

# Results of prostate biopsies in a teaching hospital in Western Saudi Arabia

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## ABSTRACT

**Objective:** To evaluate the prostate cancer detection rate in 45 patients who underwent transrectal ultrasound scan (TRUS) guided biopsies at King Abdul-Aziz University Hospital (KAUH), Jeddah, Kingdom of Saudi Arabia (KSA) and compare it with the previously reported national and international rates.

**Methods:** Forty-five charts reviewed for patients underwent TRUS guided biopsies in the period between July 1997 through to November 2002 at KAUH. Patients were entered in the study either as of high serum prostatic specific antigen (PSA) or abnormal digital rectal examination (DRE), or both. Cases with large prostate size or suspected elevation of PSA due to causes other than prostatic cancer was excluded from the study.

**Results:** Out of the 45 patients who underwent TRUS guided biopsy; cancer of the prostate was detected in 13 (28.8%). The cancer detection rate in patients presented with

abnormal DRE alone was 7.6%, and was 15.3% in the group with elevated PSA but normal DRE (stage T1c). When PSA was elevated to 4-10ng/ml TRUS guided biopsy detected cancer in 21.4%, elevation of PSA to 10-20ng/ml lead to cancer detection in 40% of the patients, and when PSA was above 20ng/ml all cases were positive for cancer.

**Conclusion:** Cancer prostate is common in Western countries; national studies reported a low incidence of prostate cancer in KSA. Yet in our local patients using this precise method of investigation, our study confirms that the detection rate of prostate cancer through TRUS guided biopsies match the results of previously reported national studies and still lower than the international rates. Although the number of cases are small to draw solid and final conclusions; this study should stimulate further research and more reports on this important subject.

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Measurements of serum Prostatic Specific Antigen (PSA) are widely used for the early detection, diagnosis, and for monitoring of prostate cancer while prostatic transrectal needle biopsy is performed to confirm or exclude the presence of cancer. Prostate biopsy is currently performed under the guide of Transrectal Ultrasound Scan (TRUS) which yields a high degree of precision. The management of patients with elevated serum PSA or hard nodules on clinical examination can be a problem when the first set of prostate biopsies were reported as negative since prostate cancer is often multimodal and the volume sampled by

the standard sextant biopsy technique is relatively small, and there is a real possibility that these individuals may harbor cancer. All cases with suspicious malignancy need repeat biopsy as cancer detection rate on repeat biopsy ranges between 10-20%.<sup>1-3</sup> No biopsy protocol is present up till now is capable of diagnosing all prostate cancers at first set of biopsies, repeat biopsy may be necessary in many patients. Recent reports describing modifications in the technique of prostate biopsy to include different strategies in order to cover all regions of the prostate with at least 8 or 11 systemic biopsies.<sup>4-6</sup> Nevertheless, in some patients who later on proved to

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definitely harbor cancer, initial systemic biopsies without positive results do occur. This might be a major drawback for the individual patient, as the only certain method of reducing mortality and morbidity from prostate cancer is early cancer detection, especially while cancer is still organ confined.<sup>4-6</sup> Transrectal ultrasonography continues to play an important role in the evaluation of the prostate malignancy and also it is critical in ensuring accurate sampling of the gland.<sup>7,8</sup> Comparing 2D with 3D ultrasound imaging, early results 3D gray scale ultrasound did not show a significant clinical improvement for the detection and staging of prostate cancer over 2D gray scale ultrasound.<sup>9</sup> In patients with normal digital rectal examination (DRE) and PSA serum level between 4.1-10ng/ml, they represent the diagnostic grey zone, in which the total PSA has low specificity, yield a cancer detection rate of 25.4% while when the serum PSA level is between 10.1-20ng/ml. The detection rate is 30-37.7%.<sup>10-12</sup> Cancer detection rate increases up to 60.1% when serum PSA and DRE were abnormal.<sup>12</sup> The cut off level of total serum PSA for detection of prostatic cancer lowered, cancer is detected in patients even when serum PSA level is less than 4ng/ml. When this lowered level cutoff is used in combination with free PSA less than 18% of the total PSA, frequently lead to detection of prostate cancer in its curable state. Patients diagnosed at this early organ confined stage are usually candidates for both nerve and continence sparing surgery.<sup>13</sup>

