ANALYSIS OF THE HISTOLOGICAL PROSTATE BIOPSY FINDINGS RELATED TO THE NUMBER OF SPECIMENS AND BIOPSY PROCEDURE METHODS

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ANALIZA HISTOPATOLOŠKIH NALAZA BIOPSIJA PROSTATE U ODNOSU NA BROJ UZORAKA I METODU UZIMANJA UZORAKA

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SAŽETAK
Histopatološke (Hp) lezije u biopsijama prostate mogu se srasati u četiri kategorije: benign (B), premaligne (PM), maligne (M) i adenocarcinom prostate (AP). Cilj je bio da usmerimo evaluaciju Hp lezija prostate nadenih u seksant biopsiama (SB) i da utvrđimo vrednost i značaj SB prostate nadenih pod kontrolom transrektalne ultrasonografije (TRUS). Izražavanji materijal čini 96 bolesnika sa uzračenom biopsijom prostate. Biopsije su u obziru na broj i metodu uzimanja uvećanih anatomskih podataka (TRUS). Primanjene su patomorfološke metode istraživanja. U I g AP je naden 0 ul (12.5%), u II g 6 ul (25%), u III g 6 ul (25%) i u IV g 5 AP je naden u 14 sl. (58.3%). U I g od 3 AP u 1 sl. (33.3%) naden je peri-neuralna invazija (PNI), u II g od 6 AP u 2 sl. (33.3%) i u IV g od 14 AP, PNI je naden u 9 sl. (64%). PM lezije u I g su naden u 8 sl. (33.3%), u II g u 11 (44%), u III g u 1 (47.8%) i u IV g 15 sl. (62.5%). Od 29 sl. sa ultra sonogramom su zajedno naden i PM lezije (19 ul. ili 65.5%). B lezije su naden u I g u 1 sl. (4.2%), u II g u 3 (12%), u III u 4 (17.4%) i u IV g u 6 sl. (25%). Detekcija PM i M lezija prostate raste sa brojem uzetih uzoraka. SB vodene TRUS, imaju za M i PM lezije najveći i najbolji stepen Hp detekcije i mogu obezbediti maksimalne Hp informacije o patološkim lezijama prostate.

Prijedlog reči: seksant biopsija, karcinom prostate, premaligne lezije prostate.

INTRODUCTION
Wide application of the test on the prostatic specific antigen and digital rectal examination led to the substantial increase of the prostate needle biopsy application. Every year large number of male population undergoes the prostate biopsies in order to make diagnosis. In studies, when the examination of results of the pathological reports and the interpretations of the pathological findings of the prostate specimens is made, they could be generally classified into four categories: benign, prostatic carcinoma, premalignant lesions and suspiciously malignant (1, 2). These findings determine the further course of the treatment for the patient. In other words, the prostatic intraepithelial neoplasia, premalignant lesions, atypical and suspicious on carcinoma, require biopsy as a rule and searching for the associated or the occult prostatic carcinoma. The biopic findings can be useful for the strategy of biopsy with the topographic localization of the pathological lesions in prostate. Consequently the pathological report on the biopic sample can provide for all relevant information necessary for the clinician to develop the strategy of diagnostic testing, monitoring or treatment of the patient.

Certainly the pathological report is often limited by the lack of material and technique of taking the sample of tissues. Many examination studies of the prostate biopsy technique in order to provide all the necessary information were made. This led to the optimal method of taking the sample enabling the pathologist to have the adequate material for analyzing the prostate samples, which is the most indispensable to the patient and clinician in obtaining the precise diagnosis and strategy planning for the patient with the prostate disease. Today, the most accepted prostate biopsy is so-called sextant prostate biopsy led by transrectal ultrasonography (2-5). During recent years the premalignant lesions have been given a great consideration due to the high predictive significance for development of the prostatic adenocarcinoma (PC), and significant association with AP. In the study, the prostatic intraepithelial neoplasia was stated as

