

Comparative Analysis of Complications While Using Various Biopsy Techniques of Prostate Gland

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Abstract:

Nowadays the increase in the incidence of prostate cancer on last decade is more than half of situations of PCa. The average annual growth rate is 7.76%. Great importance in diagnosis and subsequent choice of treatment tactics for the patient has histological verification of prostate cancer. Currently, the most common method is transrectal “blind” ultrasound-guided prostate biopsy, which does not have sufficient sensitivity and specificity for detecting prostate cancer, and the morphological result contains limited information about the aggressiveness and stage of the disease. Multiparametric magnetic resonance imaging is currently the most sensitive and a specific imaging method for diagnosing prostate cancer, techniques are increasingly used in clinical practice targeted prostate biopsy.

Keywords: prostate cancer, prostate biopsy, magnetic resonance imaging, saturation prostate biopsy, transperineal combined biopsy.

Introduction

Prostate cancer (PCa) – 2nd leading cause of death from cancer and the most commonly diagnosed malignant tumor in men. PCa According to its biological structure, it is a heterogeneous disease, and its forms vary from indolent to highly aggressive. In this regard, timely verification of the diagnosis is very important. Modern diagnostic approach consisting of serum prostate specific antigen (PSA) level testing, digital rectal examination and ultrasound study followed by standard transrectal ultrasound biopsy [1], does not have sufficient sensitivity and specificity when prostate cancer is detected, and the morphological material has limited information about the stage and clinical aggressiveness of the disease [2, 3]. The results of most studies showed that concept of increasing the number of biopsy points due to puncture of the peripheral parts of the prostate gland (PG), it significantly improves the diagnosis of prostate cancer [4]. This strategy was called extended pancreatic biopsy, consisting of 10–18 cores. Theoretically, an increase in the number of injections with extended biopsy should lead



to an increase in the detection of prostate cancer. Scheme with maximum detection of clinically significant prostate cancer and the smallest number of points is optimal pancreatic biopsy.

Due to the multifocality of prostate cancer, the difficulty of visualizing tumor foci in the organ, the relatively low specificity of the ultrasound method and the low information content of the standard biopsy, as well as the high sensitivity of multi-parametric magnetic resonance imaging (mpMRI) has been introduced into urological practice fusion biopsy using MRI/TRUS (magnetic resonance imaging/transrectal ultra sound). Targeted biopsy under MRI/TRUS navigation allows for more accurate localization oncological process, predict the volume and the degree of malignancy of the tumor, which may be used to plan treatment tactics.

There are 2 approaches to pancreatic biopsy methods: transrectal and perineal (transperineal) [5]. The transrectal method is widely used for a long time, but despite the simplicity of execution and small invasiveness, this intervention cannot be called absolutely safe [6]. Adverse events include pain, acute prostatitis and orchiepidemitis, hematuria, hemospermia, acute urinary retention, rectal bleeding. Analysis of literature data demonstrated that the frequency of infectious complications is 4.8% [6], serious infection after transrectal biopsy is observed in less than 1% of cases [7], acute urinary retention is observed in 0.3–2.1% of patients [8], rectal bleeding – in 28.0%, hematuria – in 66.3% [9]. Often these conditions do not require hospitalization and treatment and resolve on their own [10].

Theoretical advantages of transperineal access compared to transrectal associated with the procedure performed under aseptic conditions due to the absence of contamination of intestinal microflora and higher quality material collection due to longitudinal location of the pancreas [11, 12]. When studying modern literature on this issue 2 opposing opinions have been identified that the prointernal method even with saturation biopsy is one of the safe ones [13–15], and vice versa [16–18]. The purpose of the study is to estimate the prevalence complications and comparison of adverse events with various biopsy methods: standard transrectal, perineal mapping and whole transperineal fusion using MRI/TRUS navigation.

Materials and methods. A comprehensive examination of 142 patients with suspected prostate cancer was carried out, including those with a previously performed biopsy, based on the results in which tumor pathology was not detected. Indications for repeat biopsy: history of negative biopsy results, but persistent suspicion; precancerous conditions after primary biopsy – atypical small acinar proliferation and prostatic intraepithelial neoplasia.

In most cases, the reason for a repeat biopsy was an increased serum level of blood PSA and/or pathological changes according to mpMRI (PI-RADS score (Prostate Imaging Reporting And Data System) ≥ 3). Previously, all patients underwent standard TRUS-guided biopsy. Patient age was 44–74 years old (mean age 62.0 ± 6.5 years).

