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Role of Duplex Ultrasound in Diagnosis of Prostate Cancer and Localization for Biopsy

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ABSTRACT

Background: Prostate cancer is a common malignancy among men and is one of major problem of health care system. Ultrasonography is useful, safe, and available method for evaluation of prostate problem. The aim of present study was to evaluate the role of duplex ultrasound in diagnosis of prostate cancer and localization for biopsy. **Methods & Materials:** In a descriptive analytical study, 27 patients with increased level of PSA, who were referred to ultrasonography ward of Imam Reza Hospital for prostate biopsy, were included in the study and examined with color doppler and duplex ultrasonography. Biopsy was done for all patients using transrectal guided ultrasonography. Resistance index (RI), pulsatility index (PI), prostate volume, and pathology findings of biopsy, were evaluated. **Results:** Among 27 patients, 12 patients (44.4%) had prostate cancer and 15 patients (55.6%) had benign prostatic hyperplasia (BPH). In evaluation of RI & PI in prostate arteries, there were no significant differences between patients with malignancy and patients with BPH (P>0.05). Mean volume of prostate in patient with prostate cancer was 36.56±3.13 ml and in patients with BPH was 54.76±5.42 ml. Mean volume of prostate in patients with BPH was significantly more than patients with prostate cancer (P=0.020). **Conclusion:** Based on the findings of present study; there is no significant correlation between vascular features of prostate arteries and prostate malignancy, and volume of prostate in patients with BPH was significantly higher than patients with prostate cancer.

INTRODUCTION

Prostate cancer is one of the commonest cancers among elder men and is the second cause of cancer related deaths among men. Incidence of prostate cancer in the life of male persons is one out of six men (1, 2). Many tests and methods are proposed for assessing prostate, in order to diagnose prostate cancer at early stages such as serum prostate specific antigen (PSA) test, percent free PSA, digital rectal examination and transrectal ultrasonography (TRUS). The precise diagnosis of prostate cancer is done by transrectal ultrasound guided biopsy of prostate (3). Many studies are conducted in order to find a sensitive method to distinguish prostate cancer from prostate benign process at a very early stage.

Recently impressive progress in color doppler and duplex ultrasonography (CDUS and DUS) has led to more precise survey of anatomy of vascularity of organs such as prostate. Transrectal CDUS is a noninvasive method for study of vascular anatomy of prostate in a real-time and reproducible pattern (4). Some studies have reported that color flow of a normal prostate at CDUS is generally low or absent and presence of a focal hypervascularity at peripheral zone of prostate at CDUS should interpreted as a suspicious focus for malignancy; however some other studies revealed that some inflammatory or infectious process may have similar view on CDUS (5,6). It is known that capsular and urethral branches of prostatic arteries are the main source of prostate blood flow (7).

In this study we are aimed to assess the role of CDUS findings of capsular and urethral arties including pulsatility index (PI) and resistive index (RI) of these arteries in distinguishing malignant and benign process of prostate; as there are very few studies in this regard.

METHODS AND MATERIALS

Twenty seven patients who were referred to ultrasonography ward of Imam Reza Hospital, Tabriz, Iran by urology specialist due to abnormal digital rectal exam and elevated prostate specific antigen (PSA) for ultrasonography guided transrectal biopsy of prostate, were entered to the study. Transrectal ultrasonography, color doppler transrectal ultrasonography and transrectal prostate biopsies were done for patients. These ultrasonographic examinations were performed using LPC-1530, ALOKA Corporation, Japan ultrasonography machine using a 5MHz transrectal probe. Patients were prescribed a gastrointestinal tract cleaning en-

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ema on the morning of examination; and were told to empty the bladder before the examination.

