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Evaluation of the pathologic results of prostate biopsies in terms of age, Gleason score and PSA level: Our experience and review of the literature

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Summary
Objective: To evaluate the pathologic and clinic results of our large series of transrectal prostate biopsies in relation to Gleason score, age and PSA level.

Materials and Methods: We reviewed the pathologic results of transrectal prostate biopsies performed because of high PSA levels and abnormal digital rectal examination findings between January 2008 and February 2012.

Results: The pathologic result of 835 prostate biopsies was benign in 82.2% and malign in 17.8%. Furthermore in 3.7% high grade PIN (Prostatic Intraepithelial Neoplasia) or ASAP (Atypical Small Acinar Proliferation) was shown. In the interval of total PSA values between 4 and 10 ng/dl, that is the so-called grey zone, cancer detection rate was 12.4%. There was a significant relationship between cancer detection and cancer stage at all levels of PSA also in the grey zone. The most common Gleason score observed was 3 + 3 with a rate of 7.4% whereas the second most commonly observed score was 3 + 4 with a rate of 2.5%. In the patients with abnormal digital rectal examination findings but normal PSA levels according to age the cancer detection rate was 8.7%, in patients with only high PSA levels the rate was 41.2% and in the patients with both high PSA levels and abnormal digital rectal examination findings, the rate was 49.3%.

Conclusion: Our study underlines the relationship between age, PSA level and pathologic stage of prostate cancer and also the importance of digital rectal examination.

Key words: Prostate biopsy; Gleason score; Prostate specific antigen.

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INTRODUCTION
Prostate cancer, is the most common cancer observed in men and when deaths due to cancer are considered, prostate cancer ranks second after the lung cancer (1, 2). In 2008, 340,000 patients were diagnosed with prostate cancer and over 70,000 deaths were reported due to prostate cancer in European Union countries (3). Early diagnosis of prostate cancer is important as it gives direction to the treatment improving long-term survival (4). Serum PSA level is the most commonly used screening test for prostate cancer (5).

Prostate biopsy is the main method for the diagnosis of prostate cancer and higher PSA levels and abnormal digital rectal examination findings are the indications of prostate biopsy (4, 6). In the United States of America it is reported that over 1 million prostate biopsies are performed annually (3). Pain, infection and hemorrhage are some of the complications of transrectal ultrasonography-guided prostate biopsy (6). Gleason score of prostate cancer is used for determining treatment and follow-up modalities (7, 8). In this study, we reviewed the pathologic results of prostate biopsies and their relationships with Gleason score, age and PSA level.

MATERIALS AND METHODS
The results of prostate biopsy performed between January 2008 and February 2012 were reviewed retrospectively. The indications to prostate biopsy were higher PSA levels according to age and abnormal digital rectal examination findings. In our clinic, transrectal ultrasonography-guided prostate biopsies were performed for the patients under the age of 50 when PSA level was over 2.5 ng/dl, for the patients with age between 50 and 60 when PSA was over 3.5 ng/dl and for the patients over the age of 60 when PSA level was over 4 ng/dl. Biopsies were also performed for the patients with abnormal digital rectal examination findings regardless of PSA level. After digital rectal examination, biopsies were performed in the left lateral decubitus position. Four ml lidocaine (2%) or prilocaine (2%) were used for local anesthesia. Disposable or re-usable guides and 18-gauge biopsy needles were used for the biopsies. Biopsies were performed taking 12 cores (6 for right lobe, 6 for left lobe). Detailed consent forms were obtained from the patients who were given detailed information before the biopsy procedure. After the procedure the patients were directed to the uro-oncology polyclinic with the results of biopsies and treatment modalities were decided according to the results.

No conflict of interest declared
**RESULTS**

The results of 835 prostate biopsies showed 656 benign findings (78.5%), 4 Gleason 2+3 adenocarcinomas (adenocarcinoma) (0.5%), 1 Gleason 3+2 adenocarcina (0.1%), 61 Gleason 3+3 adenocarcina (7.4%), 21 Gleason 4+3 adenocarcina (2.5%), 14 Gleason 4+3 adenocarcina (1.7%), 16 Gleason 4+4 adenocarcina (1.9%), 1 Gleason 5+3 adenocarcina (0.1%), 20 Gleason 4+5 adenocarcina (2.5%), 6 Gleason 5+4 adenocarcina (0.7%) and 4 Gleason 5+5 adenocarcina (0.4%). Finally High Grade PIN or ASAP were reported in 31 patients (3.7%) (Table 1).

