Role of Magnetic Resonance Spectroscopy in Differentiating Benign From Malignant Nodules of Thyroid Gland, Using Tissue Diagnosis as Gold Standard

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ABSTRACT

Objective: To analyze the diagnostic accuracy role of Magnetic Resonance Spectroscopy in differentiating benign from malignant nodules of thyroid gland by using tissue diagnosis as a gold standard.
Study Design: Co-relational Analytical study.
Place and Duration: At Department of Radiology, Children Hospital and Institute of Child Health, Multan from 1st October 2017 to 1st October 2018.
Methodology: A total of seventy patients (of both genders) were recruited for this study who clinically presented with palpable thyroid nodule. The patients who had any previous surgery of thyroid, thyroid malignancy (proven by biopsy), claustrophobic and with contraindications to Magnetic Resonance Spectroscopy that is cardiovascular implanted electronic devices were excluded. Magnetic Resonance Spectroscopy was done for Choline Peak and Choline/Creatine ratio to assess thyroid nodule and results were then compared with tissue diagnosis.
Results: among total of 70 patients, malignant thyroid nodules diagnosed in 51 (72.85%) and Magnetic Resonance Spectroscopy shows true positive in 96.07% (n=49) patients and with and among them 93.87% (n=46) were found to be true positive while 6.13% were false positive. Among 24 Magnetic Resonance Spectroscopy negative patients, 16 were true negative while 05 were false negative patients (p=0.0001). Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of Magnetic Resonance Spectroscopy in diagnosing malignant thyroid nodule taking tissue diagnosis as gold standard was 93.51%, 84.35%, 95.24%, 79.51% 91.40% respectively.
Conclusion: Magnetic Resonance Spectroscopy is an extremely sensitive and noninvasive tool which gives accurate method for diagnosing malignant thyroid nodules.
Keywords: Magnetic Resonance Spectroscopy, Thyroid Nodules, Benign, Malignant, Tissue, Diagnosis, Sensitivity

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INTRODUCTION

Thyroid nodules are swellings which can commonly occur in an otherwise normal thyroid gland. A thyroid nodule can appear in any part of the gland. Prevalence of palpable nodules was found to be 4-7% in adults and about 50% have non-palpable nodules.[1,2] In patients with thyroid nodules timely diagnosis is of vital significance as it is one of the most treatable malignancies.[3,4] Fine Needle Aspiration Cytology (FNAC)is considered to be the most important pre-operative method to differentiate between malignant and benign thyroid nodules.[5] But compared to FNAC, Magnetic Resonance Imaging (MRI) is a non-invasive technique to give immediate and detail information.[6]

MRI has emerged as the most competent and adaptable imaging tool for diagnosis, prognosis, evaluation of treatment, progression of disease and treatment planning.[7] Another imaging technology, Magnetic Resonance Spectroscopy (MRS) uses to measure biochemical changes and molecular composition of tissue and can identify malignant nodules.[8,9] MRS

uses strong magnetic fields to measure biochemical changes and molecular composition within body.[10,11]

Moreover, tumor characterization depends on their biochemical changes and molecular composition, in vivo assessment recognizes just two basic metabolites (choline and creatine). For diagnosis of thyroid cancer, two basic metabolites (either choline alone or the choline/creatine ratio) have 100% sensitivity and 88.88% specificity.[12-14] In malignant lesions, there is a high concentration of choline, indicating increase membrane synthesis and cell turnover.[12]

Among the major life-threatening endocrine carcinomas, thyroid malignancy is the second most common lethal disease globally after ovarian malignancies.[15,16] Previous studies were done to emphasize the noninvasive radiological methods which help the management of thyroid nodules. These studies produced interesting results but still the parameters needs to be tested in clinical setting. When examinations are done in vivo, several issues may come across such as bearing the financial load of MR scan of whole body used as screening, magnetic susceptibility effects, movement of lump as a result of breathing, and artifact from surrounding fat. These limitations indicate that in vivo examination is although helpful but may only be applied in large tumors.[11]

These facts suggest this problem to be of high severity and demand an accurate, non-invasive imaging modality for pre-operative assessment of the thyroid malignant lesions. In this context, it may be hypothesized that Magnetic Resonance Spectroscopy is an accurate diagnostic test to identify benign and malignant thyroid nodules.

The result of this study will may fill the gap of the non-availability of an authentic evaluation tool in the perceptual paradigm of lethal thyroid malignancies which may also help the surgeons to plan an accurate treatment accordingly. Therefore, this study was conducted with an objective to analyze the diagnostic accuracy role of Magnetic Resonance Spectroscopy in differentiating benign from malignant nodules of thyroid gland by using tissue diagnosis as a gold standard.

