

Correlation between MR spectroscopy and histology in detection of prostatic carcinoma

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Abstract

Objective: To determine the diagnostic accuracy of magnetic resonance spectroscopy in the detection of prostatic carcinoma.

Methods: This descriptive, cross-sectional study was conducted at the Jinnah Postgraduate Medical Centre, Karachi, from July 24, 2014, to January 23, 2015, and comprised patients who had been screened for prostate cancer. Using non-probability purposive sampling, all magnetic resonance spectroscopy scans were interpreted by three radiologists. Male patients aged 45-70 years, diagnosed with suspicious heterogeneous mass in peripheral zone on ultrasound and who had prostatic specific antigen levels value >4.0 ng/ml were included. Three dimensional magnetic resonance spectroscopy imaging data was acquired. Data was analysed using SPSS 21. Diagnostic accuracy of the procedure was determined by taking histopathology as the gold standard.

Results: There were 224 patients with an overall mean age of 55.63±6.34 years (range: 45-70 years). The strong perfect correlation of 0.82 was found by Kappa statistics between magnetic resonance spectroscopy and histopathology results and a good diagnostic accuracy (92.8%) of magnetic resonance spectroscopy testing was observed for the detection of prostate carcinoma. Pooled sensitivity was 92.2% and specificity was 94.6% for the diagnosis of prostate carcinoma.

Conclusion: A strong correlation was found between magnetic resonance spectroscopy and histopathology results to detect prostate carcinoma.

Keywords: Prostatic carcinoma, Histopathology, MR spectroscopy, Prostate specific antigen (PSA). (JPMA 68:986; 2018)

Introduction

Prostate cancer is the most common malignancy among males worldwide and foremost reason of death in North America, Europe, Latin America and Africa. It is the second leading cause of cancer deaths among men in the United States. In 2015, it was predicted that more than 200,000 fresh cases of the cancer will be detected in the United States. This is approximately a quarter of all the malignancies among males and around 27,000 were expected to die from the disease. A man's lifetime risk of developing prostate cancer is one out of seven.¹ Like other countries, it is very common cancer among males in Pakistan, too. Most prostate cancers are slow growing; however, some grow relatively fast. The percentage of men diagnosed with prostate cancer varies around the world. However, it is the second-most common types of cancer among males with 15 out of every 100 males suffering from the disease. The number of men dying from the disease has gone up from around 150,000 deaths in 1990 to around 250,000 deaths in 2010. Not surprisingly, it is one of the most common forms of cancer

in men, affecting one of every six men suffering from cancer.^{2,3} In Pakistan prostate cancer is the third type of malignancy for men, but fortunately the diagnostic and therapeutic facilities limit its prevalence. A lack of availability of resources or access to healthcare, lack of public awareness and lower life expectancy may be causes of lower incidence of prostate cancer in Pakistan compared with worldwide incidence rates.^{4,5} During 1998-2002, prostate cancer was the fourth common malignancy among males in Karachi, with an age standardised incidence rate of 10.1 per 100,000 men, whereas mean age of the cases were 67.4 years.⁶ This is similar to Asia-Pacific region's incidence of 9.9 per 100,000, but less than the world's 32.8 per 100,000.⁷ The serum prostate-specific antigen (PSA) test, being one of the best non-invasive tests, is currently widely used as a screening method for early detection of prostate cancer.^{8,9} However, although PSA level has high sensitivity for prostate cancer detection, but its specificity is insufficient when PSA levels are within the so-called "gray zone" of 4-10 ng/mL. Therefore, about 70% of men may undergo unnecessary biopsies.¹⁰ Accurate detection of prostate cancer thus has the potential for decreasing unnecessary biopsies.

Magnetic resonance spectroscopy (MRS) is a powerful

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tool for exploring the cellular chemistry of human tissues.¹¹ MRS is considered one of the most promising areas in prostate imaging research. Accordingly, proton MRS (1H-MRS) is a diagnostic modality that is based on in vivo metabolic information and has been shown to improve detection of prostate cancer.^{12,13} The current study was planned to determine the diagnostic accuracy of MRS in detecting prostatic carcinoma using histopathology as the gold standard.

