International Journal of Advanced Biotechnology and Research (IJBR)
ISSN 0976-2612, Online ISSN 2278–599X,
Vol-9, Issue-2, 2018, pp490-496
http://www.bipublication.com

Research Article

Diagnostic accuracy of magnetic resonance spectroscopy (MRS) in diagnosing malignant breast lesions

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ABSTRACT

Objectives: To determine the diagnostic accuracy of magnetic resonance spectroscopy in malignant breast lesions.
Materials & Methods: This descriptive cross sectional study was conducted at Department of Radiology, D.G. Khan Hospital, D.G. Khan from January 2017 to June 2017.A total of 158 patients with breast lesions on US and on mammography and age 30-50 years were included. Patients who took chemotherapy for primary or secondary breast cancer, pregnant or breast feeding females, patients with renal failure, h/o of any trauma to breast tissue and contraindication to MRS were excluded. All the patients were then underwent MRS. Magnetic resonance spectroscopy findings were correlated with histopathological findings.
Results: Mean age of 41.27 ± 5.48 years. MRS supported the diagnosis of malignant breast lesions in 80 (50.63%) patients. Histopathology confirmed malignancy in 83 (52.53%) cases. In 80 MRS positive patients, 74 (True Positive) had malignant breast lesions and 06 (False Positive) had no malignancy on histopathology findings. Among, 78 MRS negative patients, 09 (False Negative) had malignant breast lesions on histopathology where as 69 (True Negative) had benign lesions on histopathology.Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of MRS in malignant breast lesions was 89.16%, 92.0%, 92.50%, 88.46% and 90.51% respectively.
Conclusion: This study concluded that magnetic resonance spectroscopy is a highly sensitive and accurate modality for diagnosing malignant breast lesions.

Keywords: Breast lesions, malignant, imaging modality, non-invasive, sensitivity.

INTRODUCTION

Patient complaints of breast lumps or lumpiness are common, ranging from 40% to 70% in women seeking advice. A breast lump, either self detected, screen detected or clinician detected, raises the fear of breast cancer in any woman, irrespective of age.[1] Fortunately, the vast majority of breast lumps are benign, but this does not negate the need for evaluation of any palpable breast lesion.[2] The main motive behind the evaluation of such a newly detected palpable lump is basically to rule out malignancy. Evaluation of breast lumps involves the rational use of a detailed history, clinical breast examination, imaging modalities and tissue diagnosis.[1,2]Cancer of breast is the most common cancer affecting women worldwide and is the second most common cause of cancer death next to lung cancer. It also usually presents as lump or nipple discharge.[3] Baltzer PA et al in his study has shown the prevalence of breast cancer in 65% patients presenting with breast lesions.[4] Noninvasive diagnosis of breast cancer remainsa major clinical problem. In the

case of a potential malignancy, imaging studies are useful to define the extent of the malignancy and to identify non-palpable masses elsewhere in the breast or on thecontralateral side. These findings may alterthe therapeutic approach, especially thechoice of local therapy.[5] Mammography andsonography are currently the most widely usedmodalities for detecting breast cancer.[6] But the limitations of mammography and sonography and the great desire not to miss a malignant lesion in the early stage of disease lead to aggressive biopsy, but the biopsy rate for cancer is only 10% to 30%. This means that 70% to 90% of breast biopsies are performed for benign diseases, which induce unnecessary patient discomfort and anxiety in addition to increasing costs to the patient.[7,8]

Magnetic resonance imaging (MRI) avoids exposure to radiation, has a sensitivity superior to that of mammography and is more accurate than both mammography and ultrasonography in determining the size of a breast cancer mass.[9] Proton magnetic resonance spectroscopy (^{1}H MRS) of the breast has been proposed as an adjunct to the magnetic resonance imaging (MRI) examination to improve the specificity of distinguishing malignant breast tumors from benign breast tumors.[8,10-12] In a study, the sensitivity and specificity of magnetic resonance spectroscopy (MRS) in differentiation of malignant from benign breast lesions is found to be as 89.5% and 92.3% respectively.[11]

There was very little research available on this topic, so the rationale of this study was to determine the diagnostic accuracy of magnetic resonance spectroscopy (MRS) in diagnosing malignant breast lesions in local population. If its diagnostic accuracy would be found high, then our general population would be provided with a non invasive pre-operative diagnostic technique for accurate diagnosis which would help the clinicians to take proper management protocols for these particular patients in order to reduce the morbidity and mortality of these patients. Moreover, it would also help to reduce pure diagnostic biopsies in breast lesions which would not only reduce complications of this invasive procedure but also decrease unnecessary patient discomfort, anxiety and increasing costs to the patient.