METHODOLOGY

This Co-relational Analytical study was conducted over a period of one year (1st October 2017 to 1st October 2018) at Children Hospital and Institute Of Child Health, Multan. A total of seventy patients (of both genders) were recruited for this study who clinically presented with palpable thyroid nodule, whereas, patients who had any previous surgery of thyroid, history of thyroid malignancy (proven by biopsy), claustrophobic patients and patients with contraindications to MRS i.e. cardiovascular implanted electronic devices were excluded. Sample size was calculated by using WHO calculator taking 95% confidence level and 80% power of study.

After clinical examination, study participants were referred to the Department of radiology of the same institution. Later, after taking informed consent and history from all the patients, subjects went through MRS for the thyroid gland for choline peak and Choline/Creatine (Cho/Cr) ratio. The proton Magnetic Resonance Spectroscopy (1H MRS) was conducted using 1.5 Tesla Magnetic resonance system with gradient strength of 33 mT/m. A scout scan was taken and the technique used in the scan was point-resolved Magnetic Resonance Spectroscopy single-voxel technique. After this water suppression pulses and data acquisition were obtained.

For interpretation, all the images were then consulted by the radiologists having at least 7 years of post-fellowship experience in MRS. On MRS, presence of increased choline level and reduced NAA level on MR Spectrum with increased 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 malignant. Each MRS report was then correlated with gold standard histopathology report.

Data Analysis: Quantitative variables were taken as mean and standard deviation. Qualitative variables were taken as frequency and percentage employing SPSS version 20.0 software. The 2x2 contingency table was used to calculate sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of MRS in differentiating malignant thyroid nodule taking tissue diagnosis report (as gold standard).

RESULTS

Out of the recruited 70 patients, 52 were females (74.29%), 18 were males (25.31%) and female to male ratio were 1.89:1. The patients' age ranged between 30-70 years with a mean age of 46.53 ± 9.15 years. The ages of almost 50% of patients were between 41-50 years. Mean duration of disease was found to be 0.83 ± 0.35 years.

MRS diagnosed malignant thyroid nodules in 49 (70.0%) of the patients. Histopathology findings confirmed malignant thyroid nodules in 51 (72.86%) cases whereas, 19 (27.14%) patients were found to be with benign thyroid nodules. Choline/Creatine ratio for the malignant nodules was identified to be 2.82±1.20 to 5.12 ±2.21**.**

Table I describes that in MRS positive patients, 46 True Positive (TP) had malignant thyroid nodule and 03 False Positive (FP) had benign thyroid nodules on histopathology. Among 24, MRS negative patients, 05 False Negative (FN) had malignant thyroid nodules on histopathology whereas, 16 True Negative (TN) had benign thyroid nodules on histopathology (p=0.0001).

The overall sensitivity, specificity, PPV, NPV and diagnostic accuracy of MRS in differentiating malignancy of thyroid nodule from benign using tissue diagnosis was 93.51%, 84.35%, 95.24%, 79.51% and 91.40% respectively. (Figure-I)

Table-I-: Comparison of results of Magnetic Resonance Spectroscopy and Histopathology (N=70)

Results of MRS	Positive results of histopathology	Negative results of histopathology
MRS Positive	46 (TP)*	03 (FP)***
MRS Negative	05 (FN)**	16 (TN)****
*TP = True Positive	**FP = False Positive	
***FN = False Negative	****TN= True Negative	

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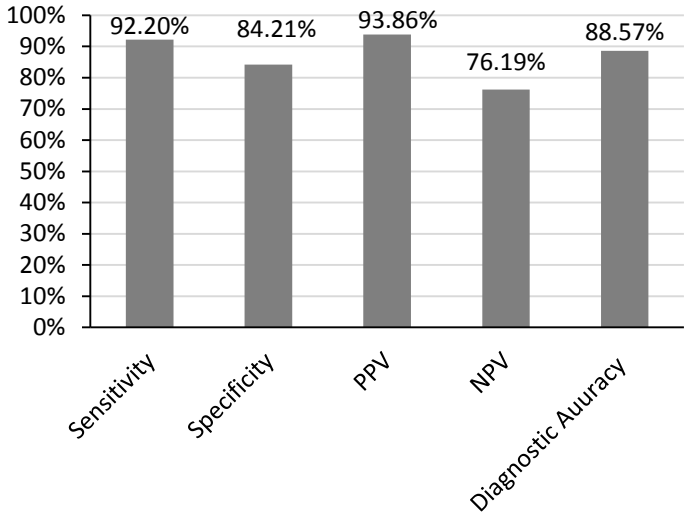