A gray scale transrectal ultrasonography was performed assessing the parenchymal echogenicity of the prostate in both coronal and sagittal views, measuring the dimensions and volume of prostate and investigating any abnormality in echo texture of prostate as hyperecho or hypoecho nodules. Color doppler and duplex ultrasonography (CDUS and DUS) examinations of prostate at the largest transverse section were conducted to evaluate the vascularity of prostate gland including capsular and urethral arteries at the peripheral and transitional zones of prostate. The capsular arteries were examined at the entering site to prostate and the urethral arteries were examined parallel to the urethra. At DUS in order to identify the arteries we set the Pulse Repetition Frequency (PRF) at the lower threshold. We measure the Pulsatility index (PI) and Resistance Index (RI) of capsular and urethral arteries at both sides. Also any hypervascular of hypovascular nodules at the parenchyma of prostate was examined by CDUS and DUS.

The patients received 500mg of ciprofloxacin every 12 hours and 250 mg of Metronidazole every 8 hours on the day before sampling up to 10 following days. Biopsies were taken using an 18 –gauge, 20 cm needle from 12-core standard sampling areas (including apex, central, posteromedial, posterolateral, mediolateral and anterolateral areas of both sides). Also samples were taken from any suspicious nodules which were detected at CDUS and DUS examinations. Acetaminophen is prescribed to use if there was a pain after sampling. Samples were sent for histopathologic studies for any malignancy or benign pathologies.

Statistical Analysis

Data were analyzed using SPSS™, version 17 software. Data were explained as mean±SD, percent and frequency. In order to compare two qualitive variables, chi square test and for comparing two quantitive variables Mann-Whitney U test were used. In all test the P value less than 0.05 was considered as significant.

Ethical Considerations

This study was conducted after it is approved by the Ethical Committee of Tabriz University of Medical Sciences. The whole process of study was explained to patients before entering the study and the patients received an informed consent. Patients who had accepted the concept of study was entered the study. All information of patients including the demographical data, gray scale and color doppler ultrasonography data and the results of biopsies remained secret.

RESULTS

With respect to histopathologic outcome, patients were divided to two groups of malignant and nonmalignant groups. Patients with pathology of malignancy at least at 1 area of 12 studied areas of prostate were considered as malignant group. Of 27 studied patients, 12 patients had malignant samples and 15 patients did not have any malignancy at prostate samples. Table 1 shows the frequency of malignancy at each area of sampling.

The Mean age of all patients was 62.62 years; mean age of patients at malignant and nonmalignant groups was 63.91 and 61.60 respectively.

The mean volume of prostate in all patients was 49.69±3.71 ml; the volume of prostate at nonmalignant group was 54.76±5.42 ml which was significantly higher than mean volume of prostate at malignant group which was 35.56±3.13 ml (P value=0.020).

The results of DUS study showed that there is not any significant difference between vascular features (RI and PI) of capsular and urethral arteries at peripheral and transitional zones of prostate with prostate cancer. Our study results showed that mean RI value of capsular artery was slightly

Table 1. Frequency of malignancy in 12-core standard prostate biopsy areas

Area of prostate	Malignant	Nonmalignant
Whole prostate (Percent)	12 patients (44.4%)	15 patients (55.6%)
Right lobe (Percent)	9 patients (33.3%)	18 patients (66.7%)
Left lobe (Percent)	11 patients (40.7%)	16 patients (59.3%)
Right apex (Percent)	5 patients (18.5%)	22 patients (81.5%)
Right anterolateral (Percent)	6 patients (22.2%)	21 patients (77.8%)
Right mediolateral (Percent)	6 patients (22.2%)	21 patients (77.8%)
Right posterolateral (Percent)	7 patients (25.9%)	20 patients (74.1%)
Right posteromedial (Percent)	7 patients (25.9%)	20 patients (74.1%)
Right central (Percent)	8 patients (29.6%)	19 patients (70.4%)
Left apex (Percent)	6 patients (22.2%)	21 patients (77.8%)
Left anterolateral (Percent)	6 patients (22.2%)	21 patients (77.8%)
Left mediolateral (Percent)	6 patients (22.2%)	21 patients (77.8%)
Left posterolateral (Percent)	6 patients (22.2%)	21 patients (77.8%)
Left posteromedial (Percent)	6 patients (22.2%)	21 patients (77.8%)
Left central (Percent)	7 patients (25.9%)	20 patients (74.1%)

higher at malignant group compared to nonmalignant group (0.73 compared to 0.72) however the mean PI value at this artery is higher in nonmalignant group (1.32 compared to 1.41). The mean RI value at urethral artery is lower at malignant group compared to nonmalignant group (0.69 compared to 0.70); on the other side mean PI of this artery is higher at malignant group (1.26 compared to 1.22). However these differences were not statistically meaningful.

