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Hypoechoic versus hypervascular lesion in the diagnosis of prostatic carcinoma

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KEYWORDS
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Abstract
Objective: The goal of this study was to get a better understanding the role of Power Doppler (PDUS) and conventional Gray Scale transrectal ultrasound (TRUS) in targeting prostatic biopsy in men with high prostate-specific antigen (PSA).
Patients and methods: A prospective comparative study of 100 men, categorized according to PSA level into two groups: Group (A) with a PSA level (4.0–10.0) ng/ml (Gray zone) and Group (B) with PSA >10.0 ng/ml, above Gray zone. Gray Scale scanning was done, followed by Color Doppler and Power Doppler to test the blood flow all over the prostate and suspicious foci. Twelve systematic TRUS-guided core needle biopsies were performed, and additional biopsies of abnormal lesions on Gray Scale TRUS and PD-TRUS. The demographic data, clinical data, imaging results, laboratory investigations, histopathological report and its correlation with pathological results and any complications during or post the procedure estimated.
Results: The age of the Group (A) ranged between 50 and 75 years with a mean ± S.D. of 65.7 ± 6.8 years, while in the Group (B), it ranged between 54 and 84 years with a mean ± S.D. of 69.5 ± 6.3 years. TRUS biopsy revealed prostate cancer in 11 (35.5%) out of 31 cases of the Group (A) and 35 (50.7%) out of 69 cases of the Group (B) ($p < 0.003$). Thirty out of 39 (76.9%) from Group (B) were hypervascular in PDUS ($p < 0.04$).
PDUS sensitivity, specificity, positive predictive value (PPV) and negative predictive values were 74.5%, 85.7%, 84.4% and 76.4%.

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Conclusion: Power Doppler ultrasonography (PDUS) increase the cancer detection rate diagnosis, PDUS combination with Gray Scale TRUS-guided biopsy increases the reliability of the diagnosis of cancer prostate.

Introduction

Color flow Doppler (CFD) and Power Doppler imaging (PDI) advanced and have accepted as a tool for prostatic carcinoma diagnosis. Vascularity assessment has two methods of using PDI: total vascularity (TV) and vascular density (VD), and estimate whether quantitative Doppler vascularity correlated with prostate cancer detection. They postulated that the gross total number of blood vessels (TV) in the prostate is diagnostic than the vascular density (VD) [1]. Histology literature integrates angiogenesis in cancer through using vessel density (number of vessels per unit area of the tissue) to ass's vascular activity. A series intended to understand the differences between TV and VD of the prostate and to evaluate their correlation to pathologic diagnosis. They review how TV and VD correlate with visual evaluation of vascularity on Doppler images, how TV and VD vary from the central zone versus peripheral zone, and, whether the differences in Doppler TV or VD be used to differentiate the prostatic lesions, especially, adenocarcinoma, benign prostatic hypertrophy (BPH) as well as intraepithelial neoplasia (PIN) [2]. Hypervascularity correlated with prostate cancer due to increased angiogenesis [3]. TRUS has a high sensitivity but associated with a low positive predictive value (PPV) in the diagnosis of early malignant lesions, which lowering its strength, because hypoechoic lesions detected in a benign lesion. Various modalities investigated to reduce the cost and morbidity and to avoid unnecessary biopsies. Hypoechoic lesion on Gray Scale ultrasound only has a deficiency in the diagnosis of the most prostate malignancies [4]. Color and Power Doppler ultrasound and Gray Scale TRUS when used together, they will increase the sensitivity of detecting prostate cancer, but the specificity is not decreasing. So, the lesions which seem positive Color and Power Doppler ultrasound findings are significant for cancer detection [5].

The goal of this study was to get a better understanding the role of Power Doppler (PDUS) and conventional transrectal ultrasound (Gray Scale TRUS) in targeting Prostatic lesion in a patient with high prostate-specific-antigen (PSA).

Patients and methods

Prospective comparative study of one hundred men from outpatient clinics of Urology and Ultrasonography Unit Al-Azhar University Hospitals in the period between November 2012 and May 2015. After approval of the Medical Research Ethical Committee, an informed written consent obtained. Patients were categorized according to serum prostate - specific antigen as two groups, Group(A)with a PSA level (4.0 -10.0) ng/ml. (Gray Zone), and Group (B), with PSA >10.0 ng/ml, above Gray Zone, included in this study, while the patient had an active urinary tract infection, before the examination; infection controlled. Patients on anticoagulant therapy are not a candid for examination until the anticoagulant dosage adjusted. Also, patients on finasteride therapy were excluded.

