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The Results after Transrectal Prostate Biopsy with 12 Biopsy Cores Taken

Marina Knežević[1], Josip Galić[2], Antun Tucak[2] and Zdravko Ebling[3]

[1] Department of Urology, General Hospital »Našice«, Našice, Croatia
[2] University Department of Urology, University Hospital »Osijek«, Osijek, Croatia
[3] General Practice, Osijek, Croatia

A B S T R A C T

This report describes the clinical value of transrectal prostate biopsy during which 12 biopsy cores are taken in comparison to the classical sextant method. There were 106 patients included in the study, who had transrectal prostate biopsy (TRB) due to abnormal finding after digitorectal examination (DRE) and/or values of PSA > 4 ng/ml in the period from 4 October 2001 till 14 August 2002. There were 117 biopsies with 12 biopsy cores taken, 6 cores from each lobe. Prostate cancer was confirmed in 49 patients (46%). Out of total number of confirmed cancer cases, initial biopsy detected 94%. There were three patients who had suspicious DRE finding, with PSA value of < 4 ng/ml, but cancer was not detected in any of them. In the patient group with PSA value between 4–10 ng/ml, cancer was detected in 26% of them and in the group with PSA value > 10 ng/ml cancer was detected in 58%. The most common Gleason score in the case of cancer was 7 (43%). During the biopsy procedure, 3 patients experienced strong vasovagal reactions, meaning that out of 117 biopsies incidence of complications was 2.6%. Few days after the biopsy, two patients developed urogenital tract infections (1.7%) and right after the procedure, there was one case of strong hematuria (0.8%) and strong rectal bleeding (0,8%) that needed hospitalization. Our results regarding the incidence of complications do not differ much from the results in the literature. According to data in the literature regarding sextant biopsy, 15–34% of cancer cases remain undiagnosed at initial biopsy. The method of 12 biopsy cores fails to diagnose only 6% of all cancers, but it is important to note that in the mentioned period, re-biopsy was indicated only in 11 from 60 patients with negative biopsies.

Key words: *prostate cancer, transrectal prostate biopsy, number of biopsy cores*

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Introduction

In last few decades the biopsy technique has improved much. The very first one was finger guided puncture biopsy, replaced by transperineal biopsy under general anesthesia and nowadays we perform widely accepted transrectal ultrasound guided prostate biopsy. Hodge et al. described sextant method of transrectal biopsy in 1989 and now it is a standard procedure[1]. The procedure itself consists of 6 biopsy cores taken from prostate region where cancer more likely occurs; so there are 3 cores taken form each lobe, from apical, middle and basal part of prostate in an appropriate parasagittal line. Applying the procedure for years, the urologist realized that the sextant method had its shortcoming in cancer detection. The main complain was a high number of false negative cancer found after the initial biopsy what made doubtful its accuracy and reliability. It turned out that number of positive findings, meaning number of undetected cancers after the initial biopsy was rather high, ranging from 15–34%[2]. Numerous studies have tried to prove whether some changes of transrectal biopsy technique, including the increase in number of biopsy cores and change of prostate zones that cores are taken from, could improve the accuracy of the method in cancer detection. So far, there has not been found the most suitable method which would meet certain parameters (like significant increase in detection of cancer but without affecting increase in detection of clinically insignificant cancer, without increasing incidence of complications and not affecting patients well-being) to replace sextant method successfully.

This report presents our own results obtained after transrectal biopsy of prostate which includes taking of 12 biopsy cores and we compared the results with the those ones in the literature regarding sextant biopsy.

Material and Methods

This report is a retrospective study, showing the results of transrectal prostate biopsy, consisting of 12 biopsy cores, which were taken from October 2001 till August 2002. In this time 106 patients had transrectal biopsy and it was indicated due to abnormal DRE finding and/or due to PSA value of > 4 ng/ml.

