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Research Article

The Initial Experience of Trans-Rectal Ultrasound and Biopsy in Diagnosis of Carcinoma Prostate in Gezira Hospital for Renal Disease and Surgery (GHRDS)

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Abstract

Background: Prostate cancer prevalent cancer in males above sixty-five worldwide, this lead to the introduction of screening of the PSA and using of the transrectal ultrasound scanning, and sextant biopsy of the prostate.

Objectives: To compare the accuracy of the Transrectal Ultrasound guided biopsy (TRUS/BX) in the diagnosis of prostate cancer in Gezira Hospital for Renal Diseases and Surgery (GHRDS), with specific considerations to the digital rectal examination (DRE) findings and prostate specific antigen (PSA) level.

Materials and Methods: This is a prospective, descriptive small-scale hospital based study. A total of 297 patients with clinically symptomatic enlarged prostate underwent transrectal ultrasound guided true cut needle biopsy of the prostate were studied in (GHRDS) in the period from June2006 to June2009.

Results: The majority 188 (63.3%) of patients were between 50-70 years of age. Abnormal digital rectal examination (DRE) like obliteration of the median sulcus, and fixed mucosa revealed higher incidence of carcinoma prostate (CaP) with a significant value (p = 0.0000). PSA level showed significant relation (p = 0.0001) with the diagnosis of carcinoma prostate. Transrectal U/S findings well correlated to the histopathological results, where abnormal findings (like hypo-echoic lesions or calcifications and cysts) showed higher incidence of malignancy in 46 patients constitute 52.8% of the abnormal U/S findings.

Conclusions and recommendations: PSA level is highly sensitive but less specific in detection of prostate cancer. Normal DRE doesn't exclude prostate cancer, fixed mucosa and obliterated median sulcus has the highest predictors of cancer prostate in DRE. Presence of calcifications and cyst on trans-rectal ultrasound has the highest liability for cancer prostate in compare to the other ultrasonic findings.

Keywords: Prostate cancer, DRE, PSA level, TRUS/ BX (Transrectal ultra sound biopsy), sextant biopsy

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الملخص

الخلفية: سرطان البروستات هو سرطان منتشر في الذكور فوق سن الخامسة والستين في جميع أنحاء العالم، ولهذا السبب تم إدخال فحص بى أس أي وإستخدام المسح بالموجات فوق الصوتية عبر المستقيم، وخزعة سيكسانت من البروستات.

الأهداف: هى مقارنة دقة الخزعة المأخوذة بالموجات فوق الصوتية الموجهة عبر المستقيم في تشخيص سرطان البروستات في مستشفى الجزيرة لأمراض وجراحة الكلى، مع إعتبارات محددة لنتائج فحص المستقيم الأصبعى ومستويات فحص بى أس أي.

الطرق: فى دراسة إستباقية وصفية على نطاق صغير قائمة بالمستشفى وقد درس ما مجموعه ٢٩٧ مريضاً مع أعراض سريرية وتضخم للبروستات الموجات فوق الصوتية عبر المستقيم موجهة خياطة إبرة قطع حقيقية من البروستاتا في (غردز) في الفترة من يونيو ٢٠٠٦ إلى يونيو ٢٠٠٩.

النتائج: كانت الأغلبية ١٨٨ (٦٣,٣٪) من المرضى بين ٥٠-٧٠ سنة من العمر. فحص المستقيم الأصبعى غير طبيعي مثل طمس من التلم الأوسط، والغشاء المخاطي الماتصق كشفت عن حدوث أعلى من سرطان البروستات مع قيمة كبيرة (p = ٠,٠٠٠٠). أظهر مستوى بى أس أي علاقة كبيرة (p = ٠,٠٠٠١) مع تشخيص سرطان البروستات. وترتبط نتائج الموجات فوق الصوتية الموجهة عبر المستقيم بشكل جيد مع النتائج النسيجية، حيث أظهرت نتائج غير الطبيعية (مثل الأورام أو التكلسات والأكياس) ارتفاع نسبة الخباثة في ٤٦ مريضا حيث شكلت (٥٢,٨٪) من نتائج الموجات فوق الصوتية الموجهة عبر المستقيم الغير طبيعية.