One day before examination patient received levofloxacin 750 mg once daily and metronidazole 500 mg three times per day, to continue for two days after the procedure. A cleansing enema performed before the procedure. And non-steroidal anti-inflammatory (NSAIDS) and aspirin stopped for 3 and 5 days before the procedure.

The procedure performed by using transrectal ultrasound (TRUS Gray Scale and Power Doppler) (B&K Medical, Denmark). Transrectal imaging of the prostate completed by using an endocavitary transducer (A 5.0–7.5 MHz). Gray Scale scans are done to the prostatic tissue in the axial and sagittal sections in all patients and its adjacent structures to detect any suspicious lesion (presence of an irregular contour and an asymmetric gland recorded as an abnormal finding). With TRUS, the prostate categorized into a peripheral zone (isoechoic) and a heterogeneous central gland, (transition zone). Calcifications (corpora amylacea) are common at the boundary between the peripheral zone and the central gland. The seminal vesicles visualized as convoluted hypoechoic cystic structures. Prostate cancers visualized as hypoechoic lesions within the isoechoic normal peripheral zone, but lesions appear as isoechoic, hyperechoic, or multifocal as well as TRUS, which recorded.

Color Doppler and Power Doppler ultrasound used to estimate the blood flow among the prostatic tissue and suspicious lesion. The signals from Color Doppler classified into normal vascular, hypovascular and hypervascular foci. Grading of PDUS categorized as follows: Grade 0, no abnormal vascularity; Grade 1, low focal vascular clustering; Grade 2, intensive focal vascular clustering; and Grade 3, diffuse vascular clustering.

Twelve core biopsies taken using TRUS-guided needle biopsies by an 18-gauge biopsy cutting needle driven through a biopsy gun. Extra biopsies from areas that showed abnormality (hypoechoic or hypervascular lesion). Management of complications if occurred, during and after the procedure and evaluation of the histopathological examination reports and the data collected for analysis.

Statistical analysis

The data analyzed using statistical package for social science (SPSS version 20.0) for Windows (SPSS IBM: Chicago, IL). The results expressed as mean ± SD with 95% confidence interval by using medians for quantitative variables, and using the frequencies and percentages for qualitative ones; a P-value < 0.05 is a statis-

tically significant. Sensitivity, specificity, positive predictive value (PPV) and the negative predictive value estimated by using MedCalc1 V.7.1.0.1. Student-t-test used to compare the parametric data between the groups

Results

The age of Group (A) ranged between 50 and 75 years with a mean ± S.D. of 65.7 ± 6.8 years. While in Group (B), it ranged between 54 and 84 years with a mean S.D. of 69.5 ± 6.3 years. So, the mean age was higher in Group (B) than in group A ($p = 0.01$).

Serum PSA of Group (A) (Gray zone) ranged between 4.5 and 10 ng/dl with a mean ± S.D. of 7.9 ± 1.4 ng/dl, while in Group (B) above Gray zone, it ranged between 10.5 and more than 1000 ng/dl with a mean ± S.D. of 66.4 ± 145 ng/dl.

Digital rectal examination (DRE), 22.6% of the Group (A) and 40.6% of the Group (B) had an abnormal DRE which was statistically significant ($p = 0.04$).

TRUS biopsy revealed prostate cancer in 11 (35.5%) out of 31 cases of the Group (A) and 35 (50.7%) out of 69 cases of Group (B).

Correlation between the results of the DRE and histopathological examination revealed a statistically significant difference ($p = 0.04$).

TRUS revealed hypoechoic lesions in 40 cases, 12 out of them were of the Group (A) and 28 were of the Group (B). So, there was no statistically significant difference in hypoechoic lesion detection between the two study groups (38.7% for Group (A) vs. 40% for Group (B)) ($p = 0.6$).

Histopathological examination of cores taken from hypoechoic lesions revealed adenocarcinoma in 24 cases (6 out of them were of Group (A) and 18 were of Group (B)). So, cancer detected in 50% (6/12) of hypoechoic lesions in Group (A) and in 64.3% (18/28) of Group (B). Which was statistically significant ($p = 0.006$). Comparative study of the groups, depending on adenocarcinoma of a hypoechoic lesion, we find a statistical difference with (p-value <0.01) 25% of patients of a hypoechoic lesion in the Group (A) and 75% in the Group (B).

Color Doppler showed hypervascularity in 51 (51%) patients (15 out of them were of Group (A) and 36 were of Group (B)). The difference between both groups is statistically insignificant ($p = 0.7$).

Correlation between the cores taken from hypervascular areas and the results of histopathology revealed that cancer detected in 38 out of 51 (74.5%) hypervascular areas (8 out of them were of Group (A) and 30 were of Group (B)). So, an incidence of cancer detection in hypervascular areas in Group (B) (83.3%) was higher than Group (A) (53.3%) which was statistically significant ($p = 0.02$).