Of 27 patients 15 patients had at least one suspicious prostate nodule including 10 patients with hypervascular and 5 patients with hypovascular nodules. Of these 15 patients only 3 nodules had a site of malignancy at pathology study. The results showed that existence of nodule at prostate is not correlated with prostate malignancy (P value= 0.194). Also in hypervascular prostate nodules; we did not find any relationship between the vascular features (RI and PI) of nodule artery and the possibility of malignancy at these nodules.

The detailed comparison of DUS study results of prostate arteries and prostate nodules artery in both groups were shown at Table 2.

DISCUSSION

Prostate cancer is the commonest cancer among elder men and it has the highest incidence among cancers in males (22%). The prostate cancer is the second leading cause of mortality following lung cancer among males (11%) (8-10). As the mortality rate caused by prostate cancer increases by progression of disease, nowadays there is a large attention to early diagnosis of this disease. It is previously mentioned that many methods are being used to detect prostate cancer at early stages including PSA, Free PSA, digital rectal examination, and prostate biopsy (11). Gray scale transrectal ultrasonography is being used as the first imaging modality for localizing and visualizing anatomic aspects of prostate tumor; however its efficacy to detect this cancer at early stages is doubtful. Some studies have shown that gray scale transrectal ultrasonography has a low positive predictive value for cancer detection. At transrectal gray scale ultrasonography most prostate cancers is isoechoic or has a nonspecific irregularity of echo texture of prostate (12-14).

As previous studies have demonstrated; the growth of solid tumors is depended on angiogenesis as a result of endothelial growth factor secretion; which will result in increased vascularity of tumor and its blood flow (15-18). The study of Delongchamps et al revealed the same rule for the prostate cancer; in this study results showed increased blood flow and hyper vascularity of prostate at the malignant site due to increase in angiogenesis (19). Recently color doppler ultrasonography is being used to investigate the vascular structure of tumor and assess the site of increased vascularity. Many studies aimed to investigate the role of CDUS findings in distinguishing malignant tissue from normal tissue in cancers (17, 18). In a study by Remzi et al it is demonstrated that CDUS can detect patients without prostate cancer who has high PSA. The results of this study showed a high negative predictive value for CDUS in diagnosing prostate cancer, the authors concluded that CDUS can prevent further prostate biopsies in order to diagnose cancer (20).

As very few researches have been conducted to evaluate the role of CDUS in detecting malignant tissue in prostate, we are aimed to investigate this problem. In our study, the mean volume of prostate in malignant and nonmalignant prostate was 36.56 and 54.76 respectively; in which the volume of prostate was significantly lower at malignant prostate.

The mean PI value of capsular arteries at peripheral zone of prostate in malignant and nonmalignant prostate was 1.32 and 1.41 respectively; and the mean PI value of urethral artery at transitional zone of prostate in malignant and nonmalignant prostate was 1.26 and 1.22 respectively. The mean RI value of capsular arteries at peripheral zone of prostate in cancer cases was 0.73 which was slightly higher than mean value for non-cancer cases which was 0.72; and the mean RI value of urethral artery at transitional zone of prostate was slightly lower in malignant compared to nonmalignant prostate, which was 0.69 and 0.70 respectively. However there was a slight differences between the RI and PI values of capsular and urethral arteries of two groups of patients but our statistical analysis showed that there is not any correlation between CDUS findings (including PI and RI of capsular and urethral arteries of prostate) with prostate cancer.

