral parameters in a nodule having type III pattern of vascularity

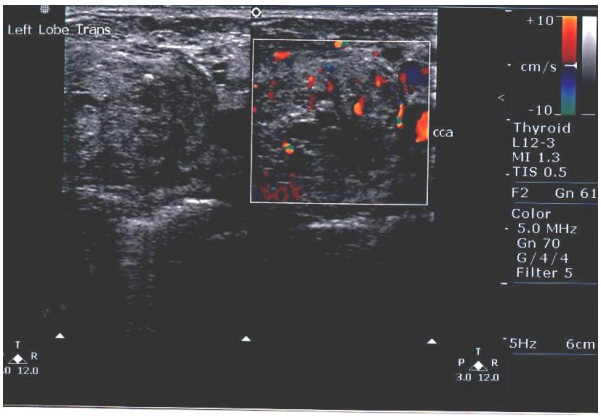

Figure 3

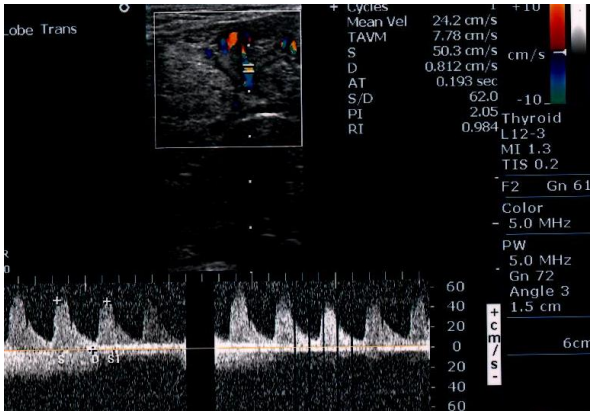

Figure 4

Figures 3, 4: showing Type IV vascularity pattern and spectral parameters in a malignant nodule

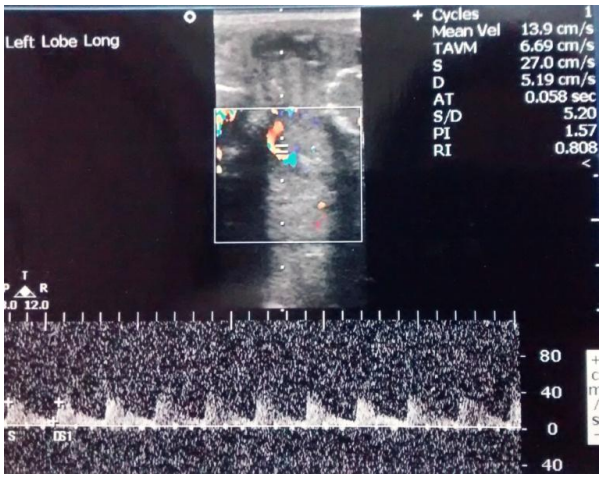

Figure 5

Figure 5: showing spectral parameters in intranodular vessel in a malignant nodule

TABLE I: SHOWING PATTERN OF VASCULARITY IN THYROID NODULES (N=40)

Pattern of Vascularity	No. of Patients	Percentage (%)
Type I Absent blood flow	1	2.5
Type II Exclusively Perinodular blood flow	7	17.5
Type III Perinodular blood flow equal to or greater then intranodular blood flow	22	55
Type IV Marked intranodular blood flow and less significant perinodular blood flow	10	25
Type V Exclusively intranodular blood flow	0	0

TABLE II : SHOWING SPECTRAL INDICES (PI AND RI) OF THYROID NODULES (39) NODULES

Characteristics	No. of Nodules	Percentage
PI		
• >1.5	10	25
• <1.5	29	72.5
RI		
• >0.75	12	30
• <0.75	27	67.5

TABLE III: COLOR DOPPLER FINDINGS IN THYROID NODULES IN CORRELATION WITH HISTOPATHOLOGICAL FINDINGS (N=39)

Characteristics	Pathological Diagnosis			
	Benign(n=31)		Malignant(n=8)	
	No.	%	No.	%
1. Pattern of Vascularity				
• Type I	1	3.125	0	0
• Type II	7	21.875	0	0
• Type III	20	62.5	2	25
• Type IV	4	9.375	6	75
• Type V	0	0	0	0
2Pulsatility Index				
• >1.5	4	12.5	6	75
• <1.5	27	84.375	2	25
3. Resistivity Index				
• >0.75	5	15.625	7	87.5
• <0.75	26	81.25	1	12.5