Prostate cancer detection rate was 17.8% in our prostate biopsy series. There was a significant relationship between higher PSA levels and cancer detection and cancer stage In the interval of total PSA values between 4 and 10 ng/dl, that is the so-called grey zone, cancer detection rate was 12.4%. When the pathologic results were reviewed by the range of serum PSA levels, in patients with benign prostatic hyperplasia (BPH) PSA level was < 4 ng/dl in 9.3%, 4-10 ng/ml in 66.8% and > 10 ng/dl in 23.9% of the patients whereas in patients with adenocarcinoma PSA level was < 4 ng/dl in 4%, 4-10 ng/dl in 49.3% and > 10 ng/dl in 52%. When pathologic data of the patients with adenocarcinoma were examined, Gleason score was higher than 7 in 33% of the patients with PSA level < 4 ng/dl, in 13.8% of the patients with PSA level > 10 ng/dl and in 46.7% of the patients with PSA level > 10 ng/dl (Table 2). When the digital rectal examination findings (DRE) were reviewed, in 71% of the patients with BPH DRE findings were normal and in 29% were abnormal, whereas in 41.9% of the patients with adenocarcinoma digital rectal examination findings were normal and in 58.1% abnormal (p < 0.005). Adenocarcinoma detection rate was 8.7% in the patients with normal PSA levels but abnormal DRE findings, 41.2% in the patients with normal DRE findings but higher PSA levels and 49.3% in the patients with both higher PSA levels and abnormal DRE findings. Furthermore, cancer was diagnosed in 7.5% of the patients under the age of 50, 14.4% of the patients between the age of 50 and 60, 27% of the patients over the age of 70. Gleason score was higher than 7 in 2.5% of the patients under the age of 50, in 3.7% of the patients with age between 50 and 70, in 10.3% of the patients over the age of 70 (p < 0.03) (Table 3).

**DISCUSSION**

Transrectal ultrasonography guided prostate biopsy is the main method used for diagnosing prostate cancer. The pathological results of 82.2% of prostate biopsies were reported as benign and in 66.8% of the cases with benign pathological results, PSA levels before biopsy procedure were between 4 and 10 ng/dl. On the other hand, according to the literature reviewing the two indications to prostate biopsy, digital rectal examination is considered a subjective parameter (10).

There are several studies about pathologic results of prostate biopsies performed because of high PSA level and abnormal DRE findings. According to the results of Ojewola et al. The total average cancer detection rate was 44% and more specifically in presence of high PSA level with normal DRE findings the rate was 30%, in presence of normal PSA level and abnormal DRE finding the rate was 17% and in presence of both high PSA level and abnormal DRE finding the rate was 62% (11). In the study of Shim et al. (12) the patients were divided in two groups: 721 patients with normal DRE findings and 192 patients with abnormal DRE findings. Prostate cancer detection rate was higher in the group with abnormal DRE findings but the result was not significant in the patients that had PSA levels between 2.5 and 3.9 ng/dl and also in the patients with age between 45 and 59 (12). In another study of Thompson et al., including 2950 patients, cancer detection rate was 6.6% for the patients with PSA level < 0.5 ng/dl, 10.1% for the patients with PSA level between 0.6 and 1 ng/dl, 17% for patients with PSA level between 1.1 and 2.0 ng/dl, 23.9% for patients with PSA level between 2.1 and 3.0 ng/dl and 26.9% for patients with PSA level between 3.1 and 4 ng/dl. The result of this study is important as it shows that prostate cancer would be detected also at lower PSA levels (13).

Another study by Catalona et al. (14) about biopsies performed only for abnormal digital rectal findings demonstrated a cancer detection rate of 0%. This rate was 6% for the study by Braver et al. (15) and 17% for another.

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**Table 1. The distribution of pathologic results and Gleason scores of the prostate biopsies.**

<table>
<thead>
<tr>
<th>Pathologic result</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>656</td>
<td>78.5%</td>
</tr>
<tr>
<td>2+3 Adenocarcina</td>
<td>4</td>
<td>0.5%</td>
</tr>
<tr>
<td>3+2 Adenocarcina</td>
<td>1</td>
<td>0.1%</td>
</tr>
<tr>
<td>3+3 Adenocarcina</td>
<td>61</td>
<td>7.4%</td>
</tr>
<tr>
<td>4+3 Adenocarcina</td>
<td>21</td>
<td>2.5%</td>
</tr>
<tr>
<td>4+4 Adenocarcina</td>
<td>14</td>
<td>1.7%</td>
</tr>
<tr>
<td>5+3 Adenocarcina</td>
<td>1</td>
<td>0.1%</td>
</tr>
<tr>
<td>4+5 Adenocarcina</td>
<td>20</td>
<td>2.5%</td>
</tr>
<tr>
<td>5+4 Adenocarcina</td>
<td>6</td>
<td>0.7%</td>
</tr>
<tr>
<td>5+5 Adenocarcina</td>
<td>4</td>
<td>0.4%</td>
</tr>
<tr>
<td>Asap/High Pin</td>
<td>31</td>
<td>3.7%</td>
</tr>
<tr>
<td>Total</td>
<td>835</td>
<td>100%</td>
</tr>
</tbody>
</table>

