Endorectal coil MRI and MR-spectroscopic imaging in patients with elevated serum prostate specific antigen with negative trus transrectal ultrasound guided biopsy

Farooq Ahmad Ganie1, Mohammad Saleem Wani2, Feroz Shaheen3, Mohd Lateef Wani1, Shabir Ahmad Ganie4, Mohd Farooq Mir5, Shadab Nabi Wani1, Masaratul-Gani4

1Department of CVTS, SKIMS, 2Department of urology, SKIMS, Srinagar, 3Department of Radiology, SKIMS, Srinagar, 4Department of Health Services, Jammu and Kashmir, India

Abstract

Background: The aim of this study was to see the efficacy of endorectal coil MRI and MR spectroscopic imaging in patients with elevated serum PSA and negative transrectal ultrasonography (TRUS)-guided biopsy.

Materials and Methods: This study was conducted on 87 patients presented with: • Elevated prostatic specific antigen levels >5 ng/ml • Symptoms and signs of prostatic carcinoma • Patients with negative TRUS-guided biopsy • Suspicious lesion on TRU. All the patients were subjected to TRUS and followed by TRUS-guided biopsy of the lesion identified on endorectal coil MRI and MR-Spectroscopy. TRUS-guided biopsy of prostate was done with a Siemens Sonoline Adana Scanner. The scanning was performed by mechanical probe 5-7.5 MHz.

Results: Out of 87 patients, 43 (49.4%) had hypointense lesion, 11 (12.6%) had hyperintense lesion. Out of 87 patients, MR-spectroscopy showed peak choline-creatine in 74 patients. Normal citrate peak was seen in 13 patients. Patients who had choline-creatine peak, among them 28 (37.8%) had peak in left peripheral zone, 23 (31.1%) had peak in the right peripheral zone, 2 (2.7%) had peak in the central zone, 17 had (23%) peak bilaterally. Four patients (5.4%) had peaks in right and central zones. The difference was statistically significant (P < 0.001).

Conclusion: Prostatic biopsy directed with endorectal coil MRI and MR-spectroscopic imaging findings in patients with elevated serum PSA and prior negative biopsy, improves the early diagnosis of prostatic carcinoma and accurate localization of prostate cancer within the gland.

Key Words: Magnetic resonance imaging, prostate, transrectal ultrasonography

INTRODUCTION

An estimated 234,460 men were diagnosed with prostatic cancer in the United States during the year 2006. Most of these cases were diagnosed after elevated serum prostatic-specific antigen (Sr. PSA) level were detected and followed by a positive conventional TRUS-guided biopsy. However, men with an elevated serum PSA have negative results at TRUS-guided biopsy. These patients are a well-recognized for diagnostic problem in urologic practice, particularly if the PSA level continues to rise or is very high. Second biopsy in these patients detects cancer in 20-30% of such patients.[1] Third and even fourth biopsies may detect cancer in 5% and 4% of patients, respectively.[2]

Patients are very much reluctant to undergo second, third biopsies because of recognized complications of conventional
TRUS-biopsy such an infection, hematospermia, hematuria and bleeding per rectum and also because of somewhat speculative concerns that biopsy may result in hematogenous dissemination of cancer cells. Many published studies have shown that additional records of conventional TRUS-guided biopsies do not seem to improve the cancer detection rate in these patients.

Sextend (six biopsies randomly in a patients were no lesion is found on TRUS) biopsies in patients with persistently increasing serum PSA show gradually decreasing results as the number of rebiopsy rounds from 23% cancer detection rate the first round, 17.6% second time and 11.7% at third time. It is positive in only 8% at the fourth and fifth round, respectively.

These shortcomings have provoked search of a new diagnostic method that might replace or supplement the conventional TRUS-guided biopsy.

Endorectal coil MRI and MR-spectroscopic imaging have shown considerable promise in the evaluation of prostatic carcinoma in patients with persistently elevated serum PSA and prior negative biopsy.

MATERIALS AND METHODS

The present study was conducted from May 2007 to April 2009 in the department of Urology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, in collaboration with departments of Radiodiagnosis and Pathology.

This study was conducted on 87 patients who presented with the following:
- Elevated prostatic specific antigen levels >5 ng/ml
- Symptoms and signs of prostatic carcinoma
- Patients with negative TRUS-guided biopsy
- Suspicious lesion on TRU.

All the patients were subjected to TRUS and followed by TRUS-guided biopsy of the lesion identified on endorectal coil MRI and MR-Spectroscopy. TRUS-guided biopsy of prostate was done with a Siemens Sonoline Adana Scanner. The scanning was performed by 5-7.5 MHz mechanical probe.

