ORIGINAL ARTICLE

To Determine The Positive Predictive Value Of Magnetic Resonance Spectroscopy In Diagnosing Malignant Thyroid Nodules By Taking Histopathology As A Gold Standard

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ABSTRACT:

Objective: To determine the positive predictive value of magnetic resonance spectroscopy in diagnosing malignant thyroid nodules by taking histopathology as a gold standard.

Methodology: This descriptive cross-sectional study was undertaken at the department of Radiology, CMH Multan from October 2014 to March 2015. 77 patients with malignant thyroid nodules on ultrasonography between ages 30-70 years, of either gender were included. Patients with previous thyroid surgery, already biopsy proven malignant thyroid nodules and, those having contraindication to magnetic resonance spectroscopy (MRS) were excluded. All the patients then underwent MRS for choline peak and choline /creatine (Cho/Cr) ratio. Findings were correlated with histopathology.

Results: Mean age of the patients was 46.53 ± 9.15 years. Out of these 77 patients, 62 (80.52%) were female and 15 (19.48%) were males with female to male ratio of 4:1. MRS supported the diagnosis of malignant thyroid nodules in 60 patients. Histopathology confirmed malignant thyroid nodules in 49 (true positive) cases where as 11 (False Positive) had no malignant lesion on histopathology. Positive predictive value of magnetic resonance spectroscopy (MRS) in diagnosing malignant thyroid nodules was 81.67%.

Conclusion: Magnetic resonance spectroscopy (MRS) is a non-invasive modality of choice with high positive predictive value in diagnosing malignant thyroid nodules. It has not only dramatically improved our ability of diagnosing thyroid lesions pre-operatively but also helps the surgeons for proper decision making.

Keywords: Magnetic resonance spectroscopy, Thyroid malignancy, Thyroid nodules

Introduction:

Thyroid nodules are lumps arising within an otherwise normal thyroid gland. Palpable nodules are present in approximately 4 to 7% of adults, and up to 50% of adults will have non-palpable nodules discovered at the time of death[1]. Multinodular goiter is the most common benign lesion of the thyroid[2]. Although most thyroid nodules are benign but Ma et al[3] in their study found the prevalence of malignant thyroid nodule to be 55%. It is important to categorize these nodules as either benign or malignant lesions before surgery. Early detection of thyroid cancer is important as it leads to better prognosis because they are at a less advanced clinical stage[4].

Ideally, diagnostic procedures should be not only of high accuracy but also non-invasive. Most commonly performed diagnostic procedure to confirm the presence of a nodule and assess the status of the whole gland is an ultrasound. Measurement of thyroid stimulating hormone and anti-thyroid antibodies help to decide whether there is a functional thyroid disease, such as Hashimoto's thyroiditis, a known cause of a benign nodular goiter[5]. Measurement of calcitonin is necessary to exclude the presence of medullary thyroid cancer.

Fine needle aspiration (FNA) for cytology is considered the most valuable method preoperatively in differentiating malignant from benign thyroid lesions[6]. Compared with FNAC, magnetic resonance imaging (MRI) has the advantage of being non-invasive and giving immediate information[7]. Focal nodular lesion characterization with MRI is based on their morphology, signal intensity on different sequences and their behavior with para-magnetic contrast agents[8].

Magnetic resonance spectroscopy (MRS) allows biochemical characterization of scanned tissue and has been proved to be a sensitive method in identifying malignant nodules[6,9]. Malignant lesions usually have elevated choline concentrations, reflecting increased membrane synthesis and a higher cell turnover[9]. In a study by Gupta et al, positive predictive value of magnetic resonance spectroscopy (MRS) in identifying malignant thyroid nodule was found to be 89%[10].

As the available literature on the problem discussed was very scarce, this study was conducted to determine the positive predictive value (PPV) of magnetic resonance spectroscopy in diagnosing malignant thyroid nodules taking histopathology as gold standard. The results of this study could give the surgeons an accurate, non-invasive imaging modality for pre-operative assessment of thyroid malignancy so that they could plan the treatment accordingly. Grey scale ultrasonography despite having high predictive values is an operator dependent technique with wide range of positive predictive values (for characterization of thyroid nodules) ranging from 56% to 95%[11]. MR spectroscopy is more standardized technique having lower operator

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dependency and subjective variability. Thus, this study was conducted to gauge whether MR spectroscopy has the potential to fill in this diagnostic vacuum or not.