OPERATIONAL DEFINITIONS:

1. **Malignant Breast Tumour:** Breast tumour was considered as malignant if there was choline peak on magnetic resonance spectroscopy and choline/creatine ratio was be >1.5.
2. **Benign Breast Tumour:** Breast tumour was considered as benign if there was no choline peak on magnetic resonance spectroscopy and choline/creatine ratio was ≤ 1.5.
3. **Histopathological Findings:** presence of all of the following was considered as positive; cellular atypia (peomorphism), mitotic activity, increase in nuclear cytoplasmic ratio.
4. **True Positive:** Patients with malignant breast lesion on MRS as well as on histopathology.
5. **True negative:** Patients with benign breast lesion on MRS as well as on histopathology.
6. **False Positive:** Patients with malignant breast lesion on MRS but benign on histopathology.
7. **False Negative:** Patients with benign breast lesion on MRS but malignant on histopathology.
8. **Diagnostic Accuracy:** was measured in terms of;

a. **Sensitivity** = $\frac{TP}{\text{All positive cases on histopathology}}$ x 100

b. **Specificity** = $\frac{TN}{\text{All negative cases on histopathology}}$ x 100

c. **Positive Predictive Value (PPV)** = $\frac{TP}{\text{All positive cases on MRS}}$ x 100

d. **Negative Predictive Value** = $\frac{TN}{\text{All negative cases on MRS}}$ x 100

MATERIAL AND METHODS

This descriptive cross sectional study was conducted at Department of Radiology, D.G.

Khan Hospital, D.G. Khan from January 2017 to June 2017. Total 158with breast lesions of any size on US (presence of all of the following; speculations, deeper than taller, punctuate calcifications, duct extension and non-compressibility) and on mammography (all of the following; irregular shape, low fat density, indistinct margins and speculations), having age range from 30-50 years with duration of disease <3 months were selected. Patients who took chemotherapy for primary or secondary breast cancer, pregnant females (assessed on history and ultrasonography), H/o of prior irradiation to breast, patients with any chronic disease i.e. tuberculosis, chronic renal failure diabetes mellitus (assessed on history and medical record), patients with h/o of any trauma to breast tissue, patients with already proven histopathology, patients who have contraindication to MRS i.e. MRS incompatible prosthesis or cardiac pacemaker holders (assessed on medical record), patients not willing for biopsy were excluded from the study. Study was approved by review committee. After taking informed written consent and relevant history, proton magnetic resonance spectroscopy (1H MRS) was performed in every patient using 1.5 Tesla MR system with gradient strength of 33 mT/m. A fast scout scan in sagittal, axial, and coronal planes were obtained. The scan technique used was the point-resolved spectroscopy single-voxel technique. Each MR spectroscopy was interpreted by consultant radiologist (with at least 5 years of post-fellowship experience) and was looked for benign or malignant breast lesions (as per-operational definition) taking histopathology report as gold standard. All this data was recorded on a specially designed proforma.

Collected data was analyzed through computer software SPSS 20.0. Mean and standard deviation were calculated for quantitative variables i.e. age, duration of disease, size of lump and BMI. Frequency and percentage were calculated for qualitative variables i.e. benign and malignant breast lesion. 2×2 contingency table was used to calculate sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of magnetic resonance spectroscopy (MRS) in breast lesion taking histopathology as gold standard.

RESULTS

Age range in this study was from 30-50 years with mean age of 41.27 ± 5.48 years. Majority of the patients 90 (56.96%) were between 41 to 50 years of age as shown in Table I. Mean duration of disease was 1.23 ± 0.85 months (Table II). Mean size of lump was 4.83 ± 2.35 cm (Table III). Mean BMI was 29.74 ± 5.35 kg/m^2 (Table IV).

All the patients were subjected to magnetic resonance spectroscopy. MRS supported the diagnosis of malignant breast lesions in 80 (50.63%) patients. Histopathology confirmed malignancy in 83 (52.53%) cases. In 80 MRS positive patients, 74 (True Positive) had malignant breast lesions and 06 (False Positive) had no malignancy on histopathology findings. Among, 78 MRS negative patients, 09 (False Negative) had malignant breast lesions on histopathology where as 69 (True Negative) had benign lesions on histopathology as shown in Table V.Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of MRS in malignant breast lesions was 89.16%, 92.0%, 92.50%, 88.46% and 90.51% respectively (Figure I).