Preparation for endorectal MRI and MR-spectroscopy
1. Patient took light diet on the day prior to and on the day of examination
2. Cleansing enema early morning at home/hospital
3. Metal and electronic objects were not allowed in examination room like jewelry, watches, credit cards, hearing aids, metal zippers, pens, pocket knives, and eye-glasses
4. Endorectal coil was covered with latex condom to prevent contamination
5. 50 ml syringe with normal saline
6. The anus and endorectal coil was adequately lubricated with xylocaine jelly.

The endorectal coil was then inserted. As the coil has the tendency to migrate cephaladly when the balloon is inflated, this was counteracted by gentle traction on the coil as the balloon was inflated with 70-80 ml of normal saline to hold the coil. The endorectal MR-imaging and MR-spectroscopy were performed with a 1.5 T unit (magnetom Avento, Siemens, Erlangen, Germany) by using a combined endorectal and body phased-array coil. The prostate was examined with a T2-weighted turbo spin-echo sequence at angulated transverse and coronal section orientations (by using 16 × 16 cm and 20 × 20 cm fields of view, respectively) and with an angulated transverse T1-weighted spine-echo sequence by using a 16 × 16 cm field of view. The section thickness was 3.0 mm with an intersection gap of 0.9 mm. An imaging matrix was used in all examinations.

The MRI and MR-spectroscopic imaging findings were analyzed by two radiologists who were blinded to the findings of TRUS.

The MR-imaging and MR-spectroscopic imaging findings were analyzed prospectively in patient by patient manner. The angulated transverse and coronal T2-weighted images were evaluated for hypointense regions in the peripheral zone. Confluent hypointense areas were classified as inconclusive findings. On the T1-weighted images, regions were classified as suspicious only when they were to be isointense relative to the surrounding tissue. On the basis of the suspicious areas identified, the entire prostate was classified as suspicious, inconclusive, or negative for cancer. Suspicious lesions were localized by assigning them as right peripheral left peripheral zone, and central zone.

MR-spectroscopic imaging
After review of transverse T2-weighted images, a spectroscopic imaging volume was selected to maximize coverage of the prostate while minimizing the inclusion of periprostatic fat and rectal air. Three-dimensional MR-spectroscopic data were acquired using a water and lipid-suppressed double-spin-echo point-resolved spectroscopy sequence, which was optimized for quantitative detection of both choline and citrate, water and lipid suppression was achieved by using the spectral-spatial pulses capable of both volume selection and frequency selection.

Outer voxel saturation pulses were also used to eliminate signals from adjacent tissues, especially prostatic lipids and rectal wall tissue.
Data sets were acquired as 16 × 8 × 8 phase-encoded spectral arrays (1024 voxels; nominal spatial resolution, 0.34 cm³ 1000/130) acquisition time 20 min, the total examination time was 50-65 min, including coil placement and patient positioning.

Three-dimensional MR-spectroscopic imaging data were processed aligned with the corresponding MR-imaging data, displayed, and analyzed by using Software. The raw spectral data were apodized with a 1-Hz Gaussion function, and Fourier transformation was performed in the time domain and three spatial domains. The estimation of choline, creatine, and citrate peak parameters (i.e. peak area, peak height, peak location, and line width) was accomplished by using aniterative procedure that allowed initial identification of significant peaks, choline, creatine, and citrate peak areas were obtained with numerical integration over a frequency range determined with the metabolic peak location and width in regions of healthy tissues. The polyamine peak that resonates between choline and creatine could not be sufficiently resolved and it was incorporated in the areas of the peak choline-plus-creatine. A software upgrade allowed us to use the voxel shifting capability to better align the spectral data with the anatomy.

**MR-data analysis**

MR-spectroscopic imaging data were overlaid on the corresponding transverse T2-weighted MR-images and evaluated in consensus by two radiologists to determine which voxels were suitable if they were not contaminated by insufficiently suppressed water or lipids. Suitable spectroscopic voxels were rated as optimal fair, or poor on the basis of spectral quality and they were subsequently scored according to a recently developed standardized five-point scale. Specifically, a study was considered to be optimal spectral quality if the signal-to-noise ratio of all metabolites was greater than 10. All metabolic resonances were well resolved, and there were no baseline distortions due to residual water or lipids. A study was considered to be of fair spectral quality if the signal-to-noise ratio of all metabolites was between 8 and 10. All metabolic resonances were reasonably well resolved, or there were minimal baseline distortions due to residual water or lipid studies with lower signal-to-noise ratios and substantial lipid contamination were considered to be of poor spectral quality.