الإستنتاجات: مستوى البى أس أي حساس للغاية ولكن أقل تحديداً في الكشف عن سرطان البروستات. فحص المستقيم الأصبعى الطبيعى لا يستبعد وجود سرطان البروستات، والغشاء المخاطي المثبت وطمس وسط التلم لديهما أعلى تنبؤات من سرطان البروستات في نتائج فحص المستقيم الأصبعى . وجود التكلسات والكيسات على الموجات فوق الصوتية عبر المستقيم لديه أعلى مسؤولية عن سرطان البروستات مقارنة للنتائج الأخرى من الموجات فوق الصوتية.

1. Introduction

Prostate cancer is more common in countries with higher proportions of elderly men in their population, and so accounts for around 15% of cancers in men in developed countries, but only 4% in developing countries [1].

In Sudan prostate cancer was not considered among the top 10 commonest cancer in Sudan in the period (1967-1984), but in the period (1984-2004), it was listed at the bottom of the top 10 common male cancers [2].

Prostate cancer in Gezira state, Sudan, was studied in patients diagnosed and treated in the National Cancer Institute & GHRDS in Wad Medani in the period 2002-2007, comprised 8% of all cancer in the period before TRUS introduction. It jumped to 14% in the first year after introduction of TRUS/BX. The prostate cancer became number one

male cancer compared to number three cancers before TRUS was introduced. However, no other study was reported in Sudan regarding TRUS/BX [2].

Before TRUS improvements and serum PSA testing became widespread, clinicians relied mainly on digital rectal examination to establish a diagnosis of prostate cancer and performed digitally directed lesion biopsies. The presence of focal nodules on digital rectal examination still will prompt a biopsy using the TRUS technique regardless of PSA levels. TRUS-directed prostate needle biopsy remains the gold standard for diagnosis of prostate cancer [3]. The risk of a positive DRE turning out to be cancer is dependent greatly on the PSA value. This was shown by the nomogram, which showed an increase in the positive predictive value as the PSA level increase from 0 to 10 ng/ml [4].

PSA-based screening programs have markedly improved early prostate cancer detection. These initiatives were significantly increase the rate of organ-confined and potentially curable disease [6]. Currently, most clinicians recommend biopsy once a patient's serum PSA rises above 4.0 ng/mL [4]. Evidence for lowering the PSA threshold from work by Catalona's group showed higher rates of organ-confined disease at the time of radical retropubic prostatectomy in men sampled with PSAs in the 2.6- to 4.0-ng/mL range [7]. These findings have led many urologists to recommend prostate biopsy to men younger than 60 years of age once their PSA level rises above 2.5 ng/mL [4]. There is a general trend toward allowing older men (70 years or older) to have slightly higher "normal" PSAs, in the range of 5.5 to 6.5 ng/mL, although this is not universally accepted [8, 9]. Patients with a serum PSA value between 4.0 and 10.0 ng/mL, using a percentage of free PSA thresholds of less than 25% detected 95% of cancers while eliminating 20% unnecessary biopsies, and within this group, the risk of prostate cancer increased dramatically as the percentage of free PSA level declined [10]. Regardless of initial PSA value, a PSA velocity greater than 0.75 to 1.0 ng/mL per year is frequently associated with prostate cancer and warrants biopsy [9], whereas an elevated PSA density and PSA density-Transitional zone have both been shown to increase the likelihood of diagnosing prostate cancer on repeat biopsy [11]. The original sextant biopsy scheme, (one core from the base, mid, and apex bilaterally) significantly improved cancer detection over digitally directed biopsy of palpable nodules and ultrasound-guided biopsy of specific hypo- echoic lesions) [12, 13]. Taken in the parasagittal plane these cores sampled a portion of the peripheral zone but also included a significant amount of tissue from the transitional zone, with subsequent studies of radical prostatectomy specimens demonstrating that the vast majority of adenocarcinomas arise in the posterolateral peripheral zone [14], thus explaining some of the false-negative results of standard sextant biopsy [15].