Through these criteria, patients who had a hypoechoic and hypervascular lesions cross-tabulated with adenocarcinoma, we find a highly significant difference in the incidence of adenocarcinoma between hypoechoic, hypervascular lesions than in hypoechoic non-hypervascular lesion according to the histopathology with (p-value <0.001).

Similarly, as well as we find (p-value <0.001) in patients with non-hypoechoic and hypervascular Lesions cross-tabulated with adenocarcinoma according to histopathology, that meant there was a highly significant difference in the incidence of adenocarcinoma among non-hypoechoic hypervascular lesions than non-hypoechoic, Non-hypervascular lesions according to the histopathology (p-value 0.01) (Tables 1 and 2).

PDUS guided biopsies missed three cases, one of which appeared as a non-vascular, non-hypoechoic in Gray Scale TRUS in the Group (A). The other two adenocarcinoma cases were neither hypoechoic in Gray Scale TRUS nor hypervascular in PDUS in the Group (B). The three missed cases demonstrated with systematic TRUS biopsy.

According to hypervascularity grading, 51 cases diagnosed, 15 from Group (A) and 36 from Group (B) out of the 38 patients diagnosed as adenocarcinoma (3 G0 7.9%, 7/38 18.47% G1, 10/38 26.3% G2 and 18/38 47.3 G3) (Fig. 1A–C).

Power Doppler Ultrasound (PDUS) sensitivity, specificity, positive predictive value (PPV) and negative predictive values were 74.5%, 85.7%, 84.4% and 76.4%, respectively. PDUS had greater sensitivity and specificity than TRUS (60% and 66.7%, respectively) and identified cancer cases more accurately (Table 3).

Discussion

The most commonly used methods for detection of prostatic carcinoma is the conventional transrectal ultrasound (TRUS-guided prostate biopsy). TRUS has several benefits including safety, portability, low-cost, and the ability to do real-time imaging and image-guided procedures in an office setting. A hypoechoic lesion which appears on the Gray Scale ultrasound, is the most common appearance of prostate cancer, but it is isoechoic in up to 30% of patients. One study compared GSU and PDU with 620 radical prostatectomy specimens and revealed combination of PDU and GSU make efficient specificity from 47 to 74% [6].

In this work, Gray Scale scanning performed for 100 patients all over the entire prostatic tissue, as well as the surrounding structures to look for areas that appear suspicious. The Gray Scale assessment in our study shows that 40 (40%) patients had hypoechoic lesions, 12 (30%) patients in Gray zone of PSA (Group (A)) and 28 (70%) patient above Gray zone (Group (B)). The results of the histopathological examination of the biopsies showed adenocarcinoma in 24 (60%) patients from patients with hypoechoic lesions and 24 (24%) patients from the total number of all patients. Six (25%) patients were in the Gray zone and, 18 (75%) patients above the Gray zone. When we used Color and Power Doppler US in our series, we found 51 (51%) patients with hypervascular lesions, 15 (29%) patients in the Gray zone and 36 (71%) patient above Gray zone, the results of the histopathological examination of the biopsies detect adenocarcinoma in 38 (74.5%) patients from patients with hypervascular lesions and 8 (21%) patients in the Gray zone and 30 (79%) patients above Gray zone [7].

The hypoechoic lesions which appeared on Gray Scale ultrasound may appear hypervascular or non-hypervascular and hypervascular lesions which appeared in PDUS may be hypoechoic or non-hypoechoic. So, we have four characters for prostatic lesions, hypoechoic, hypervascular lesions (23 patients), hypoe-

Table 1 Correlation between Gray Scale, Power Doppler and histopathology in Group (A).

Gray Scale	Doppler	Adeno.	BPH	PIN	Total	*p*-Value
Hypoechoic	Hypervascular	5 (71%)	2 (29%)	0 0%	7 (100%)	0.04
Hypoechoic	Non-hypervascular	2 (40%)	3 (60%)	0 0%	5 (100%)	0.05
Non-hypoechoic	Hypervascular	3 (37.5%)	5 (12.5%)	0 0%	8 100%	0.03
Non-hypoechoic	Non-hypervascular (*Systematic core*)	1 (9.1%)	10 (90.9%)	0 0%	11 100%	0.09

Adeno. = adenocarcino, BPH = benign prostatic hyperplasia, PIN = prostatic intraepithelial neoplasia.

Table 2 Correlation between Gray Scale, Power Doppler and Histopathology in Group (B).