Table-I: Age distribution

Age (years)	No. of Patients	%age
30-40	68	43.04
41-50	90	56.96
Total	158	100.0

Table-II: Distribution of patients according to duration of disease

Duration of disease	No. of Patients	%age
≤ 1 month	76	48.10
>1 month	82	51.90

Table-III: Distribution of patients according to size of lump

Size of lump	No. of Patients	%age
≤ 5 cm	93	58.86
>5 cm	65	41.14

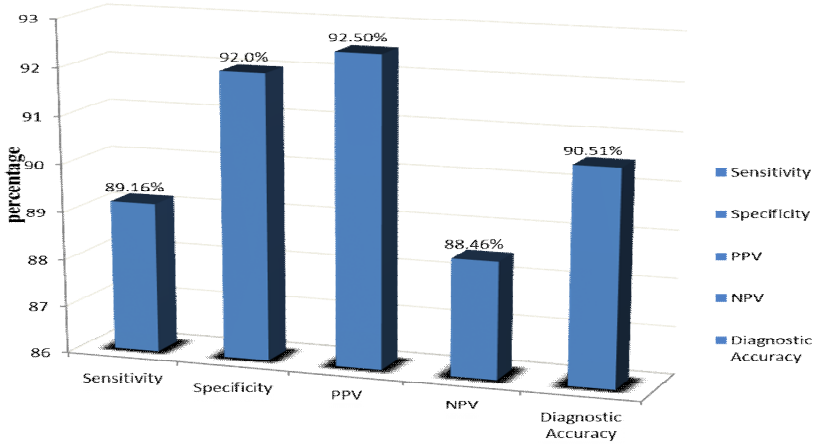
Table-IV: Distribution of patients according to BMI

BMI	No. of Patients	%age
≤ 30 kg/m^2	71	44.94
>30 kg/m^2	87	55.06

Table-V: Summary of Results

Histopathology	Positive on MRS	Negative on MRS	P-value
Positive Histopathology	74 **(TP)***	09 **(FN)*****	**0.736**
Negative Histopathology	06 **(FP)****	69 **(TN)******	

Figure-I: Diagnostic accuracy of Magnetic Resonance Spectroscopy in malignant breast lesions



DISCUSSION

In our study, MRS supported the diagnosis of malignant breast lesions in 80 (50.63%) patients. Histopathology confirmed malignancy in 83 (52.53%) cases. In 80 MRS positive patients, 74 (True Positive) had malignant breast lesions and 06 (False Positive) had no malignancy on histopathology findings. Among, 78 MRS negative patients, 09 (False Negative) had malignant breast lesions on histopathology where as 69 (True Negative) had benign lesions on histopathology. Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of MRS in malignant breast lesions was 89.16%, 92.0%, 92.50%, 88.46% and 90.51% respectively. In a study, the sensitivity and specificity of magnetic resonance spectroscopy (MRS) in differentiation of malignant from benign breast lesions is found to be as 89.5% and 92.3% respectively.[11]

The use of MRS as an adjunct to MRI in the evaluation of breast lesions was first investigated by Cecil et al (2001)[13] In the study (level III-1 diagnostic evidence), MRS was acquired as part of an MRI examination of 38 women, all who presented with a suspicious mass in the breast of 1cm in diameter or larger (as revealed by a palpable mass or abnormal mammographic finding). Using biopsy results as the gold standard, the authors found that blinded review of MRI results predicted tumour malignancy with a sensitivity and specificity of 95 and 86 per cent respectively. Blinded review of spectroscopy results alone was also found to be fairly accurate, with sensitivity and specificity reported to be 83 and 87 per cent respectively. The authors noted that if tubular adenomas, a well-known source of false positive readings on MRS, had been excluded by the MRI, the specificity and positive predictive value of MRS would have improved to 93 and 95 per cent respectively.

Katz-Brull R et al,[14] published a non-systematic review and meta-analysis of fiveclinical studies, examining the utility of MRS to distinguish benign andmalignant breast lesions. In this meta-analysis, pooled results of five clinical studiesfrom 153 lesions gave an estimated sensitivity for MRS of 83% [95% confidenceinterval (95% CI) 73%–89%) and specificity of 85% (95% CI 71%–93%) in thedifferentiation of benign and malignant breast lesions.Recently, Haddadin IS et al[15] reported 73% sensitivityand 77% specificity of magnetic resonance spectroscopy for distinguishing benign from malignantlesions.