ABSTRACT
Histological (Hp) findings in prostatic needle biopsy may be placed into four major categories: benign (B), premalignant (PM), atypical and suspicious for cancer and prostate cancer (PC). The study material consists of 96 cases (c) with performed needle biopsy (NB) of the prostate. We analyzed 4 groups (g) of NB specimens (S) related to the number of NB: I g 1 S (24 c), II g 2 S (25 c), III g 3–4 S (23) and IV g sextant biopsy (SB)(24 c) transrectal ultrasound (TRUS) guided. Hp findings were categorized in three groups (g): B, PM (High grade prostatic intraepithelial neoplasia – HCPIN, atypical adenomatous hyperplasia – AAH) and PC. We applied histological methods of investigations. In I g PC was found in the 3 c (12.5%), in II g PC in the 6 c (24%), in III PC in the 6 c (24%) and in IV PC was found in the 14 c (58.3%). In I g out of 3 PC we found perineural invasion (FIB) in 1 c (33.3%), in II g out of 6 PC FIB was in 2 c (33.3%), in III g out of 6 PC FIB was in 2 c (33.3%) and in IV g out of 14 PC FIB was in 9 c (57%). PM lesion was found in I g in 8 c (33.3%), in II g in 11 c (44%), in III g in 11 c (47.8%) and in IV g in 15 c (62.5%). Out of 29 c PC in high percentage we found coexistent PM lesion (19 c or 65.5%). B lesion we found in I g in 1 c (4.2%), in II g in 3 c (12%), in III in 4 c (17.4%) and in IV g in 9 c (30%). Detection PM and M lesion increase with number of biopsy S. Hp findings for TRUS guided SB had for M and PM highest rate of Hp detection and may provide the best information of pathological lesion of the prostate.

Key word: sextant biopsy, prostatic carcinoma, premalignant lesion.
the most important premalignant lesion (PIN) (6). Today PIN is divided into two stages: low-grade PIN (LGPIN) and high-grade PIN (HGPIN). In keeping with the available data, HGPIN is highly significantly associated with PC and it is considered as the most important PC precursor. Also during recent years the group of atypical small acinar proliferations, which are difficult for differentiation from PC, are characterized by the definition of two morphological entities: The atypical adenomatous hyperplasia (AAH) and the atypical small-acinar proliferation (ASAP) (7, 8). Their role as precursors of carcinoma is still controversial. These lesions are considered as probable prostate malignant lesions due to their increasing incidence when associated with PC (8).

Our aim was to do the evaluation of the histological findings in the prostate needle biopsies. We wanted to analyze the prostate pathological lesions in correlation with the number of taken tissue samples, as well as the method of taking the tissue samples.

Our aim was to determine the sensitivity of the biopsy samples regarding the number of the tissue samples and the method, according to whether they were benign, premalignant, atypical and suspicious on malignant and prostate carcinoma.

Especially, we wanted to analyze prostate lesions in the sextant prostate biopsies and to establish the sextant prostate biopsies value and significance performed by the control of transrectal ultrasonography (TRUS).

MATERIAL AND METHODS

The material consists of 96 needle prostate biopsies during the period between 2002 and 2003, done on the Department of Urology, KBC Kragujevac. The biopsies were divided into four groups according to the number of taken samples: I group – one sample (24 patients), II group - 2 samples of the prostate tissue obtained by the needle (25 patients), III group 3–4 samples (23 patients) and IV group of sextant prostate biopsy (24 patients). In the fourth group are the biopsies with 6 samples of prostate tissue taken by the transrectal ultrasonography conduct of biopsies (4, 9). In the cases with 2 tissue samples, one by one was taken from the left and the right lobe. Also, in the cases with 3–4 tissue samples were taken 1 or 2 tissue samples from the left or right lobe and at the sextant biopsies were taken 3 tissue samples from the left and right lobe.

We divided histological findings into three groups: benign, premalignant lesions (AAH, ASAP i HGPIN), and prostate adenocarcinoma.

The pathomorphological research methods were applied. The obtained sample tissues were fixed in 4% buffered formalin, patterned in paraffin blocks, and cut on the microtome into preparations of 4–6 micrometers thickness. The standard method of haematoxilin eosin dying was applied, as well as the histochemical methods of Alcian blue, Masson and Van Gieson elastica (2, 6).

All the provided results were statistically processed by Student's test for the two independent samples.

