The author discusses preparations for ultrasound guided prostate biopsy, its technique conditions and the process of performing a biopsy. Every author proposes the use of preoperative antibiotics based prophylaxis. Differences may be found in the type, dosage and the time span of preoperative application. For anaesthesia mostly lidocaine was proposed, which may be a gel applied in the rectum or used in the form a prostate infiltrate. The widest debate goes on in respect of defining the number of biopsies needed. Recently 8 or rather 10 samples are proposed to be taken. Twelve biopsies do offer an advantage compared to 6 although in case of 8 this isn’t so. According to the site of sample taking the apex, the base and the middle part are proposed. In case of a palpable nodule or any lesion, made visible by TRUS an additional, targeted, biopsy has to be performed. Certain new techniques like the 3D Doppler, contrast, intermittent and others shall also be presented. A repeated biopsy shall be necessary in case of PIN atypia, beyond that the author also discusses other indications for a repeated biopsy. We may expect the occurrence of direct postoperative complications and it is necessary to know how to treat these.

Key words: ultrasound, biopsy, prostate cancer

INTRODUCTION

Prostate cancer has become the most common cancer in the male population and the second leading cause of cancer – mortality. In USA 300.000 new prostate cancers are registered yearly, more than 4000 in Hungary. Initially the disease is symptoms free, an elevated prostate specific antigen (PSA) level or a palpable hard nodule found by rectal digital exams indicate a need to perform a prostate biopsy in order to prove or exclude prostate cancer.

The usual cut off value is 4 ng/ml, although in case of younger male patients it would be better to use a lower cut off value while in aged male ones a bit higher one taking the previously advised age specific PSA cut off values in consideration. We are going to tend to determine a lower cut off value in order to find the cases in most early stage.

The prostate biopsy is one of the most frequently performed urological interventions. Certain technical aspects of it are under discussion, discussions about these, individual experiences and convictions recur in the literature on a regular basis.

The procedure itself is the reason of these, at times contradictory, standpoints; the efforts to achieve a possibly most high rate of hits; the endeavour to have possibly the least number of cancers missed, the cost- benefit effect and the issue of effects and side effects complicate this relatively simple intervention.

In the United States about 500.000 prostate biopsies are performed annually. It is understandable that this process is in the centre of interest.

PATIENTS’ PREPARATIONS FOR BIOPSY

It is important to provide the patient with information prior to a prostate biopsy for several reasons. The patient must be informed that the indication of the biopsy and the intervention itself do not mean a cancerous illness by necessity, more than one half of the histological tests do not verify any malignity. The patient must also be informed that biopsy is but a minor intervention. The percentage of mild complications is high although they pass without any treatment in most of the cases. We may also reassure the patient that a local or brief intravenous narcosis will insure the painlessness of the intervention.

We have to indicate the upper age limit of the intervention as well. It is variable in the European countries, should be about 75 years.
Administering a pre-operative enema on the day of biopsy, in the morning or at least three hours before the intervention, may reduce the danger of infection, but a full ampulla of the rectum may also hinder the visualisation of the prostate.

In our practice we perform the enema on the day of the biopsy. We also verify that the patient does not take any anticoagulant drug.

**PROPHYLACTIC ANTIBIOTICS**

Opinions in literature agree upon the fact that in order to prevent postoperative infection and to preclude a possibly emerging sepsis prophylaxis by antibiotics is necessary.

According to Matlaga et al. 1 24 hours before biopsy fluoroquinolon was administered, continuing for 24 hours after biopsy. Lee-Elliott et al. used a simple 1 g metronidazole suppository and 500 mg ciprofloxacin twice daily for 3 days and 1 hour before the procedure.

Cormio et al. compared short-term parenteral prophylaxis with piperacillin/tazobactam (P-T) with long term oral therapy with ciprofloxacin in preventing infective complications. The P-T dose was 2250 mg intra-muscularly twice daily for 2 days, the administered ciprofloxacin (500 mg orally) was given twice daily for 7 days, beginning both in the evening before biopsy. Following the biopsy bacteruria occurred in 2 and in 3 cases respectively. From the point of the costs involved; the short prophylactic procedure is advised.

Galetti et al. use sulfametoaxazol 800 mg+ trimetoprimg 160 mg twice a day; starting 12 hours before the procedure and continued for 5 days afterwards. A mere 1 % rate of symptomatic infection could be observed.