2. Materials and Methods

This is a prospective, descriptive, hospital based study-carried out in (GHRDS) in Wad Medani, Gezira state, Sudan. Gezira hospital for renal disease and surgery it serves patients from Gezira state which is the second popular state in Sudan with population of 4 million capita, also serves patients coming from nearby states .

All patients, were above fifty, presenting with lower urinary tract symptoms suggestive of prostatic problems, were seen in the referred clinic. History, clinical examination including digital rectal examination (DRE) was done, investigations including, prostate specific antigen, and abdominal ultrasound were done. Patients indicated for TRUS/BX are selected, prepared through clinical work up, including history and examination to exclude contra-indications like bleeding tendency, painful anorectal conditions, and urinary sepsis. Written consent for the procedure and the study were obtained. Patients used to come early in the morning fasting, enema were routine, followed by an intravenous injection of gentamycin. In left lateral position with flexed right hip and knee-rectal probe, covered with sterile condom was introduced lubricated with xylocaine jelly. Sextant biopsy was taken according to the Sudanese guidelines policy. More biopsies were taken in the presence of when palpable nodules, or suspicious hypo-echoic, hyper-echoic, calcifications or cyst formation. The procedure of TRUS/BX was done by the urologist. Biopsies were preserved in formalin (10%) containers sent for histopathology. Data were statistically analyzed using SPSS packages, the Chi square test was used for categorical variables .Variable was considered to be significant if the P value was 0.05 or less. The sensitivity and specificity and positive predictive value were calculated by using the formula:

Sensitivity = TP/TP+FN

Specificity = TN/FP+TN

Positive predictive value = TP/TP+FP

TP = True positive

FN = False negative

TN = True negative

FP = False positive

3. Results

The study included 297 patients who underwent transrectal ultrasound and biopsy at Gezira Hospital for Renal Diseases and Surgery, during the period from June 2006 to June 2009. The ages of the patients ranged between 50 – 70 years.

DRE was found in 145 (48.8%) to be normal, 135 (93.1%) of them had histopathology results but 10 (6.9%) revealed cancer of the prostate .

DRE	Histopathology			Total
	Benign	Adenocarcinoma	Inflammatory	
Normal	135 (93.1%)*	10 (6.9%)	0	145
Hard nodular	81 (87.1%)*	9 (9.7%)	3	93
Obliteration median sulcus	17 (53.1.1%)	15 (46.9%)	0	32
Fixed mucosa +pelvic extension	6 (23.1%)	21 (76.9%)*	0	27
	239	55	3	297

Table 1: The relation between the DRE findings and the histopathology of 297 patients had TRUS/BX. *DRE sensitivity = 78.6%, DRE specificity = 56.3%, *P value=0 .000.*

PSA ng/ml	Histopathology			Total
	Benign	Adenocarcinoma	Inflammatory	
< 4	16 (84.2%)*	3 (15.8%)	0	19
4 to 10	115 (90.6%)*	12 (9.4%)	0	127
11 to 100	106 (70.7%)*	41 (27.3%)	3	150
> 100	1 (100%)	0	0	1
	238	56	3	297

Table 2: The histopathological distribution of 297 TRUS/BX biopsies according to the PSA level. *PSA sensitivity = 94.5%, PSA specificity = 76.0%, *P value=0.001.*

Patients with abnormal DRE findings comprise 151 (50.8%), of them 107 (70.9%) had benign and 44 (29.1%) had malignant, as shown in Table (1), the sensitivity of DRE was 78.6 and the specificity was 56.3.

PSA less than 4 ng/dl was found in 19 (6.4%) case, 3 (15.8%) had cancer prostate on histopathology, PSA level 4-10 ng/dl was found in 127 (42.8%) case, 12(9.4%) of them had cancer prostate. PSA level 11-100 ng/dl was found in 150 (50.5%) case, 41(27.3%) of them had cancer prostate, and 3 cases showed inflammatory changes. One case (0.3%) has reported more than 100 ng/dl of PSA, but his histopathology result was benign. The relation between stocktickerPSA and histopathology results was significant (P= 0.001) as shown in Table 2, the PSA sensitivity and specificity were 94.5% and 76.0 **%** respectively.