Primary scores ranged from 1 to 5 and they were assigned on the basis of the mean healthy ratio of the choline-plus creatine-to-citrate ratio. The mean choline-plus-creatine-to citrate ratio was defined as 0.22 ± 0.013 on the basis of a previously published study that used the same MR-spectroscopic data acquisition and processing used in this study. A score of 1 was assigned to the voxels with a choline-plus-creatine-to-citrate ratio greater than an equal to 1. standard deviation of the mean healthy value. A score of 2 was assigned to voxels with a choline-plus-creatine-to-citrate of more than/ and less than or equal to 2-standard deviations above the mean healthy value. A score of 3 was assigned to voxels with choline-plus-creatine-to-citrate ratio of more than 2 and less than or equal to 3 standard deviations above the mean healthy values. A score of 4 was assigned to voxels with choline-plus-creatine-to-citrate ratio of more than 3 and less than or equal to 4 standard deviations above the mean healthy value. A score of 5 was assigned to voxels with a choline-plus-creatine-to-citrate ratio of more than 4 standard deviations above the mean healthy value.

Prostatic biopsy directed with endorectal coil MR-imaging and MR-spectroscopic imaging findings

All the patients with hypotensive areas in peripheral or central zone on T2-weighted MR-images and patients with abnormal MR-spectroscopic imaging voxel underwent biopsy after patient preparation (which included cleansing enema and administration of local anesthetic).

US-transverse scans were obtained to reproduce the same gland, morphologic findings obtained with T2-weighted transverse MR-image to better localize the suspicious MR-spectroscopic findings. These scans were obtained by using internal and external anatomic landmarks (i.e. external sphincter, verumontanum, surgical and anatomic capsule, urethra, neurovascular bundle, hypertrophic central gland nodules and seminal vesicles). Additional useful topographic information was obtained with the correlation of the transverse images with the midsagittal T2-weighted scout view. By using these criteria, the suspicious MR-spectroscopic areas were projected as accurately as passable on US scans, and transrectal US-guided biopsy was performed. To facilitate the correlation of both methods, similar image zoom factors were used to obtain a similar peripheral zone thickness. Direct voxel guided biopsy was then performed, with removal of two or three cores from the areas classified as abnormal with MRI and MR-spectroscopic imaging all biopsies were performed by two radiologists who were also involved in acquisition and interpretation of the MR-images and MR-spectroscopic images. The biopsy cores were labeled to reflect the location of the biopsy. All patients subsequently received an extended-pattern biopsy scheme, To evaluate the accuracy of transrectal US-guided biopsy-directed MR-imaging and MR-spectroscopic imaging.

**Histopathologic analysis**

Histopathological analysis was performed for all biopsy samples and used as the standard of reference for MR-imaging and
MR-spectroscopic imaging findings. The pathological analysis included determination of the number of positive cores.

All the data was subjected to statistical analysis.