In the past the standard biopsy technique, conducted at the Department of Urology, University Hospital »Osijek«, was a transperineal method which consisted of 6 and later 12 biopsy cores. In October 2001 we introduced the transrectal biopsy method and did not perform transperineal any more, except when the transrectal method cannot be technically performed (for e.g. if there are severe hemorrhoid piles, or after abdominoperineal rectum resection) or when patient is prone to infections (for e.g. serious diabetic patients, or patients with implanted heart valves). We have had only one case so far, a patient with abdominoperineal rectum resection.

All patients were given written instructions at the examination prior to the procedure, with detailed explanations of the biopsy procedure and possible complications. It is emphasized that the procedure does not require any other special preparation of the patient, except to stop with anticoagulant therapy 7 days before, to have a full bladder and emptied colon (but without laxative or enema) before the biopsy. The patient must have a lab analysis done, not older than a month. Transrectal biopsy is done in outpatients, without anesthesia. Prior to biopsy, patients are given an antibiotic prophylaxis. The choice is intramuscular injection of cefazolin (Kefzol) in a dose of 1 g, except in the case of beta-lactam antibiotics allergy. These patients are given fluoroquinolone orally during 3–5 days after the procedure.

During the procedure the patient is lying in the left lateral position, with bended legs in hips and knees and the rectal probe with needle guidance is inserted in rectum. Prior to it, the probe is covered with a condom, filled with ultrasound gel, then the needle guidance is fixed on the probe and then comes another condom with gel over the entire instrument (Brüel & Kjær Medical). Biopsy is performed using an 18 Gauge biopsy needle driven by a biopsy gun, which enables to take 12 biopsy cores, 6 from right and 6 from left lobe. There are 3 cores from each lobe as it is typical for classical sextant method, with additional 3 cores from each lobe which are pointing even more to lateral parts of peripheral regions. We can determine precisely which prostate part we want to take samples from with the help of the dotted line on the screen. We usually take random, systematic cores, but if we visualize hypoechoic zones in the prostate, we take a targeted sample which is already included in mentioned 6, actually 12 samples. One hour after the procedure the patients could empty their bladder and if there is no severe hematuria, they are discharged, but asked in the case of any complications to come back to the hospital. However, temporary hematuria, blood in stool and sperm could be expected.

Results

Out of 106 patients who had biopsies in the mentioned period, cancer was detected in 49 patients (46%). Figure 1 shows distribution of patients according to age and number of patients with cancer in each group. In 3 patients who underwent biopsies due to suspicious DRE, with PSA value of < 4ng/ml, no cancer was detected. In the group of patients who had PSA value of 4–10 ng/ml, cancer was detected in 26%. The highest number of patients had PSA > 10 ng/ml and cancer was detected in 40 of them (58%). These results can be seen in the Table 1.

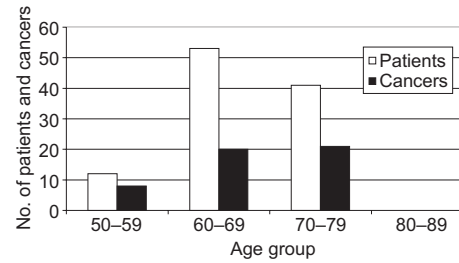

Fig. 1. Distribution of patients according to age and number of patients with prostate cancer in each age group.

The most common Gleason score was 7 (43%). Figure 2 shows cancer distribution according to the Gleason score. Two patients developed urogenital infections few days after the procedure (one prostatitis and one orchiepididymitis), meaning 1.7% of infection rate in 117 biopsies. During the procedure in 3 patients vasovagal reactions with loss of consciousness occurred (2.6%), one patient had severe hematuria (0.8%) and one had rectal bleeding (0.8%) which has to be treated in hospital. The complications are presented in the Table 2.