We especially wanted to analyze prostate lesions detected in the sextant biopsies and define value and importance of the sextant prostate biopsies performed under the control of transrectal ultrasonography (TRUS).

RESULTS

The main proportion of 96 analyzed patients (Figure 1) were in the seventh decade (34 patients or 36.2%) and in the eighth decade of life (45 patients or 47.9%). Nine patients (9.6%) were in the sixth decade, 6 patients (6.4%) in the ninth decade of life and for 2 patients we didn't record the age.

The types of histological lesions detected in 96 analyzed prostate biopsies are shown in Table 1. PC was found in 29 cases (30.2%). From the premalignant lesions HGPIN was detected in 35 cases (36.5%), LGPIN in 19 (19.8%), AAH in 9 cases (9.4%), ASAP in 2 cases (2.1%). From the benign lesions, the prostate benign hyperplasia (PBH) in 13 cases (13.5%) and in 13 (13.5%) the material obtained by biopsy was inadequate for the histological diagnostics.

Also HGPIN was detected at the same time in 19 (65.5%) of 29 cases. In 2 cases, ASAP was associated with HGPIN, and in 5 cases AAH was detected at the same time with LGPIN.

When the all patients were interpreted according to histological diagnoses; benign, malignant and premalignant lesions. It was a question of the carcinoma in 29 (30.2%), in 41 cases (42.7%) about premalignant prostate lesions.
and in 26 (27.1%) about benign lesions and the inadequate material for histological diagnostics.

The parallel analysis of the detected histological lesions in the needle prostate biopsies compared with the number of prostate samples was presented in Table 2.

**Table 2.** The parallel analysis of the detected pathological lesions compared with the number of prostate samples

<table>
<thead>
<tr>
<th>The types of histological lesions</th>
<th>1 sample – 24 cases</th>
<th>2 sampl. – 25 cases</th>
<th>3–4 sampl. – 25 cases</th>
<th>6 sampl. – 24 cases</th>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma prostate</td>
<td>3</td>
<td>12.5</td>
<td>6</td>
<td>24.0</td>
<td>6</td>
<td>26.1</td>
<td>14</td>
<td>58.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HGPIN</td>
<td>7</td>
<td>29.2</td>
<td>8</td>
<td>36.0</td>
<td>9</td>
<td>39.1</td>
<td>11</td>
<td>45.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LGPIN</td>
<td>2</td>
<td>8.3</td>
<td>6</td>
<td>24.0</td>
<td>5</td>
<td>21.7</td>
<td>6</td>
<td>25.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AAH</td>
<td>1</td>
<td>4.2</td>
<td>2</td>
<td>8.0</td>
<td>2</td>
<td>8.7</td>
<td>4</td>
<td>16.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PBH</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>12.0</td>
<td>4</td>
<td>17.4</td>
<td>6</td>
<td>25.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASAP</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>2.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Material obtained for the histological diagnostics</td>
<td>11</td>
<td>45.8</td>
<td>1</td>
<td>4.0</td>
<td>1</td>
<td>4.3</td>
<td>-</td>
<td>-</td>
<td></td>
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</tbody>
</table>

The total of 96 prostate biopsies were analyzed. In 24 cases (25.8%) it was a question of one prostate tissue samples, in 25 (25.8%) two prostate tissue samples (left and right lobe), in 23 cases (23.65%) 3–4 prostate tissue samples and in 24 cases (24.73%) sextant prostate biopsies.

The detection of premalignant (PM) and malignant prostate lesions in our material shows the increase in the number of prostate sample tissues obtained by the needle biopsy, especially in the sextant biopsies, and it is presented in Table 2. In other words, PC was detected in the I group in 3 cases (12.5%), in the II in 6 cases (24%), in the III in 6 cases (26.1%) and in the IV group PC was detected in 14 cases (58.3%). In the I group from 3 cases PC in 1 case (33.3%) PNI was detected, in the II group from 6 PC in 2 cases (33.3%) and in the IV group from 14 PC, PNI was detected in 9 cases (64.3%). PM lesions in the I group were detected in 8 cases (33.3%), in the II group in 11 (44%), in the III group in 11 (47.8%) and in IV group 17 cases (70.8%). At the same time from 29 cases PC in a high percentage were detected PM lesions (19 cases or 65%).