We administer in our department 1 day 500 mg ciprofloxacin prophylactic therapy.

**Anaesthesia**

Many urologists tend to point out that the pain associated with this intervention is so mild that local anaesthesia is not necessary. However 65-90 % of patients undergoing TRUS guided biopsy of the prostate experience discomfort and pain, that are often severe.

Several authors published techniques for local anaesthesia for TRUS guided prostate biopsy. Matlage et al. (1) administered 10 ml 2 % lidocain jelly 10 minutes before the biopsy or 20 ml of 1 % lidocain in local injection mixed with 2 ml 8.4 % sodium bicarbonate, 5 minutes before the biopsy. 5-5 ml were infiltrated into the left and right nerve plexuses located junction of the seminal vesicle and prostate and 5 ml into the gentourinary diaphragm as well as 5 ml between the rectal wall and prostate. Compared to the jelly treated group: in the infiltration group the overall pain decreased significantly (0.0001).

Adamakis et al. compared a group without anesthesia (using only a sonographic gel), another group was given an infiltration of lidocain-pilocain gel, and a third received a periprostatic 10 ml 2 % lidocain injection. The pain scores were 5.1, 4.8 and 2.5 in the different groups respectively. Compared to groups 1 and 2 the score was significantly lower in the case of group 3.

Lee-Elliott et al. compared periprostatic infiltration of 10 ml 10 % lidocain to 5 ml 1 % lidocain mixed with 5 ml 0.25 % bupivacain and adrenalin. A cross-sectional comparison showed no differences between the groups in terms of the mean pain scores immediately after biopsy, however there was a significant rebound on a visual - analogue scale at 1 hour in the lidocain but not in the (long-acting) lidocain-bupivacain group.

Periprostatic local anaesthesia requires at least 2 or more needle punctures. Öbek et al. investigated the postoperative bleeding in patients receiving local anaesthesia or with no anaesthesia. The periprostatic anaesthesia did not increase the risk of urethral bleeding, however bacteriuria and fever were more common in the local anaesthesia group.

In our practice we administer 5-10 mg Diazepam combined with 1.0 mg/bw Propophol intravenously. With this we accomplish a full relaxation, stop the patient’s anxieties and in case of a possible repeated biopsy the patients has no adverse memories and will not be afraid of the intervention. A five minutes long narcosis shall be sufficient for 6-8 or even 10 scores.

In selected cases, upon request of the patient we perform biopsy in local anaesthesia (lidocain gel) as well.

**TECHNIQUE OF THE BIOPSY**

There is no doubt that ultrasound is available everywhere today and the TRS guided biopsy is a technique of choice. There is practically no indication to perform perineal prostate biopsy.

Ultrasonography is the most suitable process for imaging the prostate. All three regions, i.e.: the central zone, transition zone and peripheral zone, as described by McNeal, can in most cases be visualised by ultrasound.

Adenocarcinoma can sometimes be recognised as hypoechoicogenic lesions. Some tumours can be hyperechogenic as well. The isoechogenic tumours, up to 50 % of all cases, can not be targeted directly, the cancer can only be proved by the use of random biopsy, but it can be missed as well.

Rifkin and Peters investigated 650 men who have undergone a TRUS-guided biopsy of the prostate. Each area undergoing biopsy was characterised as: 1- appearing normal-, 2-hypoechoic, 3-mixed echogenic, 4-subtly hyperechoic (containing no calculi) or 5-isoechoic. 197 patients' specimen were proved as being tumorous (32 %). Ninety nine (50.2 %) of these patients had hypoechogenic lesions as the primary site. Twenty five (12.7 %) had mixed echogenicity, 9 (4.6 %) had hyperechoic foci and 23 (11.7 %) had isoechoic biopsy proven –foci. Twenty (0.8 %) patients with adenocarcinoma had normal ultrasound findings. Results suggest that 50 % of clinically significant prostate cancers are not purely hypoechoic, and 37 % of all diagnosed cancers contain no hypoechogenic elements.