In a more recent study, Meisamyet al[16] retrospectively investigated the diagnostic properties of MRS and MRI in 55 patients who had previously undergone biopsy (level III-2 diagnostic evidence). In the study, four radiologists were required to individually estimate the probability of breast malignancy based on MRI results, and make a hypothetical recommendation based on these results as to whether a patient should undergo confirmatory biopsy. The radiologists were then required to re-examine their decisions following the disclosure of MRS results. For all four radiologists, the addition of MRS to the breast examination resulted in higher sensitivity, specificity and accuracy (as indicated by the area under the ROC curve) regarding the malignancy of the lesion. Two of the four radiologists recorded significant improvements in sensitivity over the two conditions, while all four radiologists demonstrated significant improvements in diagnostic accuracy. The weighted mean sensitivity and specificity for the initial interpretations was 87 and 51 per cent respectively, whereas in the second interpretation, the weighted mean sensitivity and specificity improved to 94 and 57 per cent respectively.

Sardanelli F et al[17] in his study has shown the sensitivity and specificity of magnetic resonance spectroscopy in diagnosing malignant breast lesions as 90.0% and 92.0% respectively. In a meta analysis, nineteen studies were used for general data pooling. The studies included a total of 1183 patients and 1198 lesions (773 malignant, 452 benign). Pooled sensitivity and specificity were 73% (556 of 761; 95% confidence interval [CI]: 64%, 82%) and 88% (386 of 439; 95% CI: 85%, 91%), respectively. The pooled diagnostic odds ratio (DOR) was 34.30 (95% CI: 16.71, 70.43). For breast cancers versus benign lesions, the area under the symmetric summary receiver operating characteristic curve of MR spectroscopy was 0.88, and the Q* index was 0.81.[4]

In perhaps the most relevant study into the clinical utility of MRS, Bartellaet al[18] investigated the diagnostic performance of MRS and MRI in 56 patients with 57 distinct lesions (level III-2 diagnostic evidence). Of the 57 lesions examined in the study, 40 had been classified as suspicious by MRI and had been referred for further biopsy, while 17 of the lesions had already proven to be cancerous by biopsy. Using biopsy as a gold standard, 31 and 26 of the 57 lesions were found to be malignant and benign respectively. A choline peak was found in all 31 biopsy-proven malignant lesions (100 % sensitivity), while peaks were absent in 23 of 26 benign lesions (88% specificity). To determine the effect the introduction of MRS would have had on biopsy referrals, the authors investigated the 40 lesions initially classified as suspicious by MRI. In these lesions, the use of MRS as an adjunct to MRI would have significantly improved the positive predictive value of biopsy referrals from 35 to 82 per cent ($p < 0.01$). If biopsy had only been performed on those lesions with a choline peak, biopsy recommendations would have been spared in 23 of 40 lesions (58 %) and not a single malignant lesion would have been missed (i.e. a negative predictive value of 100%).

In a study, fifty-two patients (57 lesions; 42 malignant and 15 benign) were analysed. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), of predicting malignancy were 100, 73.3, 91.3, and 100%, respectively, using DCE-MRI and 95.2,

93.3, 97.6, and 87.5%, respectively, using SV (1)H MRS. The tCho cut-off for receiver operating characteristic (ROC) curve was 0.33 mmol/l. The relationship between tCho levels in malignant breast lesions with their histopathological subtypes was not statistically significant ($p = 0.3$).[19]Similarly, in a conference paper, Brennan S et al[20] suggested that if MRS had been used, biopsy would have been spared in 59% with BI-RADS 4 lesions and in 87% with BI-RADS 4 lesions that were benign, without missing any cancers.So, our study concluded that Magnetic resonance spectroscopy (MRS) has revolutionized the diagnosis and management of malignant breast lesions. So, being non invasive and a highly sensitive tool of investigation, it should be used for screening and accurate pre-operative identification of breast lesions in these particular patients in order to reduce morbidity and mortality.

CONCLUSION

This study concluded that magnetic resonance spectroscopy (MRS) is a highly sensitive and accurate modality for diagnosing malignant breast lesions, and has not only dramatically improved our ability of diagnosing breast cancer but also improves patient care by accurate and timely diagnosis for taking proper treatment options for these particular patients. So, being non invasive and a highly sensitive tool of investigation, we should recommend it as a primary screening tool for accurate screening and pre-operative identification of breast lesions in these particular patients in order to reduce morbidity and pure diagnostic biopsies in breast lesions which would consequently reduce complications of such procedures.

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