TABLE 1
DISTRIBUTION OF PATIENTS ACCORDING TO PSA-VALUES AND NUMBER OF PATIENTS WITH PROSTATE CANCER IN EACH GROUP

PSA (ng/ml)	No. of patients	No. of cancers (%)
< 4	3	0
4 – 10	34	9 (26)
> 10	69	40 (58)

All patients had at least one biopsy. The cancer was detected with the initial set in 46 cases (94%). In the mentioned period, re-biopsy was indicated in 11 patients and in 3 patients the diagnosis was

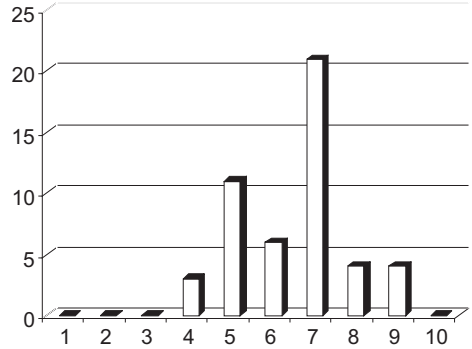

Fig. 2. Distribution of cancer according to Gleason score.

cancer. These data show that our percentage of detected cancer with initial biopsy is 94%, suggesting that we only did not detect 6% of all detected (other patients to whom re-biopsy was not indicated in this period, were not included).

Discussion

We introduced transrectal prostate biopsies at the time when the sextant protocol was exposed to strong criticism. Since we had good results with transperineal biopsies in taking 12 cores, we decided to take 12 cores also in the case of transrectal biopsy[3,4]. Out of all patients who had biopsies, cancer was detected in 46% patients and 94% of cancer cases was diagnosed by the first biopsy. We consider this as a rather significant outcome in comparison to the results obtained by sextant biopsy because it fails to detect 15–34% clinically significant cancers with the first biopsy set[2]. This high percentage of positive re-biopsies in the sextant protocol inspired creation of new protocol in order to detect cancer more successfully. These new techniques were created as a result of the low accuracy of the sextant method, which could not provide representative parts of prostate tissue for pathohistological examination in relation to prostate volume and could not supply enough prostate tissue from lateral parts of peripheral zone. The total volume of 6 biopsy cores in case of larger prostate is only a small portion of total volume of prostate tissue and can be considered suboptimal, affecting likehood of cancer detection[5]. Djavan et al. say that 6 cores are insufficient if the volume of the prostate is higher than 45 grams, so in the case when initial sextant biopsy is negative, re-biopsy should be considered as well[6]. The opinion of Uzzo et al. is that if the volume of the prostate is lower than 50 grams, the percentage of cancer detection is 38%, but if prostate volume is higher than 50 grams only 23%[7]. Eskew et al. mentioned that increasing the number of the samples from 6 to 10, improves the accuracy of cancer detection from 26% to 40%[8]. Ravery et al. talk about improved cancer detection after taking 10 or 12 samples unlike sextant method, especially among the patients whose PSA is > 10 ng/ml, normal DRE and prostate volume bigger than 50 grams[9]. On the contrary, Naughton et al. did not find a significant difference in cancer detection among the patients who had 6 cores taken (26%) and those who had 12 (28%) cores taken[10]. It is undisputed that an increase of bioptic samples from 4 to 6 improves accuracy of cancer detection. Nevertheless, there is no consensus how big the number of samples should be and to what extent it should be increased so that cancer can be more successfully detected. Some authors have improved the likehood of cancer detection once when they

TABLE 2
COMPLICATIONS AFTER TRB REQUIRING HOSPITALIZATION

Complications	No. (%)
Infections	2 (1.7)
Vasovagal episodes	3 (2.6)
Severe hematuria	1 (0.8)
Rectal bleeding	1 (0.8)

increased the number of samples up to 18[11]. Vaski et al. and Djavan et al. have suggested the so called Vienna nomogram, so that the number of samples corresponds with prostate volume, patients' age and should vary from 6–18. It is believed that this biopsy method improves cancer detection up to 90%[12]. The increased number of the biopsy cores could maybe increase the detection of clinically insignificant cancers. In order to reach that conclusion, serious analysis is required that would compare cancers from one group with those of the other and comparison criteria should include volume of tumor tissue and pathological tumor stage (after radical prostatectomy), DNA ploidia of tumor cells etc. Chan et al. think that increased number of samples does not improve the likehood that insignificant cancer would be detected, but only helps to detect cancer in its earlier stage[13].