Gray Scale	Doppler	Adeno.	BPH	PIN	Total	*p*-Value
Hypoechoic	Hypervascular	14 (82.3%)	2 (12.5%)	1 6.25%	17 (100%)	0.04
Hypoechoic	Non-hypervascular	3 (33.3%)	6 (50%)	0 0%	9 (100%)	0.05
Non-hypoechoic	Hypervascular	16 72.7%	6 (30%)	0 0%	22 100%	0.03
Non-hypoechoic	Non-hypervascular (*Systematic core*)	2 (9.5%)	18 (85.7%)	1 4.8%	21 100%	0.09

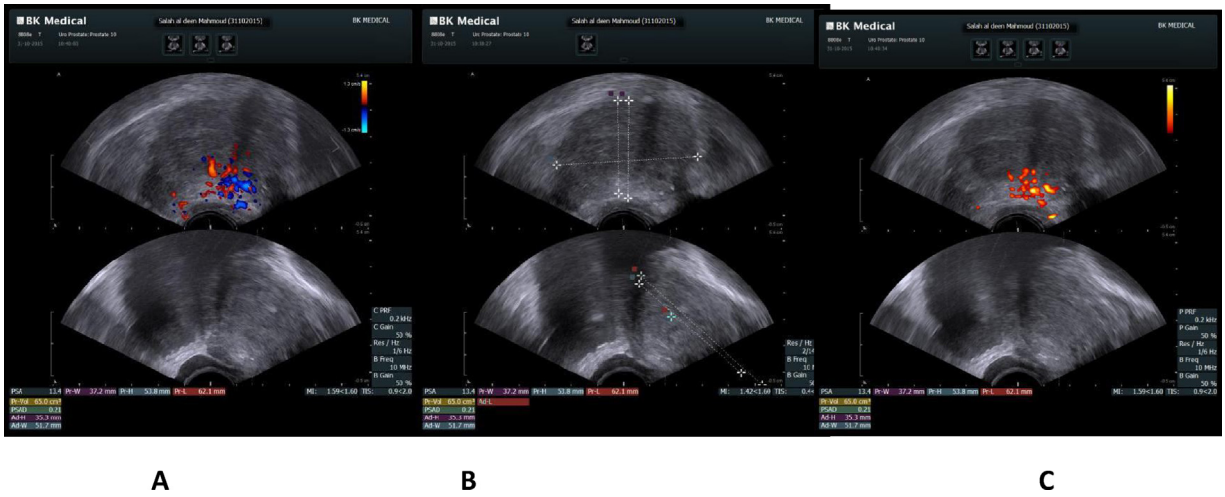

Fig. 1 Color, Power Doppler and Gray Scale transrectal ultrasound. (A) Color scale ultrasound (hypervasculer lesion). (B) Gray Scale ultrasound (no hypoechoic lesion). (C) Power Doppler ultrasound (hypervasculer lesion). PSA, 13.4 ng/ml. Pathology: poorly differentiated prostatic adenocarcinoma, Gleason score 9 (5 + 4).

Table 3 Sensitivity, specificity, PPV, NPV of Gray Scale TRUS and PDUS methods.

Method	Sensitivity	Specificity	PPV	NPV	Accuracy
Gray Scale	60%	66.7%	75%	76.5%	46.58%
PDUS	74.5%	85.7%	84.4 %	76.4%	79.66%

PPV = positive predictive value, NPV = negative predictive value.

Table 4 Summary of histopathology according to modalities for taking biopsies.

Modalities to take Biopsy		Histopathology						
		Adeno.	BPH	PIN	Total	No lesion	Total	*p*-Value
According to Gray Scale only (hypoechoic)	Count	24	15	1	40	60	100	
	%	24.0%	15.0%	1.0%	40.0%	60.0%	100.0%	
According to Color and Power Doppler only (hypervascular)	Count	38	12	1	51	49	100	
	%	38.0%	12.0%	1.0%	51.0%	49.0%	100.0%	
								0.03
According to systematic biopsy only (12 core)	Count	3	28	1	0	32	32	
	%	9.3%	87.5%	3.1%	0%	100%	100.0%	
According to Gray Scale, Color and Power Doppler (hypoechoic and hypervascular)	Count	43	23	2	68	32	100	
	%	43.0%	23%	2.0%	68.0%	32.0%	100.0%	

choic, non-hypervascular lesions (17 patients), hypervascular, isoechoic lesions (28 patients) and isoechoic, non-hypervascular prostate (32 patients).

The sensitivity of GSU for prospective tumor detection varies by experience has reported up to 60% of tumors appear hypoechoic, isoechoic in 35–39%, which is a limitation on Gray Scale ultrasound cancer detection rate [8].