TABLE IV: DIAGNOSTIC INDEX FOR INDIVIDUAL COLOR DOPPLER CRITERIA OF THYROID NODULES

Characteristics	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
PATTERN OF VASCULARITY	75	87.5	60	93.33	85
SPECTRAL PARAMETERS					
PI	75	87.1	60	93.1	82.5
RI	87.5	83.87	58.33	96.3	82.5
PI +RI	85.71	86.67	60	96.3	80
PATTERN OF VASCULARITY +SPECTRAL PARAMETERS	83.33	93.1	71.43	96.42	80

TABLE V
COLOR DOPPLER FINDINGS IN 40 MALIGNANT AND BENIGN THYROID NODULES (N=40)

Characteristics	Pathological Diagnosis				p value
	Benign(n=31)		Malignant(n=8)		
	No.	%	No.	%	
1. Pattern of Vascularity					
• Type I	1	3.125	0	0	
• Type II	7	21.875	0	0	
• Type III	20	62.5	2	25	0.003
• Type IV	4	9.375	6	75	
• Type V	0	0	0	0	
2Pulsatility Index					
• >1.5	4	12.5	6	75	0.0003
• <1.5	27	84.375	2	25	
3. Resistivity Index					
• >0.75	5	15.625	7	87.5	0.000096
• <0.75	26	81.25	1	12.5	

On statistical analysis, all the three parameters on color Doppler examination were found to be statistically significant for predicting malignancy in thyroid nodules. PI was found to be having p <0.001 and hence highly significant while p value for RI was found to be less than 0.0001 and hence very highly significant.

DISCUSSION

Qualitative analysis: probability of malignancy was seen increasing with increase in intranodular blood flow. This can be attributed to increase in intranodular vascularity with high cellular proliferation in malignancy. Exclusively intranodular Type V flow was not found in any of the nodules we examined. In our opinion this can be attributed to the smaller sample size we have taken.

Type I or II pattern of vascularity was not shown by any malignant nodules. Mixed perinodular as well as intranodular vascularity was present in >70% of benign and 100% of malignant nodules; but this was type IV (intranodular > perinodular) in 75 % of malignant nodules and type III (perinodular > intranodular) in 62% of benign nodules.

In present study, pattern of vascularity had specificity of 87.5% and positive predictive value (PPV) of 60%, while sensitivity was 75%, negative predictive value (NPV) was 93.33% and accuracy was 85% for predicting malignancy.

In study by Papini et al [6] sensitivity and specificity of pattern of vascularity as predictor of malignancy was 74.2% and 80.8% respectively while PPV was 24%. Fukunari et al [7] reported that pattern of vascularity had specificity of 74.2% and PPV of 46.57%, while sensitivity was 88.9%, NPV value was 95.78% and accuracy was 81%. Chammas et al [3] reported that pattern of vascularity was 97.62% specific for malignancy (PPV-78.57%, NPV 98.4%) with sensitivity of 84.61%

Quantitative analysis: Evaluation of pattern of vascularity can be operator and equipment dependent. Analysis of quantitative parameters of spectral parameters brings more objectivity in color doppler evaluation.

PI>1.5 for predicting malignancy had specificity of 87.1% and PPV of 60%, while sensitivity was 75%, NPV was 93.1% with accuracy of 82.5% in present study.

Fukunari et al [7] reported that PI as predictor of malignancy had specificity of 79% while sensitivity was 69.1% and accuracy was 78%. Miyakawa M et al [8] reported that PI was 92% specific for malignancy with sensitivity of 87.5%

In present study, RI for predicting malignancy had specificity of 83.87% and PPV of 58.33%, while sensitivity was 87.5%, NPV was 96.3% and accuracy was 82.5%.

De Nicola H et al [9] reported that RI had specificity of 96% and PPV of 62%, while sensitivity was 50%, NPV was 93% and accuracy was 91%. Chammas et al [3] reported that RI was 88% specific for malignancy with sensitivity of 92.3%

Introduction of elements of subjectivity and lack of difficulty of reproducibility due to technical parameters of color doppler was avoided by using parameters as per a pre determined protocol.

CONCLUSION:

Evaluation of pattern of vascularity and pulsed Doppler parameters can predict malignancy in thyroid nodules sufficiently. Amongst the used quantitative and qualitative parameters, we found RI to be the most useful parameter showing p value <0.0001 on statistical analysis.

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