It is not clear whether the increased number of cores in case of bigger prostate volumes improves the likelihood of cancer detection or it is more important of which region of the prostate are the samples are taken from. Norberg et al. have concluded that sextant method successfully detects 82% of clinical significant cancers, but if only 6 cores were taken along the sagittal line which is more laterally than the line cores are usually taken from in case of sextant method, only 70% of the cancers would be detected. The combination of these two methods, taking 12 cores, would improve detection up to 96%[14]. Our protocol reflects exactly this core taking and 94% of detected cancers with the initial biopsy, supports this theory.

Gretzer et al. consider that about 25% of the patients who have PSA value between 4–10 ng/ml have cancer, as well as 67% of the patients with PSA > 10 ng/ml[15]. Our results correspond with those mentioned and show frequency of cancer detection in 26% and 58% in appropriate PSA groups. The same authors mention that the likelihood of the cancer in the group with PSA value of < 4ng/ml is about 18%, but we did not have enough patients (only 3), so we could not compare the results. Studying the incidence of some Gleason scores, we have noticed that in 6% of the cancers the Gleason score was 2–4, in 35% Gleason score was 5–6, in 59% Gleason score was 7–10. Emiliozzi et al. mention a similar incidence in the group of low, middle and high grade[16].

Based on 117 biopsies we can say that we had a 1.7% infection rate, 2.6% vasovagal episodes, 0.8% rectal bleedings and 0.8% severe hematuria. The reported complications required either an immediate treatment or hospitalization of the patient. We did not keep a record of mild complications, since they were short and healed spontaneously. There were two patients who had urogenital infections few days after the biopsy (1.7%). They were successfully treated with antibiotics and symptomatically. The infection has not been clearly defined in the literature, as some authors describe it as high temperature, fever, sepsis or symptoms of urogenital tract infection. Sieber et al. report 0.1% of infection rate[17] and Rodriguez et al. about 2.5%[18]. The vasovagal reactions we recorded included loss of consciousness, drop of blood pressure that were treated with i.v. infusions, but milder reactions included sweating, tachicardia, moderate fall of blood pressure, without loss of consciousness and fast recovery, we did not include in the study. There were 3 patients who suffered from these severe reactions (2.6%). Djavan et al. mention 2.8% of vasovagal episodes[19]. Speaking of hematuria, only one patient had its severe form and was hospitalized (0.8%). We hospitalized one patient due to rectal bleeding (0.8%). Djavan et al. describe 0.5% of strong hematuria, 2.1% of rectal bleeding[19]. As we have mentioned, patients were informed about potential

temporary hematuria and rectal bleeding. Therefore we did not follow nor include milder cases of one or the other complication, which in spite of being frequent, heal fast and do not affect patient's well being.

Transrectal biopsy is performed with no anesthesia, though most of the patients expressed slight discomfort or light pain, there was no case of strong pain that would force us to take less numbers of samples. Administration of anesthesia is still discussed during TRB and the opinions are very different. There are urologists who advice the administration of local anesthesia for all patients and at the same time the those who oppose to it, saying that it is rather a pain tolerant procedure and so no anesthesia should be given. According to Aus et al. 92% of the patients did not feel any pain or they felt a slight discomfort[20]. Some authors think that anesthesia should be given only when more numbers of samples are taken, because they believe that pain is getting worse when more samples are taken. The opinion of Rodriguez et al. is young people are more sensitive to pain and anesthesia should be applied[18]. There are two most common types of local anesthesia during TRB, intrarectal administration of lidocaine gel and periprostatic local injection of lidocaine in neurovascular bundle. Vaidya et al. think that periprostatic anesthesia should be given to all patients[21]. Leibovici et al. pointed out that the patients who 10 ml of 1% lidocain had injected periprostatically, suffered from less pain than patients who were given placebo of 0.9% NaCl in periprostatic injection[22]. The results of the studies discussing the use of lidocain rectal gel are different. Issa et al. mention that patients who were given gel suffered from less pain than those who were not[23]. Chang et al. do not share this point of view because they have not notice better pain tolerance in the group given gel than in the one which had placebo[24].