Patients and Methods

This cross-sectional validation study was conducted in the radiology department of the Jinnah Postgraduate Medical Centre (JPMC), Karachi, from July 24, 2014, to January 23, 2015, and comprised patients who had been screened for prostate cancer. Correlation between the two tests was calculated according to Cohen's kappa coefficient=0.8, expected correlation (Pe) =0.5, confidence interval (CI) =95% and error tau (δ) =0.05. The sample size required to determine correlation (k) within ± 0.20 was 200 cases that were positive or negative by the histopathology and MRS method. But for the sake of statistical significance, the sample size was increased. Male patients diagnosed with suspicious heterogeneous mass in peripheral zone on ultrasound, and had prostatic specific antigen levels value > 4.0 ng/ml were included in the study. Non-probability consecutive sampling technique was used. The procedures were considered to the categorical agreement when they resulted in the same category (e.g. present or absent). A pre-designed questionnaire of clinical details of the cases were evaluated by reviewing the medical records of patients, including clinical information such as clinical history and findings of imaging in patients who were referred for magnetic resonance spectroscopy imaging (MRSI).

Data was entered analysed using SPSS 21. Mean $\pm$ standard deviation (SD) were recorded for all quantitative variables like age and PSA level. The categorical classification in terms of frequency and percentage was computed for prostatic carcinoma (present/absent) according to histopathology, MRS, age groups and PSA level category, also finding the categorical rate correlation between the outcome procedures. Percentage of discrepancies between positive and negative results was

also computed. The procedures were considered to be in categorical correlation when they resulted in the same (e.g. positive or negative). Cohen's kappa statistics was used to find percentage correlation MRS between findings and histopathology method. The correlation between the two raters was evaluated by kappa statistics for comparing both main outcome variables separately. Kappa values ranged from -1 to 1, where 1 was preferred perfect correlation between two procedures of the data sets. Chi-square test was applied to check out the significant association between two procedures. $P < 0.05$ was taken as significant. A 2*2 table was constructed to determine the value of sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV) and accuracy were calculated using the standard formula. Only those cases were taken as true positive which were positive by histopathology.

Results

There were 224 patients with an overall mean age of 55.63 ± 6.34 years (range: 45-70 years). Moreover, 107(47.8%) patients were aged ≤ 55 years and 117(52.2%) were aged >55 years. The overall mean PSA level was 15.13 ± 5.20 ng/ml (range: 4.1-27.5). Besides, 117(52.2%) patients had PSA level ≤ 15 ng/ml and 107(47.8%) patients had PSA level >15 ng/ml (Table-1).

Table-1: Frequency and Percentage & descriptive among age, PSA Level, Histopathology & MR Spectroscopy.

Demographics Variables	Parameters	f(%)
Mean Age	Mean $\pm$ SD (95% C.I)	55.63 $\pm$ 6.34 (54.8 to 56.47)
Mean PSA level	Mean $\pm$ SD (95% C.I)	15.13 $\pm$ 5.20 (14.4 to 15.8)
Histopathology	Present	168(75%)
	Absent	56(25%)
MR Spectroscopy	Positive	156(69.6%)
	Negative	68(30.4%)
Age Groups	<55 Years	107(47.7%)
	>55 Years	117(52.3%)
PSA Category	<15 ng/ml	117(52.3%)
	>15 ng/ml	107(47.7%)
Total	224	100%

PSA: Prostate-specific antigen

MR: Magnetic resonance

SD: Standard deviation

CI: Confidence interval.

Table-2: Correlation between MR Spectroscopy and histopathology findings for the diagnosis of prostate carcinoma (n=224).

MR Spectroscopy Finding	Histopathological Findings		Cohen's Kappa Agreement	P-value
	Present (n=168)	Absent (n=56)		
Present (n=158)	155(69.2%)	3(1.3%)	0.82	P<0.001*
Absent (n=66)	13(5.8%)	53(23.7%)		

MR: Magnetic resonance.