**Methods.** We studied 45 cases of TRUS guided biopsies as a selected group underwent exclusion criteria in the period between July 1997 and November 2002. We excluded from the study those patients with serum PSA higher than 4ng/ml due to benign prostatic enlargement of an exceedingly large adenoma or due to advanced age (age-related PSA elevation), we followed the age-adjusted PSA values recommended by the Michigan prostate institute as shown in **Table 1**.<sup>14</sup> Records of all patients were reviewed, and the following variables were studied: age, serum PSA, presenting symptoms, medications such as finestrade, urinary retention, previous history of prostatic biopsy or related surgeries such as TURP, and the histopathology results of those biopsies. Patients were divided into 4 groups: first group included all patients who had an abnormal DRE but normal serum PSA, the 2nd group included patients with serum PSA 4.1-10ng /ml with or without abnormal DRE, the third group included patients with serum PSA 10.1-20ng/ml with or without abnormal DRE, and the fourth group included patients with serum PSA higher than 20ng/ml, all of them had an abnormal DRE. Sextant prostate biopsy made by using automatic gun biopsy, biopsies of all identified hypoechoic lesions were performed before systematic biopsies, sextant biopsies were obtained in the mid lobar parasagittal plane, halfway between the lateral edge and midline of the prostate gland, and at the base, mid gland and apex,

Table 1 - Age specific references ranges for serum prostate specific antigen (Michigan Prostate Institute).

| Age range (years) | Reference range Asians (ng/ml) | Reference range Blacks (ng/ml) | Reference range Whites (ng/ml) |
|-------------------|--------------------------------|--------------------------------|--------------------------------|
| 40-49             | 0-2                            | 0-2                            | 0-2.5                          |
| 50-59             | 0-3                            | 0-4                            | 0-3.5                          |
| 60-69             | 0-4                            | 0-4.5                          | 0-4.5                          |
| 70-79             | 0-5                            | 0-5.5                          | 0-6.5                          |

while lateral biopsies were performed by positioning the probe just medial to the lateral edge of the prostate.

**Results.** The age of the patients ranged between 61-76 years old, an average of 66 years old, 23% of the patients were asymptomatic, 56% presented with irritative symptoms, and 21% with irritative and obstructive symptoms, 5 patients with an initial negative TRUS guided prostate biopsy later underwent TURP and stayed free of cancer, and 2 patients were using finestrade also had negative biopsy results for cancer. A total of 45 patients underwent TRUS guided biopsies included in our study, cancer prostate was detected in 13 patients with an overall detection rate of 28.8%. The first group was 13 patients with abnormal DRE and normal PSA. Only one patient had positive biopsy for cancer, a detection rate of 7.6%. The second group was 14 patients with serum PSA 4-10ng/ml, 6 patients had an abnormal DRE, all patients underwent TRUS guided biopsies, repeated biopsy resulted in detection of cancer in one patient, 3 patients from this group turned to be positive for prostate cancer and the cancer detection rate was 21.4%. Fifteen patients with serum PSA 10-20 ng/ml were included in group 3, 5 patients with abnormal DRE, repeated biopsy detected cancer in 2 patients, overall cancer was detected in 6 patients in this group and the cancer detection rate was 40%. Three patients in the fourth group all had a serum PSA level above 20ng/ml, varies between 26-115ng/ml, and all patients had an abnormal DRE; the cancer detection rate was 100 %. (**Table 2**). In patients in this series repeated biopsies of the prostate gland when cancer was still suspected after an initial negative first set cancer detected in 3 patients (6.6%).