In concordance to our study, the study of Alazab et al showed that the lower prostate volume is more suggestive of prostate cancer rather than prostate benign pathologies such as BPH. In this study also higher age, higher PSA value and existence of a hypoechoic area in TRUS of prostate were mentioned as other predictive factors of prostate cancer (21).

Some studies have showed that CDUS of prostate evaluating the RI and PI value of prostate arteries could inform us with good data in regard to lower urinary tract obstruction (22, 23). In a study done by Kojima et al it is revealed that the patients with BPH significantly have higher mean RI

Table 2. Comparison of DUS features of prostate arteries and prostate nodules artery in tow groups

Duplex	Whole patients	Malignant	Nonmalignant	P value
Capsular artery RI (Mean±SD)	0.73±0.087	0.73±0.091	0.72±0.087	0.71
Capsular artery PI (Mean±SD)	1.37±0.29	1.32±0.206	1.41±0.346	0.52
Urethral artery RI (Mean±SD)	0.69±0.072	0.69±0.084	0.70±0.063	0.328
Urethral artery PI (Mean±SD)	1.24±0.30	1.26±0.22	1.22±0.36	0.943
Prostate nodule artery RI (Mean±SD)	0.72±0.10	0.71±0.07	0.72±0.11	0.517
Prostate nodule artery PI (Mean±SD)	1.33±0.38	1.35±0.07	1.33±0.38	0.383

DUS: Duplex Ultrasonography, RI: Resistance Index, PI: Pulsatility Index

value compared to men with normal prostate. Of 33 patients evaluated in this study, 85% patients had RI value more than 0.7; suggesting that RI value more than 0.7 could be a predictive factor of lower urinary tract obstruction (24).

In an early report from Rifkin et al in which they have studied the correlation between spectral doppler analysis and potential of malignancy of hypervascular area of prostate; it is showed that mean RI value of arteries in these area in malignant patients (0.60) was slightly lower than mean RI value of arteries in nonmalignant patients (0.62), however this difference was not statistically meaningful (5). Our study also showed the same results, we also investigate the nodules of prostate with CDUS which were found in TRUS; the mean RI value of hypervascular nodules in cancerous patients was 0.71 which was slightly lower than non-cancerous patients (0.72), same as Rifkin study; and the mean PI value in these areas was slightly higher in cancerous patients (1.35 versus 1.33); also in our study these differences were not meaningful.

In another similar study done by Berger et al in Austria on 92 patients consist of 22 with normal prostates, 45 with BPH and 25 with prostate cancer, they studied the mean RI value of prostatic arteries in these patients which were 0.83, 0.84 and 0.81 respectively in peripheral zone and 0.66, 0.77 and 0.64 in transitional zone (25). The study of Berger et al revealed that mean RI value in transitional zone is significantly higher in benign prostate process such as BPH compared to prostate cancer. The same as our results, in which the mean RI value in transitional zone is slightly lower in malignant patients compared to BPH patients; but our studied showed no significant differences between RI values of these groups. Unlike Berger et al study, in ours the mean RI value in peripheral zone is slightly higher in patients with prostate cancer compared to patients with BPH. We think this discordance between two studies can be explained by the sample size, in which we have studied 27 patients compared to 92 patients of Berger study. Some studies have shown that the Mean RI value of prostate arteries is related with the prostate volume (22, 24, 26, and 27); so the differences between mean volumes of prostate in this study to ours (39.8 versus 49.7) could be another reason for the discordance of two studies' results.