Correlation between MRS and histopathology findings for the diagnosis of prostate carcinoma showed that 155(69.2%) patients were true positive and 53(23.7%) were true negative. In 158(70.5%) cases, MRS clearly showed the prostate carcinoma was positive and 66(29.5%) cases were found negative with prostate carcinoma. In addition, 168(75%) cases were found positive and 56(25%) cases were found negative through histopathology. According to the histopathological diagnosis, the overall sensitivity, specificity, PPV, NPV and diagnostic accuracy were 92.2%, 94.6%, 98.1%, 80.3%, and 92.8%, respectively (Table-2).

Discussion

MRSI serves as a non-invasive method of tracking down small molecular biomarkers (choline-containing metabolites, polyamines and citrate) within the intra and extracellular spaces of the prostate gland and is performed in addition with high-resolution magnetic resonance imaging (MRI).

The 1.5T MRI/MRSI has the advantage to significantly improve the local assessment of prostate cancer presence and volume and has been shown to have additive benefit in the prediction of pathological stage and post-treatment follow-up.¹⁴

The primary reason for the high death rate in prostate cancer patients is the late detection in the majority of cases combined with the fact that the disease is mostly contracted by people of an elderly age.¹⁵ Similar to other countries around the world, the prevalence of prostate cancer is common in Pakistan. It is the third-most common cancer in males, constituting about 7% of all malignancies.¹⁶ The incidence and mortality rates of prostate cancer are remarkably different in various geographic regions. Multi-regional needle biopsy of the prostate has been the gold standard for achieving a definitive diagnosis of prostate cancer, but it has the drawback of often yielding false-negative results.¹² Therefore, a sensitive screening procedure should be performed which could help in avoiding unnecessary biopsies and rebiopsy for cases in which there is a chance of missing the target lesion due to experimental staff.

According to this study, the mean age of patients was 55.63±6.34 years and 85% prostate cancer patients were found in the age group of 60-75 years. After various research works, it was determined that this type of cancer and its incidence increases with advanced age. Similar results were found in different studies conducted in Africa, the United Kingdom, the United States, Australia, India and Pakistan.¹⁷ MRS has been

shown to improve detection of prostate cancer.^{13,18} The current study was designed to determine the agreement and diagnostic accuracy between MRS and histology in the detection of prostatic carcinoma. According to this study, there was perfect positive strong Cohen's kappa agreement (0.82) for MRS and histopathology, which was consistent with the finding of Testa C. et al.,¹⁹ where they found the sensitivity, specificity and accuracy of serology at 92.2%, 94.6% and 92.8%, respectively, to diagnose prostate carcinoma.¹⁹ Another agreement reported in this study was stronger (0.82) than the results of²⁰ other studies which found the agreement between serology and histopathology at 0.45.²⁰ In this study, the sensitivity, specificity, PPV, NPV and accuracy were 92.2%, 94.6%, 98.1%, 80.3%, and 92.8% with MRS. Previous studies have reported that the combined application of MRS and biopsy can be a good method for improving the accuracy of diagnosis of localised prostate cancer. More practically, this approach allows the clinician to consider performing targeted biopsy of the prostate only at the regions that are found to be MRS-positive,²¹ or re-biopsy of sections found to be MRS-positive but biopsy-negative. However, differences between study results may in some instances be explained by differences in methodology and the choice of the gold standard. Although MRS is more expensive than transrectal ultrasonography (TRUS), its cost can be covered if an unnecessary biopsy procedure is avoided. On the other hand, if a small focus of prostate carcinoma is missed on other less expensive modality, the morbidity caused would be greater than the cost of MRS.

Conclusion

A strong perfect correlation was found between MRS and histopathology results to detect prostate carcinoma. MRS together with biopsy might improve the diagnostic accuracy of prostate carcinomas. MRSI is reasonably accurate in the diagnosis of prostate cancer in patients with an elevated serum PSA level. MRS of the prostate can be a useful diagnostic tool for detecting prostate cancer. The diagnostic and therapeutic modalities available are extremely limited in our setting.

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Conflict of Interest: None.

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References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. *Cancer J Clin.* 2015; 65:5-29.
2. Stewart B, Wild C. World Cancer Report 2014. WHO: International Agency for Research on Cancer, 2014.

3. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *cancer J clin.* 2011; 61:69-90.
4. Foley R, Hollywood D, Lawler M. Molecular pathology of prostate cancer: the key to identifying new biomarkers of disease. *Endocr Relat Cancer.* 2004; 11:477-88.
5. Ahmad MR, Pervaiz MK, Pervaiz G. Non-occupational risk factors of urinary bladder cancer in Faisalabad and Lahore, Pakistan. *J Pak Med Assoc.* 2012; 62:236.
6. Bhurgri Y, Kayani N, Pervez S, Ahmed R, Tahir I, Afif M, et al. Incidence and Trends of Prostate Cancer in Karachi South. *Asian Pac J Cancer Prev.* 2009;10:45-8.
7. Baade PD, Youlten DR, Cramb SM, Dunn J, Gardiner RA. Epidemiology of prostate cancer in the Asia-Pacific region. *Prostate inter.* 2013; 1:47-58.
8. Holmberg L, Bill-Axelson A, Helgesen F, Salo JO, Folmerz P, Häggman M, et al. A randomized trial comparing radical prostatectomy with watchful waiting in early prostate cancer. *N Engl J Med.* 2002; 347:781-9.
9. Vilanova J, Comet J, Capdevila A, Barcelo J, Dolz JL, Huguet M, et al. The value of endorectal MR imaging to predict positive biopsies in clinically intermediate-risk prostate cancer patients. *European radiology.* 2001; 11:229-35.
10. Matlaga BR, Eskew LA, McCULLOUGH DL. Prostate biopsy: indications and technique. *Journal Urology.* 2003;169:12-9.
11. Carroll PR, Coakley FV, Kurhanewicz J. Magnetic resonance imaging and spectroscopy of prostate cancer. *Reviews urology.* 2006;8:S4.
12. Saito K, Kaminaga T, Muto S, Ide H, Nishio K, Kamiyama Y, et al. Clinical efficacy of proton magnetic resonance spectroscopy (1H-MRS) in the diagnosis of localized prostate cancer. *Anticancer Res.* 2008; 28:1899-904.
13. Swindle P, McCredie S, Russell P, Himmelreich U, Khadra M, Lean C, et al. Pathologic Characterization of Human Prostate Tissue with Proton MR Spectroscopy 1. *Radiology.* 2003; 228:144-51.
14. Kurhanewicz J, Vigneron DB. Advances in MR spectroscopy of the prostate. *Magn Reson Imaging Clin N Am.* 2008; 16:697-710.
15. Giuliani L, Pescatore D, Giberti C, Martorana G, Natta G. Treatment of advanced prostatic carcinoma with cyproterone acetate and orchiectomy--5-year follow-up. *European urology.* 1979; 6:145-8.
16. Ahmad Z, Qureshi A, Idrees R, Aftab K. Prostatic carcinoma: a Pakistani perspective. *Asian Pacific J Cancer Prev.* 2009;10:323-4.
17. Zaman F, Ullah N, Aamir Q, Farooqi AA, Awan II, Mariam M, et al. *Journal of Rashid Latif Medical College.*
18. Kaji Y, Kurhanewicz J, Hricak H, Sokolov DL, Huang LR, Nelson SJ, et al. Localizing prostate cancer in the presence of postbiopsy changes on MR images: role of proton MR spectroscopic imaging. *Radiology.* 1998; 206:785-90.
19. Testa C, Schiavina R, Lodi R, Salizzoni E, Corti B, Farsad M, et al. Prostate Cancer: Sextant Localization with MR Imaging, MR Spectroscopy, and ¹¹C-Choline PET/CT 1. *Radiology.* 2007;244:797-806.
20. Scheidler J, Hricak H, Vigneron DB, Yu KK, Sokolov DL, Huang LR, et al. Prostate Cancer: Localization with Three-dimensional Proton MR Spectroscopic Imaging-Clinicopathologic Study 1. *Radiology.* 1999; 213:473-80.
21. Prando A, Kurhanewicz J, Borges AP, Oliveira Jr EM, Figueiredo E. Prostatic Biopsy Directed with Endorectal MR Spectroscopic Imaging Findings in Patients with Elevated Prostate Specific Antigen Levels and Prior Negative Biopsy Findings: Early Experience 1. *Radiology.* 2005; 236:903-10.