METHODOLOGY:

The study was conducted in the Radiology Department of Combined Military Hospital Multan, from October 2014 to March 2015. Sample size of 77 cases was calculated with 95% Confidence level. Non-probability, purposive sampling was done. The study was approved by institute's ethical committee.

All patients, of both genders, ages between 30–70 years, having thyroid nodules on clinical examination were included. Patients with history of thyroid surgery, diagnosed biopsy proven malignant thyroid, having any MRI incompatible metallic devices in their body and those having claustrophobia were excluded from study to overcome confounding factors and bias in results. Informed consent was obtained from every patient. All basic demographic information of each patient (name, age, sex, address and contact) was also noted. MR Spectroscopy was performed through single voxel technique. After water suppression, a point-resolved spectroscopy (PRESS) technique was used for localization and the studies were obtained with parameters including TE and TR of 135 and 1500 respectively. On MR spectroscopy, presence of elevated choline and reduced NAA peaks on MR spectrum with increased choline/creatine (Cho/Cr) ratio > 1.5 (Normal is 1.2) and decreased NAA/choline (NAA/Cho) ratio <1.2 (Normal is 1.6) was considered as positive. Each MRS report was correlated with the histopathology report and was assessed for confirmation of positive cases.

The collected data was analyzed statistically by using SPSS version 20. Effect modifiers like age, gender and duration of disease were controlled through stratification and post-stratification chi square was applied to see their effect on outcome. P-Value ≤ 0.05 was taken as significant.

RESULTS:

Age range in this study was from 30-70 years with mean age of 46.53 ± 9.15 years (Figure-1). Majority of the patients 35 (45.45%) were between 41 to 50 years of age. Out of these 77 patients, 62 (80.52%) were female and 15 (19.48%) were males with female to male ratio of 4:1 (Figure-2).MRS supported the diagnosis of malignant thyroid nodules in 60 (77.92%) patients. Histopathology confirmed malignant thyroid nodules in 49 (True Positive) cases, whereas 11 (False Positive) had no malignant lesion on histopathology (Table-1). Positive predictive value of magnetic resonance spectroscopy (MRS) in diagnosing malignant thyroid nodules was 81.67%. Stratification of positive predictive value with respect to age groups has been shown in Table-2, whereas gender stratification is shown in Table-3

Figure: 1
Distribution of patients according to Age (n=77)