Conclusion

Despite of many authors suggesting that increased number of biopsy cores improves the detection of prostate cancer, the biopsy protocol remains undefined. It is not clear whether improved prostate cancer detection after increasing number of cores is a consequence of increased tissue portion needed for pathohistological examination, or it is more important of which prostate regions the cores are taken from. The percentage of detected cancer on the first biopsy is 94%, justifying our decision to continue with 12 biopsy cores, especially because increased number of cores has not been accompanied with higher incidence of complications. However, what we should work on is to improve the biopsy technique so that it is suitable to every patient, regarding his age, PSA value, prostate volume and finding of transrectal ultrasound in order to avoid unnecessary increase of sample numbers by some patients.

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M. Knežević

Department of Urology, General Hospital »Našice», B. Jelačića 6, 31500 Našice, Croatia

REZULTATI DOBIVENI TRANSREKTALNIM BIOPSIJAMA PROSTATE S UZIMANJEM 12 BIOPTIČKIH UZORAKA

S A Ž E T A K

U ovom radu želimo prikazati kliničku vrijednost transrektalne biopsije prostate sa uzimanjem 12 bioptičkih uzoraka u odnosu na klasičnu sekstant metodu. Obradili smo podatke 106 pacijenata, kod kojih smo od 4.10.2001. do 14.8.2002. godine učinili transrektalnu biopsiju prostate (TRB), koja je bila indicirana zbog abnormalnog nalaza digitorektalnog pregleda (DRE) i/ili vrijednosti PSA > 4 ng/ml. U navedenom periodu smo učinili 117 biopsija sa uzimanjem 12 bioptičkih uzoraka, po 6 uzoraka iz svakog pojedinog režnja. Karcinom prostate smo dokazali kod 49 pacijenata (46%). Od ukupnog broja dokazanih karcinoma, inicijalnom biopsijom smo dokazali 94%, što znači da nam je prilikom izvođenja prve biopsije ostalo nedijagnosticirano samo 6% karcinoma. Kod 3 pacijenta biopsiju smo učinili zbog suspektnog nalaza DRE uz vrijednost PSA < 4 ng/ml, no karcinom nismo dokazali niti kod jednog od njih. U skupini pacijenata koji su imali PSA između 4–10 ng/ml, karcinom smo dokazali kod njih 26%, a u skupini pacijenata sa PSA > 10 ng/ml, karcinom smo dokazali kod 58%. Najzastupljeniji Gleason score karcinoma je bio 7 (43%). Tijekom provođenja biopsije, kod 3 pacijenta je došlo do izražene vazovagalne reakcije, što na ukupno 117 učinjenih biopsija iznosi učestalost navedene komplikacije od 2.6%. U periodu od nekoliko dana nakon biopsije, kod 2 pacijenta je došlo do razvoja infekcije urogenitalnog trakta (1.7%), a neposredno nakon provođenja postupka, u po jednom slučaju smo imali pojavu jake hematurije (0.8%) i jakog rektalnog krvarenja (0.8%), koji su zahtijevali hospitalizaciju. Naši podaci o pojavi komplikacija se ne razlikuju značajno u odnosu podatke o komplikacijama iz literature. Podaci iz literature za sekstant biopsije pokazuju da 15–34% karcinoma ostane

nedijagnosticirano inicijalnom biopsijom. Metodom sa uzimanjem 12 bioptičkih uzoraka, inicijalnom biopsijom nismo uspjeli dijagnosticirati samo 6% od ukupno dokazanih karcinoma, ali važno je naglasiti da je u vremenskom periodu koji je obuhvatila ova studija, re-biopsija bila indicirana samo u 11 pacijenata od svih sa negativnom inicijalnom biopsijom.