RESULTS

Out of 87 patients, 43 (49.4%) had hypointense lesion and 1 (12.6%) had hyperintense lesion [Table 1]. Out of 87 patients, MR-spectroscopy showed peak choline-creatine in 74 patients. Normal citrate peak was seen in 13 patients. Patients who had choline-creatin peak, among them 28 (37.8%) had peak in the left peripheral zone, 23 (31.1%) had peak in the right peripheral zone, 2 (2.7%) had peak in the central zone, 17 had (23%) peak bilaterally. Four patients (5.4%) had peaks in right and central zones. The difference was statistically significant (P < 0.001) [Table 2]. Out of 87 patients, 43 (49.4%) patients had hypo-intense lesions on T2-weighted. Thirty-six (83.7%) were positive for prostatic cancer and 7 (16.3%) were negative for prostatic carcinoma. Overall sensitivity of MRI was 83.7%, specificity was 34.1%, PPV 55.4%, NPV 68.2%, and overall accuracy was 58.6% [Table 3]. Out of 87 patients, 9 (10.3%) patients had choline-creatine/citrate ratio score of 1 (normal). Eight patients (9.2%) had choline-creatine/citrate ratio score of 2 (probably normal). Nine (10.3%) patients had choline-creatine/citrate ratio score of 3 (equivocal). Sixteen patients had choline-creatine/citrate ratio score of 4 (probably cancer). Forty-five patients had choline-creatine/citrate ratio-score of 5 (cancer) [Table 4]. In our study, 9 (10.3%) patients had choline-creatine/citrate ratio score of 1. Among them 1 was positive for prostatic cancer. Eight (9.2%) had a score of 2, among them 2 (25%) patients were positive for cancer. Nine patients (10.3%) had a score of 3, among them 5 (55.6%) were positive for prostatic cancer. Sixteen patients (18.4%) had score of 4 and among them 14 (87.5%) were positive for prostate cancer. Forty-five patients (51.7%) had score of 5, among them 43 (95.6%) were positive [Table 5]. Out of 87 patients, 61 patients had choline-creatine/citrate ratio of ≥4.57, 57 (93.3%) were positive for prostatic cancer. The overall sensitivity of MR-spectroscopy was 93.1, specificity was 61.5%, PPV 91.9%, NPV of 66.7%, and total accuracy of 87.8% [Table 6]. In our study, 43 patients had hypo-intense lesions and among them 33 had choline creatine/creatine, ratio ≥4, and among them 31 (93.9%) were positive for prostate cancer. Ten patients had score of ≤4 and among them, 5 (50%) were positive for cancer. No suspicious lesions were found on MRI in 44 patient Among them, 28 patients had a choline-creatine/citrate ratio of ≥4.26, 26 (92.9%) were positive for cancer. Sixteen patients had score of <4 and among them 13 (81.3%) were negative for cancer. The difference was statistically significant (P < 0.004) between MR-imaging and MR-spectroscopy [Table 7]. Out of 87 patients, 71 (81.6%) had MRI/MRSI lesion. Among them 62 (87.3%) had prostatic carcinoma. Sixteen (18.4%) patients had no suspicious lesion on MRI/MRSI. Among them three...
were positive for prostatic carcinoma. The overall sensitivity of MRI/MRSI was 87.3%, specificity 81.3%, PPV 95.4%, NPV 59.1%, and accuracy of 86.2%. The P value was statistically significant (P < 0.000) and odds ratio was 29.8 [Table 8].

DISCUSSIONS

Patients are very much reluctant to undergo second, third biopsies because of recognized complication of TRUS-biopsy, such an infection, hematomaspermia, hematuria, and rectal bleeding5 and also because of somewhat speculative concerns that biopsy may result in hematogenous dissemination of cancer cells.6 Prostatic carcinoma is potentially curable, when disease is limited to the prostate gland (stages A and B). Traditionally, sextant biopsy has been regarded as the standard of reference for cancer localization.7 However, the limitation of sextant biopsy is increasingly recognized.8 TRUS has produced disappointing results when used alone, because of its low specificity.9 These shortcomings has provoked search of a non-invasive diagnostic method that might replace or supplement the TRUS-guided biopsy.

Endorectal coil MRI and MR-spectroscopic imaging (MRSI) have shown considerable promise in the evaluation of prostatic carcinoma in patients with persistently elevated serum PSA and prior negative biopsy. The present study “Endorectal MRI/MR-spectroscopic Imaging in Diagnosis of Prostate Carcinoma” was conducted on both indoor/outdoor patients who presented to the Department of Urology, SKIMS, Srinagar. In our study, out of 87 (100%) patients, 43 (49.4%) patients had hypointense lesion, 11 (12.6%) had hyperintensive and no lesion on MRI was found in 33 (37.9%) patients. These findings were nearly consistent with the studies conducted by Adilson et al.,10 Yasushi et al.,11 and Delphine et al.12 In our study, out of 87 patients, MR-spectroscopy showed choline-cretine peak in 74 patients and normal citrate peak in 13 patients. In our study, 9 (10.3%) patients had a choline-cretine/citrate ratio score of 1 (normal). Eight (9.2%) patients had a choline-citrate/citrate ratio score of 2 (probably normal). Nine (10.3%) patients had a choline-creatin/citrate ratio score of 3 (equivocal). Sixteen (18.4%) patients had a choline-cretine/citrate ratio score of 4 (probably cancer) and 45 (51.7%) patients had a choline-cretine/citrate ratio score of 5 (cancer). Our findings were consistent with the studies conducted by Wefer et al.,13 Delphine et al.,12 and Adilson et al.10 In our study, 9 (10.3%) patients had a choline-cretine/citrate score of 1, 1 was positive for prostatic cancer, 8 (81.9%) were negative for prostate cancer, 8 (9.7%) had score of 2, among them 2 (25%) patients were positive for prostate cancer. Six (75.0%) patients were negative for prostatic carcinoma, and 9 (10.3%) patients scored of 3. Among them 5 (55.6%) were positive for cancer and 4 (44.4%) patients were negative for prostatic carcinoma, 16 (12.4%) patients had score of 4, among them 14 (87.5%) patients were positive for cancer and 2 (12.5%) patients were negative for prostatic cancer, 45 (51.7%) patients had score of 5, among them 43 (95.6%) patients were positive for prostatic carcinoma. Our results were consistent with the studies conducted by Delphine et al.,12 Adilson et al.,10 and Joyung et al.14 In our study, 61 patients had a choline creatine/citrate ratio of ≥4. Among them, 57 (93.4%) were positive for prostatic cancer and 4 (6.6%) were negative.
for prostatic cancer, the sensitivity of MR-spectroscopy was 93.4%, specificity 61.5%, PPV 91.9%, NPV of 66.7%, and total accuracy of 87.8%. Our results were consistent with the studies conducted by Adilson et al., Delphine et al., and Dhingra et al. In our study, 38 (43.7%) patients had hypo intense, 8 (9.2%) had hyper intense, 41 (47.1%) had iso intense lesion on T1-weighted imaging. On T2-weighted, 43 (49.4%) patients had hypo intense, 11 (26.6%) had hyper intense, and 33 (37.9%) were iso intense. Our findings were slightly variable in comparison to the study conducted by Delphine et al. In our study, 43 (49.4%) patients had hypo intense lesion on T2-weighted imaging. Among them, 42 (56.8%) lesions had also a choline-cretine peak. One (7.7%) patients had normal choline-cretine/citrate ratio. II (12.6%) patients had hyper intense lesions on T2-weighted imaging. All of them had normal choline-cretine/citrate ratio. Thirty-three (37.9%) patients had iso intense lesions. Among them, 32 (43.2%) patients peak choline-cretine/citrate ratio and I (7.7%) had normal choline-cretine/citrate. Our results were consistent with the study conducted by Delphine et al.