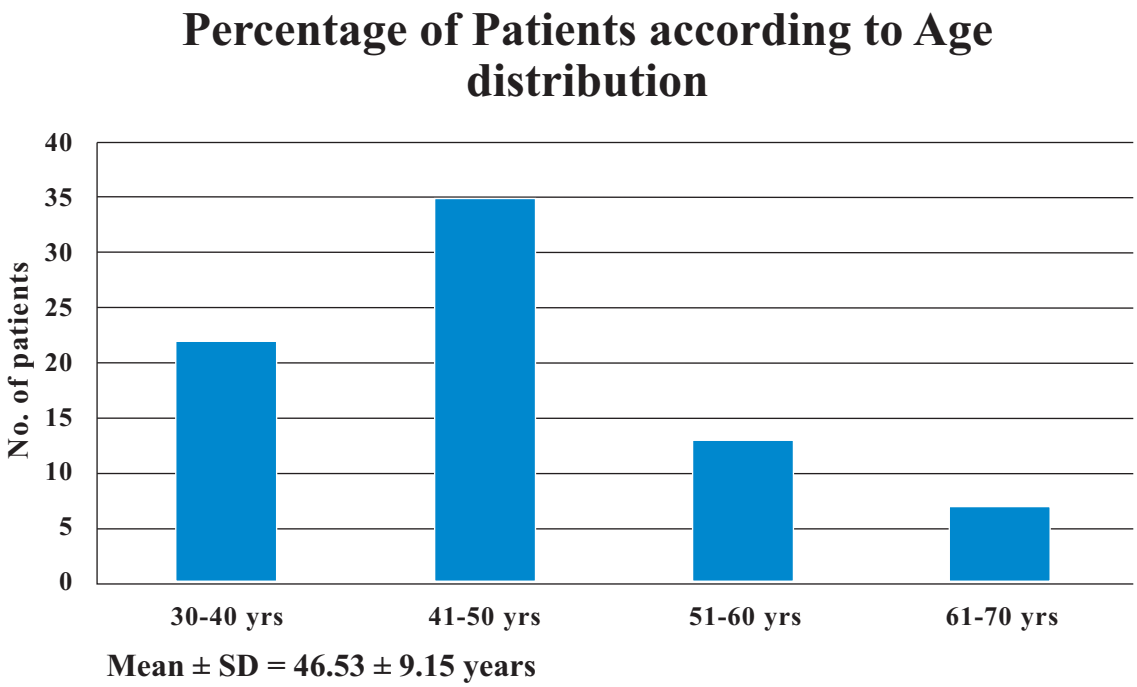

Figure: 2
Distribution of patients according to Gender (n=77)

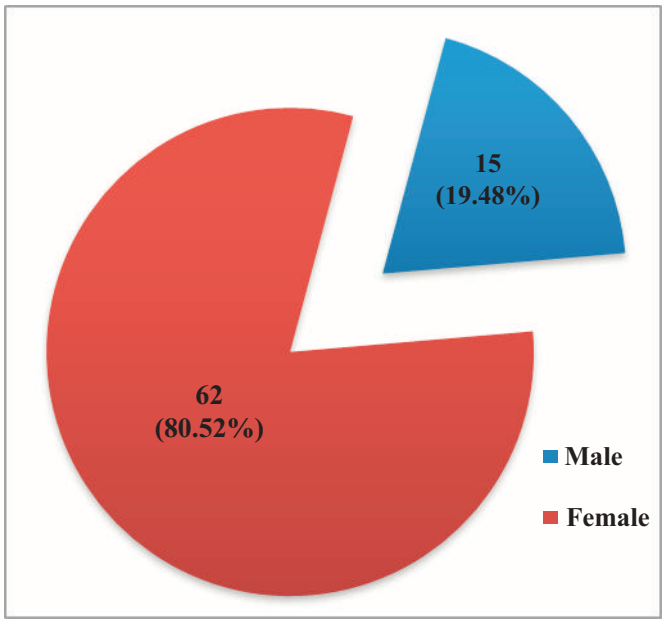

Table:1
Summary of Results (n=77)

	Positive on MRS result	Negative on MRS result	P-Value
Positive results on Histopathology	49 **(TP)***	04 **(FN)*****	**0.202**
Negative results on Histopathology	11 **(FP)****	13 **(TN)******	

*-TP=True positive **-FP=False positive ***-TN=True negative ****-FN=False negative

$$\text{Positive Predictive value} = \frac{\text{True Positive}}{\text{True Positive + False Positive}} \times 100 = \mathbf{81.67\%}$$

Table:2
Stratification of PPV with respect to age groups

Age (years)	True Positive	False Positive	P-Value
30-40	14	03	
41-50	23	05	
51-60	07	03	**0.564**
61-70	05	00	

Positive Predictive Value (PPV) for age 30-40 years: 82.35%

Positive Predictive Value (PPV) for age 41-50 years: 82.14%

Positive Predictive Value (PPV) for age 51-60 years: 70.0%

Positive Predictive Value (PPV) for age 61-70 years: 100.0%

Table: 3
Stratification of PPV with respect to Gender

Gender	True Positive	False Positive	P-Value
Male	40	09	
Female	09	02	**0.989**

Positive Predictive Value (PPV) for Male: 81.63%

Positive Predictive Value (PPV) for Female: 81.82%

DISCUSSION:

Thyroid carcinoma is the commonest endocrine malignancy and accounts for approximately 1% of all malignancies[12]. It is second only to carcinoma of the ovary, as the leading cause of death among endocrine cancers[13]. The incidence of thyroid cancer has almost tripled in the United States in the last 35 years, from 4.85 cases per 100,000 in 1975 to 12.23 cases per 100,000 in 2007[14]. This increase is mainly due to small papillary cancers, by contrast to the undifferentiated thyroid cancers that have a decreasing trend[15]. In Pakistan, thyroid cancer is responsible for 1.2 % cases of malignant tumors[16]. Papillary carcinoma is the most common and constitutes 57 to 89 % of all thyroid malignancies[17-18]. The thyroid nodules are evaluated by clinical examination, ultrasound and fine needle aspiration cytology (FNAC). Adjuncts include computed tomography (CT), magnetic resonance imaging (MRI) and more recently, fluorodeoxyglucose positron emission tomography (FDG-PET), ultrasound based elastography and magnetic resonance spectroscopy (MRS)[19-21].

Magnetic resonance spectroscopy (MRS) is a non-invasive diagnostic test that uses strong magnetic fields to measure and analyze the chemical composition of human tissues. MRS relies on the fact that chemicals in the body emit radiofrequency signals when stimulated by a strong magnetic field. By analyzing the different chemical compounds or metabolites in a diseased tissue area and comparing these with the normal metabolite composition of corresponding tissue, MRS has the potential to provide information that can assist in diagnosing pathological states and has been investigated as a feasible means of identifying malignant nodules[22]. So, this study was conducted to determine the positive predictive value (PPV) of magnetic resonance spectroscopy in diagnosing malignant thyroid nodule taking histopathology as gold standard.

A study carried out by Gupta et al[23] correlated choline peaks with the presence of malignancy with a sensitivity of 100%, specificity of 89% and positive predictive value of 90.0%. In another study[24], magnetic resonance spectroscopy was carried out in 17 benign cases, 16 follicular adenoma, and 1 colloid goiter. Of the 17 benign cases, only 1 showed choline peak; however, all 8 follicular carcinoma cases showed prominent choline peak.The sensitivity, specificity, positive predictive value and negative predictive value of magnetic resonance spectroscopy (MRS) in identifying malignant thyroid nodule was found to be 100%, 94.11%, 88.88% and 100% respectively.

Another study[22], succeeded in discriminating thyroid carcinomas from normal thyroid tissue based on the comparison of their respective MRS spectra: 8 patients with biopsy proven thyroid tumors larger than 1 cm^3 and 5 volunteers without lesions, participated in this study. MRS reported significant differences in the spectra of malignant samples. In addition to an increase of aminoacids and di- and tri-glycerides in carcinomas, the authors found that choline and creatine signals were only present in material coming from carcinomas, whereas no trace of such markers was observed in patients with normal thyroid. Therefore, choline/creatine ratio was chosen as a marker of malignancy: this ratio ranged from 1.6 (in cases of well-differentiated follicular carcinoma) to 9.4 (in thyroids with anaplastic thyroid cancer).

In the present study, MRS supported the diagnosis of malignant thyroid nodules in 60 (77.92%) patients. Histopathology confirmed malignant thyroid nodules in 49 (true positive) cases where as 11 (False Positive) had no malignant lesion on histopathology. Positive predictive value of magnetic resonance spectroscopy

(MRS) in diagnosing malignant thyroid nodules was 81.67%.

In-vivo examinations identify only two critical metabolites (choline and creatine) which have known associations with cancer. When this resonance ratio was calculated for follicular adenoma, some benign lesions also showed mildly raised values. One possible explanation was that adenoma with a malignant spectral pattern were in the process of malignant transformation. On the whole, it was concluded that MRS has high positive predictive value for diagnosing malignant thyroid lesions and method of choice for the diagnostic imaging of thyroid nodules.

CONCLUSION:

Magnetic resonance spectroscopy (MRS) is the non-invasive modality of choice with high positive predictive value in diagnosing malignant thyroid lesions. It has not only dramatically improved our ability of diagnosing thyroid lesions pre-operatively but also helps the surgeons for proper decision making. So, we recommend that magnetic resonance spectroscopy (MRS) should be done routinely in all suspected cases of malignant thyroid lesions for accurate assessment pre-operatively and opting proper surgical approach.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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