PC was detected in 29 from 96 analyzed prostate biopsy cases (30.2%) with the average patients’ age of 69.9 years, VSPIN was detected in 36 from 96 cases (37.5%), with the average patient age of 67.3 years, AAH was detected in 9 from 96 cases (9.4%) with the average patient age of 66.7 years and in 2 cases (2.1%) ASAP was detected. It is shown that the average age for HGPIN and AAH was less in comparison with PC.

The histological findings in the biopsy cases with 6 samples performed along with TRUS had for the malignant and premalignant lesions the greatest and the best degree of histological detection of the pathological lesions in prostate. The pathological finding in the prostate biopsies provides the maximal information related with the prostatic pathological lesions mostly in the sextant biopsies led by ultrasonography.

The percentage of perineural invasion in all groups is presented in Figure 2. It can be seen, according to Figure 2, that in the IV group was the greatest percentage of PNI detection.

![Figure 2. Percentage of perineural invasion (PNI) in four analyzed groups of PC](image)

**DISCUSSION**

In the analysis of 324684 biopsies during the period between 1995 and 2001., Lowe (10) detected the AP incidence in 1995 of 41% and 36% in 2001., for the age population between 70–79 years., and the incidence in the whole analyzed population is from 15% in 1995 to 34% in 2001. The published incidence HGPIN varies from 0.7 to 20% (2, 5, 11). The greatest series had Orozco et al. (11) with 62.537 patients from whom 4.1% had HGPIN and Novis et al. (2) with 15.753 patients from whom 3.9% had HGPIN. In the cases with TUR the incidence of HGPIN, varies from 2.8–33%.

Most studies show that the incidence and spreading of HGPIN is connected with the patient age, and that it is increased with years (5, 12). The carcinoma manifestation is preceded more than ten years by HGPIN (6, 13). Most of the HGPIN foci in young persons are of the low grade, with the increasing HGPIN frequency with the progress of years. Also HGPIN volume is increased with patient advanced years. In the course of time the PIN incidence at men in 80 years is 70% (6). Lee et al. (4) analyzed 256 patients who had done the prostate biopsy led by ultrasonography and identified 103 patients with carcinoma and additional 27 who had HGPIN and carcinoma. The average...
rage age of those who had PIN was 65 years, while the average age of those who had carcinoma was 70 years.

In our material PC was detected in 29 from 96 cases (30.2%) with the average age of 69.9 years. HGPIN was detected in 36 from 96 cases (37.5%), with the average age of 67.3 years. AAH was detected in 9 from 96 cases (9.4%) with the average age of 66.7 years. It can be seen that the average age for HGPIN and AAH was less in comparison with PC, corresponding to data in the studies. Also, the incidence PC and HGPIN in our material was similar to data of other authors.

HGPIN is significantly associated with the prostate carcinoma, which is consistent with all the available data in studies. The PIN frequency in the prostate with carcinoma is significantly higher than in the prostate without carcinoma. (13, 14), especially at men in the age of over 50 years (82% vs. 43%). Davidson et al. (13) in their respective study of 100 patients with HGPIN and 112 biopsies without HGPIN, find carcinoma in 35% subsequent biopsies at men with HGPIN compared with 13% at men without HGPIN (the control group). Bostwick (6) finds HGPIN in 82% of the analyzed prostates with PC on the autopsy, but they found HGPIN only at 43% of men of the same age who had PBH. The other series also found the highly predictive values of HGPIN for carcinoma. These data have the strong association of HGPIN and PC and indicate that the serious diagnostic monitoring is necessary (3, 11, 14).

Being consistent with other studies, our material also suggests that HGPIN in the cases with carcinoma (29 cases) was found in 19 cases (65.5%), while at the rest of 16 cases HGPIN was found in the cases without carcinoma.

The perineural invasion is the strong indicator of malignancy but it is not always pathognomonic, because it is extremely rare to happen in the benign prostate as well. The perineural invasion in our material was detected in 14 cases (487.3%), for that the greatest PNI percentage was in the sextant biopsies (64.3%).