To our search, the only study in this regard which has evaluated both RI and PI values of prostate arteries is a study done by Turgut AT et al at in Ankara, Turkey on 100 patients (14 malignant patients, 41 nonmalignant patients and 50 normal prostates) (28). Unlike our study, the study of Turgut et al showed no significant differences between median prostate volume between two groups (52 in malignant group and 67 in nonmalignant group); on the other side in our study the median prostate volume was meaningfully lower in patients with prostate cancer compared to patients with BPH (36.56 versus 54.76). In the study of Turgut et al mean PI value was statistically lower in malignant group (mean PI value=1.49) compared to nonmalignant group (mean PI value=1.71) in peripheral zone (P value= 0.48); similar to our study, in which the mean PI value in peripheral zone was lower in cancerous patients compared to other patients (1.32 versus 1.41) however the differences in our study was not statistically significant. In both studies mean PI value in transition zone was insignificantly higher in patients with prostate cancer (1.71 vs. 1.56 in Turgut et al study and 1.26 vs. 1.22 in our study). In Turgut study the mean RI value in patients with prostate cancer and BPH in peripheral zone was 0.78 and 0.82 respectively, and in transitional zone was 0.81 and 0.80 respectively. However the group (malignant or nonmalignant group) with higher mean RI value in both peripheral and transitional zone was completely in contrary between Turgut et al study and ours, but in both studies the differences of mean RI value between two groups of studied patients was marginal and statistically insignificant.

In conclusion our results showed that there is no relation between color Doppler ultrasonography findings of capsular and urethral arties including pulsatility index (PI) and resistive index (RI) of these arteries and prostate malignancy. Also there was not any connection between presence of prostate nodule and site of prostate malignancy; so existence of prostate nodule cannot narrow the biopsy number and sites. Our study showed that the size of prostate is meaningfully smaller in patients with prostate cancer than patients with benign prostate hyperplasia.

Considering all studies in this field, it is suggested that assessment of prostate with CDUS examination in patients with abnormal tests and clinical findings may provide useful data. Finally we recommend further studies in this regard to evaluate the role of color Doppler ultrasonography findings in prostate cancer with larger study group.

REFERENCES

1. Godley, P. A., & Schell, M. J. (1999). Adjusted odds ratios under nondifferential misclassification: application to prostate cancer. *Journal of clinical epidemiology,* 52(2), 129-136.
2. Ebrahimi, M. (2004). Prevalence of hormone dependent cancers in Iran during 1986–1997. International Journal of Gynecological Cancer, 14, 204.
3. Neumaier CE, Martinoli C, Derchi LE, Silvestri E, Rosenberg I. Normal prostate gland: examination with color Doppler US. Radiology 1995; 196:453–457.
4. Louvar, E., Littrup, P. J., Goldstein, A., Yu, L., Sakr, W., & Grignon, D. (1998). Correlation of color Doppler flow in the prostate with tissue microvascularity. Cancer, 83(1), 135-140.
5. Rifkin, M. D., Sudakoff, G. S., & Alexander, A. A. (1993). Prostate: techniques, results, and potential applications of color Doppler US scanning. Radiology, 186(2), 509-513.
6. Rubin, J. M., Bude, R. O., Carson, P. L., Bree, R. L., & Adler, R. S. (1994). Power Doppler US: a potentially useful alternative to mean frequency-based color Doppler US. Radiology, 190(3), 853-856.
7. Neumaier CE, Martinoli C, Derchi LE, Silvestri E, Rosenberg I. Normal prostate gland: examination with color Doppler US. Radiology 1995; 196:453–457.
8. Grubb 3rd, R. L., & Kibel, A. S. (2006). Prostate cancer: screening, diagnosis and management in 2007. Missouri medicine, 104(5), 408-13.