When using Gray Scale and Doppler ultrasound in our study, we found 67 (67%) patients with lesions, whether hypoechoic, hypervascular or hypoechoic only or hypervascular only. The results of the histopathological examination of the biopsies detect adenocarcinoma in 43 (64.2%) in patients with lesions (i.e. 43% patients from the total number of study patients). Ten (23.2%) patients out of them were in the Gray zone and 33 (76.7%) patients were above the Gray zone. Prostatic adenocarcinoma incidence in lesions which have the two characters hypoechoic, hypervascular were 19 patients from 23 patients (82.6%).

Power Doppler ultrasound is sensitive as to detect flow in vessels as small as 1 mm, asymmetrically increased flow patterns of the tumor with a significant increase in the number and size of vessels suggesting prostate cancer on Doppler imaging. These vessels will show an irregular orientation in contrast to the typical radial pattern of normal prostate flow [9]. The sensitivity of Gray Scale in our study was 60%, which lies in the range found in the literature (8–88%). The specificity was 86.7%, which bring a closer figure to that reported by Kuligowska et al. [10], 85%. The PPV (positive predictive value) was 75% and NPV (negative predictive value) was 76.5%, which agree with that mentioned by Russo et al. [10] 72% and 79% respectively. The sensitivity of the combined Gray Scale and Doppler together in our study was 74.5%, specificity was 85.7%, and PPV (positive predictive value) was 84.4%. So, we recommend using the two modalities, Gray Scale, and Doppler in targeting prostatic biopsies and once hypoechoic, hypervascular lesions appeared, an additionally directed biopsy performed.

PDUS has the usefulness over CDUS of detecting very low vascular flows, to get better cancer detection rates with TRUS-guided biopsy taken from abnormal vascular foci [9].

Radhakrishnan and Vinodh [11] prove that high-test performance of PDUS for prostate cancer diagnosis with 98% sensitivity and a 99% NPV. Some studies have reported that Power Doppler is a dependable method for prostate cancer detection and propose that it can also predict the tumor aggressiveness [12,13].

Color and Power Doppler US in our study, we found 51 (51%) cases with hypervascular lesions, 15 (29%) patients in the Gray zone and

36 (71%) patient above Gray zone, the results of the histopathological examination of the biopsies show adenocarcinoma in 38 (74.5%) patients from the total number of patients with hypervascular lesions and 38 (38%) cases from all patients. Eight (21%) patients in the Gray zone and 30 (79%) patients above the Gray zone.

In our study, as well as in others [14], there was a highly significant positive correlation between PSA and age ($p = 0.004$).

The sensitivity of the DRE increased when PSA is high, 20% if the PSA level less than 3.0 ng/ml. While the sensitivity of the DRE became 46% PSA level was 10 ng/ml or more [15]. Our study showed a highly significant positive correlation between abnormal DRE and prostate cancer in different studied groups, in the Group (B) incidence of prostate cancer increased with abnormal DRE than Group (A).

When examining any technique is better than the other according to the Modalities to take Biopsy, we found significant deference increased direction of using the two techniques together {Gray Scale, Color and Power Doppler (Hypoechoic and Hypervascular)}. Out of 68 patients harboring lesions either Hypoechoic or Hypervascular or both 43 patients diagnosed as adenocarcinoma (63.2%), while 3 cases out of 32 had no lesions diagnosed with cancer prostate (9.3%), p-value of 0.03. So, the percentage of systematic core biopsy for total patients diagnosed with cancer, prostate was (3/46 = 6.52%), as presented in Table 4.

Our recommendations are using Gray Scale and Doppler as a combined modality in targeting prostatic biopsies and any lesion either hypoechoic or hypervascularity estimated and a biopsy should take, in addition to the twelve core biopsies which taken as sextant biopsy. Also, we recommend any active urinary tract infection be treated before any manipulations. Patient with finasteride therapy is not a candidate for Doppler examination because one of the mechanisms of action of this drug is the decrease of vascularity.

Limitations of the study

A small number of patient of this study in which 100 patients studied. Also, a prostatic biopsy was not marked separately to show which core is positive and percentage of cancer in each core.

Conclusion

Power Doppler ultrasonography (PDUS) increases the cancer detection rate diagnosis. The diagnostic reliability of cancer prostate increased by a combination of PDUS with Gray Scale TRUS-guided biopsy. However, twelve core biopsies continued as the best diagnostic modality.

Authors' contributions

Abdel-naby Saed Elshamy – Collection and data analysis of pathological parameters.

Ethical approval

Al-Azhar Medical Research Ethics committee.

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