In 1989 Hodge et al. reported that biopsy directed at hypoechogenic areas of the prostate missed 9 % of the cancer cases detected by random systematic biopsy. The sextant biopsy has become a standard strategy for detecting prostate cancer. It seems to be realistic to assume, that more biopsy cores taken contain more cancerous tissue. The
Hodge biopsy technique involves 3 biopsies from the right and 3 from the left lobes, from the apex, basis and the mid section of the prostate. According to Palisaar et al's today’s standard is a minimum of 8 cores taken from the peripheral zone. By complementing the samples taken from the central line of 3-3 lobes by samples taken from the peripheries we may enhance the rate of hits.

It is known, that the prostate tumours arise within the peripheral zone thus the standard 45 degree biopsy angle is not optimal. By using this technique no samples are collected from the exterior and transitional zones. Therefore 20-30 % of cancer positivity rate may be characteristic of the repeated biopsy. The angel should be modified or the number of scores should be increased.

By increasing the number of biopsies and sampling the anterior and transitional zones the Hodges protocol can be improved. Meng et al advised to perform a biopsy of the apical anterior horn as a part of an 8-core biopsy providing high cancer detection.

Most of the authors were able to improve detection rate by increasing the number of cores. Beurton et al compared 6 and 12 cores biopsy and the detection rate was 22%; more tumours were found than by using sextant biopsy.

Singh et al complemented sextant biopsy with six additional peripheral biopsies in 178 patients who were also operated performing radical prostatectomy. They compared the 12 sample biopsy with the traditional sextant biopsy or rather with a biopsy involving only 6 peripheries. The 12 sample process showed a much better correlation with extra-capsular extension and the total tumour volume.

Presti et al performed more than 2000 biopsies. A total of 12 systematic biopsies of the peripheral zone were obtained in all patients, including a standard sextant scheme (mid lobar parasagittal, plane of the apex, mid se-ction and base) and laterally directed biopsies at the prostatic apex, mid section and base. Their study confirms the need for an extended peripheral zone sampling of the lateral aspect of the prostate. However Horinger et al didn’t find significant differences when comparing the taking of 10 cores to that of 14 cores (24 % versus 22 %). Nava et al reported no increase in cancer detection in case of 6 and 12 cores (15-17 %) as opposed to 18 cores (32 %).

TZ biopsy applied in addition to PZ biopsy results in an only 1.8-4.1 % higher detection rate of prostate cancer, so routine TZ-s are not justified. The Vienna nomograms advised by Djavan et al. used to determine the number of scores regarding the prostate volume and the patients’ age. An additional development is the use of colour Doppler ultrasound to detect perineural invasion.

Repeated biopsies

Subject to indication 30-80 % of all biopsies are completed with a negative result. Eighteen to thirty % of all cases lead to re-biopsy. As Rabbani et al have pointed out in case of a sextant biopsy 23 % of all tumours are not diagnosed. Therefore: if the biopsy is negative and the clinical suspicion still exists a re-biopsy has to be performed. Djavan et al found tumours in 10 % in all re-biopsies. A repeated biopsy is necessary if the sample is improper for being processed, or if it contains a too small amount of tissue and/or of improper quality of the prostate.

The biopsy should be repeated if the indication is based on PSA velocity.

In case of a high grade PIN the repeated biopsy is justified. In case of re- biopsies a tumour may be found in 23 –100%

The contraindications of a biopsy are the following: - oral anticoagulant therapy, - acetyl salicylic therapy, - bacterial prostatitis within 6 weeks (before the intervention), - thrombocytopenia, - periproctal abscess, - tumour of the rectum

To avoid complications a low molecular heparin anticoagulant should be administered in an additional antibiotic. Even in these cases hematuria may occur in 58%, blood in stool in 37%, hematospermia in 28%, obstruction of the urine in 8% and fever in 4% of all cases.

Rare and difficult cases are represented by patients who have undergone abdomino- perineal resection, but transperineal ultrasound guided random biopsy of the prostate can provide an accurate diagnosis. However the transperineal image technique is poor compared to transrectal imaging and it is not suitable for lesion directed biopsy.

 Obviously the future does not lie in the infinite increasing of the number of biopsies but in the improvement of imaging techniques. The use of Doppler ultrasound can reduce the number of biopsies. Experts considered the interpretation of 3D ultrasound superior to that of 2D ultrasound. Probably the contrast enhanced imaging provides additional benefits for the targeting of prostate biopsies in the future.

**SUMMARY**


Ključne reči: karcinom prostate, dijagnoza, ultrazvučno vodjena biopsija
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