Figure-1-: Magnetic Resonance Spectroscopy in differentiating benign from malignant thyroid nodule (N=70)

DISCUSSION

This study has described the investigative precision of Magnetic Resonance Spectroscopy (MRS) in differentiating benign from malignant nodules of thyroid gland and found positive predictive value (PPV) of MRS and therefore reported MRS to be exceedingly sensitive in this context. High Choline/Creatine ratio was observed in current study that is 2.82±1.20 to 5.12 ±2.21 suggesting a prominent diagnostic indication for confirming the thyroid malignancies. Minute difference was observed in other analogous study where reported Choline/Creatine ratio ranged from 1.3 to 5.4, in malignant nodules and was 0.9 and 1.1 in two benign nodules.[15] A study by Aydin et al. concluded almost similar Choline/Creatine ratio for the malignant nodules that was 2.95±1.54 to 5.3 ±2.38.[16]

Overall sensitivity (Sn), specificity (Sp) and PPV of MRS in this study were found to be 93.51%, 84.35% and 95.24% respectively. These findings are very close to another related study which reported the Sn of 100%, Sp of 89% and PPV of 90.0% of choline peak in detecting malignancy.[13] In another similar study, Gill et al. tested the Sn, Sp, PPV and negative predictive value (NPV) of MRS in identifying malignant thyroid nodule and was found these to be 100%, 94.11%, 88.88% and 100% respectively.[10] Elshafey et al in his study has found that all the malignant 13 nodules and 2 benign nodules (mild elevation) had choline peak while it was absent in 26 other benign nodules. The author reported the findings of these four testable variables as 96.0%, 85.0%, 92.0% and 92.0% respectively.[15] Aydin et al studied proton MRS and diffusion coefficient values and its role in diagnosing malignant thyroid nodules. He found 93.41% Sn, 89.13% Sp, 90.54% PPV, 91.05% NPV.[16] One more similar study reported that the PPV of MRS in detecting malignancy of thyroid gland is 95% compared with 100% in tissue.[17]

One more accompanying result found in the present study was the noticeable high female to male ratio which was almost 2:1 while identifying thyroid malignancies. Almost 50% of patients were between 41-50 years. Similar results were reported in a comprehensive published review which stated that thyroid cancer is among the fastest developing disease globally and it is 2.9-times more common in females than in males. The review further added that the less destructive histologic variants of thyroid malignancy are diagnosed mostly in females, while the highly violent variant showed comparable gender dissemination.[18]

One more comparable study conducted at King Faisal Specialist Hospital and Research Centre, Saudi Arabia described that the second most common cancer among females is the thyroid malignancy. This cancer accounts for almost 11% among the recently identified female cancers in Saudi Arabia. Saudi male to female ratio for thyroid malignancies was evaluated as 0.3:1 in the same study. The mean Age-Standardized Incidence Rate was reported to be 6.8 /100,000 among females and 2/100,000 in males. As far as median age was concerned it was diagnosed to be 38 years whereas the utmost incidence was found to be in the range of 30–39 years.[19]

A much recent study from China, which was conducted in 2020, reported extremely high rates of incidence and mortality for thyroid cancer among females than in males. Likewise, the same variables were much greater in urban locations than rural in areas. In context of age-specific rates, thyroid malignancies were diagnosed more in the age group of 50–54 years while the extreme mortality was seen in the age group of 80–84 years.[20]

Another important result of this current study was the almost 100% accuracy of MRS in differentiating normal thyroid gland from tumor (proven clinically or histologically). Parallel evidence has also been given in the studies of Naqvi et al. and Altaf et al[21-23]. The current study may also suggest MRS as an improved preoperative investigative measure for differentiation and characterization of thyroid lumps. This may in turn, will aid the surgeons in accurate decision making and treatment planning.

CONCLUSION

The Magnetic Resonance Spectroscopy was found to be an extremely sensitive and noninvasive tool which can give accurate method for diagnosing malignant thyroid nodules.

AUTHOR'S CONTRIBUTION

Zahra M: Conceived idea, Designed methodology, Data collection, Manuscript writing

Majeed U: Data collection, Manuscript writing

Amin M: Data collection, Manuscript writing

Islam ZU: Data collection, Data analysis, Literature review, Manuscript writing

Firdous A: Data collection, Data analysis, Literature review, Manuscript writing

Malik A: Data analysis, Critical revision and final approval of manuscript

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