In our study, 43 (49.4%) patients had hypo intense lesions on T2-weighted images, among them 36 (83.7%) patients had prostatic cancer, and 7 (16.3%) had biopsy negative for prostatic carcinoma. Sensitivity of MRI was 83.7%, specificity was 34.1%, PPV 55.4%, NPPV 68.2%, and accuracy was 68.2% and accuracy was 85.6% when MRI findings used alone; our results were consistent with the studies conducted by Delphine et al. and Dirk et al. In our study, when prostatic biopsy was directed with combined endorectal coil MRI and MR-spectroscopic imaging findings in patients, prior TRUS-negative biopsy was done. Out of 87 patients, 71 (81.6%) patients had suspicious lesions either on MRI or MRSI or on both MRI and MRSI. Among them, 62 (87.3%) were positive for prostatic cancer and 9 (12.7%) were negative for prostatic cancer. No suspicious lesions were found in 16 (18.4%) patients on MRI/MRSI. Among them 13 (18.8%) patients were also negative on systematic sextant biopsy and only 3 (18.8%) patients had biopsy positive for prostatic carcinoma on systematic sextant biopsy. The overall sensitivity of combined endorectal coil MRI/MRSI was 87.3%, specificity was 81.3%, PPV was 95.4%, NPV was 59.1% and accuracy was 86.2%. Our results were consistent with the studies conducted by, Delphine et al., Yasushi et al., Barkeley et al., Fergas et al., and Costouros et al.

In our study, 522 cores were taken on the systematic sextent pattern, among them 486 (94.4%) cores were negative for prostatic carcinoma. Only 36 (5.6%) were positive for prostatic carcinoma. 83 cores were taken for directed endorectal coil MRI/MRSI imaging findings. Among them 90 (52%) were positive for prostatic cancer and only 83 (48%) were negative for prostate cancer, the difference was statistically significant between systematic sextent biopsy pattern and biopsy directed with endo‑rectal coil MRI/MRSI findings. Our results were consistent with the study conducted by Adilson et al.

Our findings suggest that prostatic biopsy directed with endorectal coil MRI and MR-spectroscopic imaging findings in patients with elevated serum PSA and prior negative biopsy improves the early diagnosis of prostatic carcinoma and accurate localization of prostate cancer within the gland. The accurate localization of prostate cancer within the gland is of increasing clinical importance due to the development of disease‑targeted ablative therapies.

Our results suggest that addition of MRSI to MRI significantly improves the diagnostic accuracy of prostatic cancer detection in patients with elevated serum PSA and prior negative TRUS-biopsy. MRI alone had accuracy of 58.6% only, sensitivity of 83.7%, and specificity of 34.

**REFERENCES**

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