Bostwick DG and Qian J. (6) analyzed 217 prostate samples. AAH was detected in 23% cases AAH was more frequent in older patients and those whose prostate weighed more. There is ASAP in about 2.5–5.5% prostate biopsies, suspicious on PC (7, 8). Iczkowski KA et al (8) analyzed 33 cases. ASAP with at least one accompanying needle biopsy. PC was detected in accompanying biopsies in 15 from 33 cases (45%), with the average monitoring of 9 months. There are data in studies that ASAP finding during the initial biopsy significantly predictive for PC in the subsequent biopsies (7, 9). Alsikafi et al. (15) find HGPIN in 33 cases from 485 analyzed patients (6.8%), 21 (64%) had only HGPIN, Dnd 12 (36%) HGPIN with the environmental atypical glands. Three from (14%) 21 cases, with HGPIN was detected to have PC on repeated biopsies compared with 9 from 12 (75%) with HGPIN and the environmental atypical on the initial biopsies. The great predictable value ASAP for subsequent PC requires the repeated biopsies (16).

In our material AAH was detected in 9 cases (9.4%) and ASAP in 2 cases (2.1%). The average age at our patients was for AAH 66.7, and for ASAP 66.1 years. Our percentage of AAH and ASAP was lower than in some published works. This was probably the consequence of the prostatectomy elaborated samples with greater number of the tissue samples, while we diagnosed these lesions in the needle biopsies, with lesser number of tissue samples. The average age was slightly higher, but essentially approximate to data in studies.

According to data in studies (7) the PC detection in the prostate biopsies is growing with the number of the taken tissue samples and their greater volume. Also, it was shown that besides the number of the tissue samples, the greater length of the sample tissues have the impact on the greater PC detection as well. In other word, in the morphological measurements of the taken tissue samples length had shown that the detection percentage was greater at analyzed tissue samples which number is the same but the total length of the sample tissues greater (3). It was shown also that the detection degree of perineural invasion, as the significant parameter in PC prognosis in the needle biopsies, correlates with the number of taken tissue samples and their length and volume (9).

It was shown that there was a positive correlation at the number of biopptic samples, containing HGPIN and volume of multifocal HGPIN. The prostate with HGPIN in sextant biopsies contained significantly more PC than the sextant biopsy without HGPIN. The frequency of competitive PC was greater in the cases with 2 or more biopptic samples containing HGPIN (12).

The detection of premalignant (PM) and malignant prostate lesions in our material showed the increase with the number of prostate tissue samples obtained by the needle biopsy, especially in sextant biopsies. Namely, in the I group PC was detected in 3 cases (12.5%), in the II in 6 cases (24%), in the III in 6 cases (26.1%) and in the IV group PC was detected in 14 cases (58.3%). In the I group from 3 cases PC in 1 case (33.3%) was detected PIN, in the II group from 6 PC in 2 cases (33.3%), in the III group from 6 PC in 2 cases (33.3%) and in the IV group from 14 PC, PIN was detected in 9 cases (64.3). PM lesions in the I group was detected in 8 cases (33.3%), in the II group in 11 (44%), in the III group in 17 (47.8%) and in the IV group 17 cases (70.8%). At the same time in PC high percentage in 29 cases, PM lesions were detected as well (19 cases or 65.5%).

Our results correspond to the results of other authors. Namely, the percentage of detected PC and HGPIN increases with the number of taken tissue samples and shows the greatest percentage of sensitivity in the IV group. Also, the greatest percentage of PIN is detected in the IV group.

In our material PC is detected in 30.2%, HGPIN in 37.5%, AAH in 9.4% and ASAP in 2.1%. The average patient age with premalignant lesions was lower than in PC. In the significant percentage of cases in the I group, the material was inadequate for the precise histological diagnosis, and in the less percentage of cases it was in the second and in the third group.
The percentage of histological detection of HGPIN and PC increases with the number of taken prostate tissue samples, when it was significantly the greatest in the sextant biopsies done along with TRUS.

Detection of premalignant and malignant prostate lesions in the needle biopsies increases with the number of prostate tissue samples obtained by the needle biopsy, especially in the sextant biopsies.

The pathological biopsy finding can provide the maximal information related to the pathological prostate lesions mostly in the sextant biopsies led by ultrasonography.

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