**Table 2. The distribution of the patients according to pathologic results and relationship between pathologic results, DRE findings and PSA levels.**

<table>
<thead>
<tr>
<th>Pathologic result</th>
<th>Number of patients</th>
<th>Abnormal DRE findings</th>
<th>High PSA level according to age</th>
<th>Abnormal DRE (+) High PSA levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>2+3 Adenocarcina</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>3+2 Adenocarcina</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>3+3 Adenocarcina</td>
<td>61</td>
<td>30</td>
<td>54</td>
<td>24</td>
</tr>
<tr>
<td>4+3 Adenocarcina</td>
<td>21</td>
<td>10</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>4+4 Adenocarcina</td>
<td>14</td>
<td>8</td>
<td>14</td>
<td>8</td>
</tr>
<tr>
<td>5+3 Adenocarcina</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>4+5 Adenocarcina</td>
<td>20</td>
<td>14</td>
<td>17</td>
<td>11</td>
</tr>
<tr>
<td>5+4 Adenocarcina</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>5+5 Adenocarcina</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>148</td>
<td>86</td>
<td>134</td>
<td>73</td>
</tr>
</tbody>
</table>

**Table 3. The age distribution of PSA levels.**

<table>
<thead>
<tr>
<th>Age</th>
<th>PSA 0-4 ng/dl</th>
<th>PSA 4-10 ng/dl</th>
<th>PSA &gt; 10 ng/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-50</td>
<td>5</td>
<td>26</td>
<td>9</td>
</tr>
<tr>
<td>50-60</td>
<td>19</td>
<td>112</td>
<td>113</td>
</tr>
<tr>
<td>60-70</td>
<td>23</td>
<td>161</td>
<td>113</td>
</tr>
<tr>
<td>70+</td>
<td>10</td>
<td>130</td>
<td>101</td>
</tr>
</tbody>
</table>

| Total | 40 | 157 | 397 | 241 |
study by Mettin et al. (16) The cancer detection rate of
the biopsies performed only for high PSA levels was 16% in the study by Catalona et al. (14) and 19% for the study
by Brawer et al. (15) The review of the pathologic results
of the biopsies performed for the presence of both high
PSA levels and abnormal DRE findings showed a cancer
detection rate of 33% in the study by Catalona et al. (14),
16% in the study by Brawer et al. (15), and 38% in the study by Mettin et al. (16). In our study, prostate cancer
detection rate was 8.7% for the patients with normal PSA
level but abnormal DRE finding, 41.2% for the patients
with high PSA level and normal DRE and 49.3% for the
patients with both high PSA level and abnormal DRE
finding. When we look at the results of our study; the
rate for the patients with only abnormal DRE finding is
consistent with the literature, but the rates for the
patients with only high PSA level or with both two indica-
tions, are higher than the rates of literature. The rate in
presence of two indications was higher than in presence
of only one of the indications. This results shows the
importance of DRE although it is a subjective parameter.

Pain, hemorrhage and infection are some of the complica-
tions of prostate biopsy as it is an invasive procedure
and the rate of temporary bacteremia is 70% and the
rate of bacteremia is 53% (6, 17, 18). According to our
previous observations there was a significant relationship
between presence of prostate cancer and risk of bleeding
complication after prostate biopsies (19). Furthermore
the bleeding complication was observed at higher rates
for the patients with higher Gleason scores (19).

Serum PSA level and digital rectal examination are
important parameters for the diagnosis and the choice of
the method of treatment of prostate cancer. The cancer
detection rates are higher when are present both high
PSA levels according to age and abnormal digital rectal
examination findings. Other results of our study that are
consistent with the literature, are the increase of PSA
levels with age and the increase of Gleason score with age.

There are several limitations about our study and the most
important is that the free/total PSA ratio was not evaluat-
ed for the patients with the PSA level between 4 and 10
ng/dl. In fact free PSA values for some patients were not
found and accordingly this parameter was excluded from
the analysis. Another important limitation was that the
analysis was not extended to PSA levels in the follow-up
and to re-biopsy requirements for the patients with nor-
mal pathologic results. Despite all these, we think that the
results of this study are relevant as they show the relation-
ship between age, PSA level and pathologic stage and also
the importance of digital rectal examination.

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