9. Simon, H. B. (2004). On call. My doctor gave me a prescription for Uroxatral to treat my enlarged prostate. I tried to look up this medicine in your Harvard Medical School Guide to Men's Health, but I couldn't find it. What can you tell me about Uroxatral? Harvard men's health watch, 8(11), 7.
10. Ward, J. F., Slezak, J. M., Blute, M. L., Bergstralh, E. J., & Zincke, H. (2005). Radical prostatectomy for clinically advanced (cT3) prostate cancer since the advent of prostate-specific antigen testing: 15-year outcome. BJU international, 95(6), 751-756.
11. Controversies in transrectal ultrasonography and prostate biopsy. Ultrasound Q 2006; 22:169–175.
12. Shinohara K, Wheeler TM, Scardino PT. The appearance of prostate cancer on transrectal ultrasonography: correlation of imaging and pathological examinations. J Urol 1989; 142:76–82.
13. Sadeghi-Nejad H, Simmons M, Dakwar G, Dogra V. Coley CM, Barry MJ, Fleming C, Mulley AG. Early detection of prostate cancer, part I: prior probability and effectiveness of tests. The American College of Physicians. Ann Intern Med 1997; 126:394–406.
14. Raja J, Ramachandran N, Munneke G, Patel U. Current status of transrectal ultrasound-guided prostate biopsy in the diagnosis of prostate cancer. Clin Radiol 2006; 61:142–153.
15. Bigler SA, Deering RE, Brawer MK. Comparison of microscopic vascularity in benign and malignant prostate tissue. Hum Pathol 1993; 24:220–226.
16. Siegal JA, Yu E, Brawer MK. Topography of neovascularity in human prostate carcinoma. Cancer 1995; 75:2545–2551.
17. Kurjak A, Shalan H, Kupesic S, et al. Transvaginal colour Doppler sonography in the assessment of pelvic tumour vascularity. Ultrasound Obstet Gynecol 1993; 3:137–154.
18. Obwegeser R, Berghammer P, Lorenz K, Auerbach L, Kubista E. Color Doppler sonography of the lateral thoracic (breast-feeding) arteries: a new approach to the diagnosis of breast disease. Ultrasound Obstet Gynecol 2001; 18: 515–519.
19. Delongchamps NB, Peyromaure M, Dinh-Xuan AT. Role of vascular endothelial growth factor in prostate cancer. Urology 2006; 68:244–248.
20. Remzi, M., et al. & European Society for Oncological Urology ESOU. (2004). Can power Doppler enhanced transrectal ultrasound guided biopsy improve prostate cancer detection on first and repeat prostate biopsy?. European urology, 46(4), 451-456.
21. Al-Azab, R., Toi, A., Lockwood, G., Kulkarni, G. S., & Fleshner, N. (2007). Prostate volume is strongest predictor of cancer diagnosis at transrectal ultrasound-guided prostate biopsy with prostate-specific antigen values between 2.0 and 9.0 ng/mL. Urology, 69(1), 103-107.
22. Tsuru, N., Kurita, Y., Suzuki, K., & Fujita, K. (2005). Resistance index in benign prostatic hyperplasia using power Doppler imaging and clinical outcomes after transurethral vaporization of the prostate. International journal of urology, 12(3), 264-269.
23. Zhang, X., et al. (2012). Resistive index of prostate capsular arteries: a newly identified parameter to diagnose and assess bladder outlet obstruction in patients with benign prostatic hyperplasia. The Journal of urology, 188(3), 881-887.
24. Kojima, M., Ochiai, A., Naya, Y., Okihara, K., Ukimura, O., & Miki, T. (2000). Doppler resistive index in benign prostatic hyperplasia: correlation with ultrasonic appearance of the prostate and infravesical obstruction. European urology, 37(4), 436-442.
25. Berger AP, Horninger W, Kektic J, et al. Vascular resistance in the prostate evaluated by colour Doppler ultrasonography: is benign prostatic hyperplasia a vascular disease? BJU Int 2006; 98:587–590.
26. Özdemir H, Onur R, Bozgeyik Z, Orhan I, Ogras MS, Ogur E. Measuring resistance index in patients with BPH and lower urinary tract symptoms. J Clin Ultrasound 2005; 33:176–180.
27. Tsuru N, Kurita Y, Masuda H, Suzuki K, Fujita K. Role of Doppler ultrasound and resistive index in benign prostatic hypertrophy. Int J Urol 2002; 9:427–430.
28. Turgut AT, Olcucuoglu E, Kosar P, Geyik PO, Kosar U, Dogra V. Power Doppler ultrasonography of the feeding arteries of the prostate gland: a novel approach to the diagnosis of prostate cancer? J Ultrasound Med. 2007;26(7):875-83.