Ultrasound was reported 210 cases as normal echo texture of the prostate,10 (4.8%) of them had cancer prostate. The abnormal ultrasound findings was in 87- patient

Ultrasound Finding	Histopathology			Total
	Benign	Adenocarcinoma	Inflammatory	
Large normal texture	199	10 (4.8%)	1	210
Hypo-echoic lesion	37	17 (19.5%)*	2	56
Calcification + cyst	2	29 (33.3%)*	0	31
	238	29+17=46 (52.8%)*	3	297

Table 3: TRUS findings correlated to the histopathology of 297 TRUS/BX. *TRUS sensitivity = 91.1%, TRUS specificity = 83.1%, P value = 0.000.*

46(52.2%) of them were adenocarcinoma .Hypo-echoic lesions were found to be in 56- case, 17 of them had cancer prostate , and only two cases were inflammatory. Calcifications and cysts were seen in 31-case, 29 (33.3%) of them had cancer prostate. The relation between TRUS and histopathology results was significant (P value 0.000). The sensitivity and specificity of TRUS in this study were 91.1 and 83.1 respectively as shown in Table 3.

4. Discussion

Introduction of PSA screening, and TRUS/BX in GHRDS changed the picture in detecting cancer prostate patients in an earlier stage, together with the ability to increase the number of patients who are candidates for prostatic biopsy i.e. to include patients with abnormal digital rectal examination findings, patients with stocktickerPSA level more than 4ng/ml, and patients with abnormal transrectal ultrasound echo texture. This practice consisted with the European guidelines of Urology. DRE is the most important part in assessing patients with prostate enlargement, and remained an essential predictor of cancer prostate. This is well documented in this study, which showed significant correlation between abnormal DRE findings and cancer prostate (CaP) (P-Value 0.000). PSA is an important predictor of prostate cancer, since the introduction of PSA as an screening tool, the incidence of cancer prostate jumped to be the leading cancer in males above 65 years old [1]. We consider the level 4ng/ml as a cut off value, but as shown in many studies [7] levels between (2 to 4 ng/ml) in younger ages i.e. less than 60 years old have significant number of cancer prostate. Therefore, we should reduce the cutoff value for younger patients, and at the same time take higher levels for old patients [4]. To increase the sensitivity of PSA as a predictor for cancer prostate, we can use more sensitive predictors like free PSA level/Total PSA ratio, PSA density, and PSA density of the transitional zone. This will reduce about 20% unnecessary biopsies [9, 10]. Transrectal ultrasound screening of the prostate improved the biopsy technique very much, where you can direct the needle targeting specific areas like the para sagittal zone to take the sextant biopsies , also you can direct the needle towards suspicious areas detected by the ultrasound screen i.e. hypo-echoic, hyper-echoic regions, and cysts or calcification zones. Transitional zone can be included with sextant biopsy, this explain the high negative biopsies in the classical sextant biopsies [15].

The combination of DRE, PSA, and TRUS as diagnostic procedures used to screen population for cancer prostate, showed that the positive predictive value increases as the number of abnormal modalities increases i.e. if one of the modalities is abnormal the positive biopsy rate is 6-25%, with two abnormalities it is 18-60%, and if all three modalities are positive, it is 56-72%. This shows that combination of the three diagnostic modalities give the highest chance for detecting early cases of cancer prostate, and this what was done in our study [16, 17].

5. Conclusions

PSA level is highly sensitive but less specific in detection of prostate cancer. Normal DRE doesn't exclude prostate cancer, fixed mucosa and obliterated median sulucus has the highest predictors of cancer prostate in DRE. Presence of calcifications and cyst on trans-rectal ultrasound has the highest liability for cancer prostate in compare to the other ultrasonic findings.

6. The Author Contributions

i. Study concept and design:

1. Walaa Eldin Ibraheem
2. Prof. Mustafa Omran
3. Dr.Sami Mahjoub Taha

ii. Collection of data:

1. Walaa Eldin Ibraheem
2. Dr.Sami Mahjoub Taha

iii. Analysis and interpretation of data:

1. Walaa Eldin Ibraheem
2. Dr.Sami Mahjoub Taha

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