**Discussion.** In 1997, Mosli<sup>15</sup> reported in a review of the national literature, a low incidence of prostate cancer, whereas only a small number of cases have been uniformly reported from most medical centers in KSA over the last 20 years. Since 1984, PSA is in use not only for follow up but also to detect early cancer. Unfortunately, PSA may also rise in benign hyperplasia (B.P.H) and prostatitis and may lead to unnecessary

Table 2 - Shows the results of 45 patients who underwent transrectal ultrasound scan guided biopsies.

| PSA in ng/ml | n of patients | Positive for cancer n (%) | Abnormal DRE | Positive cancer by repeated biopsy | TURP     |
|--------------|---------------|---------------------------|--------------|------------------------------------|----------|
| <4           | 13            | 1 (7.6)                   | 13           | 0                                  | 0        |
| 4-10         | 14            | 3 (21.4)                  | 6            | 1                                  | 2        |
| 10-20        | 15            | 6 (40)                    | 5            | 2                                  | 3        |
| >20          | 3             | 3 (100)                   | 3            | 0                                  | 0        |
| <b>Total</b> | <b>45</b>     | <b>13 (28.8)</b>          | <b>27</b>    | <b>3</b>                           | <b>5</b> |

PSA - prostatic specific antigen, DRE - digital rectal examination, TURP - transrectal ultrasound scan

biopsies, until today there is no other means to diagnose or to exclude cancer except by biopsies.<sup>16</sup> We are using the sextant biopsies technique described by Hodge et al<sup>17</sup> were 6 biopsy. Sites were taken from the apex, middle, and base of the prostate bilaterally; in addition we performed biopsies of the hypoechoic areas or abnormally palpable but isoechoic lesions not seen on ultrasound. Eleven core multisite directed biopsy technique incorporate 5 biopsies from 3 alternate sites and the conventional sextant biopsies, 8 biopsy techniques incorporate sextant biopsies and biopsies at mid and base of the prostate, both technique need multicentric studies to proof the superiority in cancer detection rate.<sup>5,6</sup> In our study the overall prostate cancer detection is 28.8% by combination of DRE, PSA, and TRUS guided biopsy, Alhazmi et al<sup>18</sup> reported 35% detection rate, while Alotaibi et al<sup>19</sup> 27.5 %. Gretzer and Partin<sup>20</sup> reviewed the literatures written worldwide regarding PSA and screening for prostate cancer, stated that wide spread use of PSA for early detection of cancer has resulted in clinical stage T1c becoming the prevalent stage, for PSA values 4-10ng/ml there exist a 22-27% likelihood of cancer, while those above 10ng/ml. Up to 67% chance of cancer, patients with abnormal DRE and PSA level 0-4ng/ml have a chance of prostate cancer up to 25%.

In our study cancer was detected in 2 patients out of 11 patients with normal DRE and PSA less than 20ng/ml; for example stage T1c, overall rate 15.3%, Mosli<sup>21</sup> reported an incidence of 9%, and in another study A1-A2 in 7.2%.<sup>22</sup> Our own biopsy based cancer detection rate for stage T1c, and for levels of PSA ranging between 4-10ng/ml, or 10-20ng/ml still lower than the international reported rates.

The evidence of detection of cancer in cases with serum PSA less than 4ng/ml, 7.6% in our study, while in Mosli<sup>21</sup> study 15% both studies results in cases trigger the point of considering this fact in managing our patients.

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**Abstract**

Although the medical literature contains adequate accounts of the pathophysiology of various benign prostatic disorders, it is often necessary to revisit these lesions, to reexamine the relationships between known benign lesions and more sinister, malignant disorders, in the light of new advances in our understanding of the processes. We carried out a histopathological review of prostatic surgical pathology material seen over a 7 year period in our hospital. Our findings show that benign enlargement of the prostate or benign prostatic hyperplasia (BPH) is initially fibromuscular in many cases, becoming glandulostroma with advancing age. While we found no relationship between prostatitis and age, individual gland necrosis tended to occur relatively early and correlated well with stromal repair, which we believe forms the basis of fibromuscular hyperplasia. Epithelial hyperplasia may result from glandular regeneration, and basal cell hyperplasia, papillary hyperplasia and cribriform hyperplasia all showed significant correlation with prostatic intraepithelial neoplasia (PIN). On the other hand, only cribriform hyperplasia showed correlation with atypical adenomatous hyperplasia (AAH), and also demonstrated an increase in incidence with advancing age. Our findings underline the positive relationships between benign events such as glandular necrosis with repair and epithelial hyperplasia, which may itself predispose to recognized premalignant lesions such as PIN.