Clinical research methods included the study of complaints, medical history and life of the patient, objective examination data, including digital rectal examination, laboratory results (PSA level and its fraction) and radiation (TRUS and mpMRI) research methods. All patients were divided into 3 groups. Patients of group 1 (n = 49) underwent repeated standard transrectal



biopsy of the pancreas; patients of group 2 (n = 39) – perineal mapping biopsy. In patients of group 3 (n = 54), the results of mpMRI revealed focal changes in the pancreas tissue with a category on the PI-RADS_vs scale not lower than 3, they underwent transperineal fusion biopsy under MRI/TRUS navigation. In patients of group 3, they used simultaneously 2 transperineal biopsy methods: random and targeted, which is associated with the desire to determine the likelihood of multifocal growth of adenocarcinoma. Technique for performing transperineal. We have described fusion biopsies under MRI/TRUS navigation in detail [19].

In the last 10 years, mpMRI of the pancreas has undergone significant technical changes. This method is all has become increasingly used to select patients who require repeat biopsy by identifying areas of interest as targets and to target image-guided biopsies. Generalized sensitivity and specificity of mpMRI in diagnosis PCa, according to the literature, is 78–82 and 79–82% respectively. The main goals of mpMRI are diagnosis and determination of the localization of foci that correspond to clinically significant PCa. The results of recent studies have shown that depending on the location and degree of change In pancreatic tissue, mpMRI can detect moderate and high degrees of aplasia with tumor size <5 mm. According to published guidance PI-RADS_v2 should be remembered that the feasibility. Targeted biopsy of the pancreas can be considered if the PI-RADS category is at least 3. With the PI-RADS 1 or PI-RADS 2 categories, a biopsy is considered inappropriate. In cases with installed PI-RADS category 3 question about ordering a biopsy is decided not only on the basis of mpMRI data, but also according to the results of laboratory tests, digital rectal examination, medical history, etc. Suspicious areas were assessed according to the PI-RADS scale: 9 (16.7%) lesions with 5 points, 12 (22.2%) lesions with 4 points and 33 (61.1%) lesions with 3 points.

The age of patients in group 1 was 65.5 ± 5.8 years, 2nd – 62.6 ± 4.6 years, 3rd – 61.6 ± 7.8 years. At the time of the manipulation, the PSA level in patients of group 1 averaged 9.7 ± 5.8 ng/ml, 2nd – 13.52 ± 4.6 ng/ml, 3rd – 10.7 ± 4.2 ng/ml. Most patients have previously had at least one pancreatic biopsy was performed, 5 (12.8%) patients of group 2 and 12 (22.3) patients of group 3 did not have history of biopsies (see table). The pancreatic volume in patients of group 1 averaged 42.7 ± 12.4 ng/ml, 2nd – 63.1 ± 14.4 ng/ml, 3rd – 55.8 ± 15.7 ng/ml. In this study, in addition to traditional medical criteria we tried to evaluate the opinion the patient regarding subjective feelings through questioning. The following parameters were assessed: 1) without danger of manipulation; 2) urination disorders; 3) blood in the stool; 4) blood in urine; 5) manifestation of lower urinary symptoms paths; 6) manifestation of symptoms of inflammatory diseases of the testicles and appendages (pain, local hyperthermia, increase in organ volume); 7) carrying out additional medicinal methods treatment and inpatient care.

Pain parameters were assessed using a scale from 0 to 10 points, where 0 is no pain, 10 is unbearable pain, relieved by narcotic analgesics; symptoms 2 to 4 were assessed on a scale from 0 to 3 points, where 0 – no violations, 1 – minor, 2 – significant disorders requiring additional drug treatment, and 3 – severe disorders requiring hospital treatment and additional surgical interventions.



Statistical data processing was performed on an individual computer using Microsoft Excel spreadsheets and the Statistica application package for Windows 6.0 (StatSoft Inc., USA).

All obtained data were processed using the variation statistics method. At the beginning of the statistical analysis, all quantitative characteristics were assessed for the normality of their distribution using the dispersion method analysis. For cross-correlation analysis of methods performing a biopsy, their relationship with the results mpMRI used correlation coefficient Spearman.

Results

Average duration of a biopsy procedure in patients of group 1 was 10.6 ± 2.4 minutes, 2nd – 28.9 ± 8.4 min, 3rd – 56.7 ± 10.9 min. General number of biopsies obtained from patients Group 1 amounted to 516, Group 2 – 1039, Group 3 – 1369. Prostate cancer was verified in 64 (45.1%) patients: in 13 (26.5%) patients of the 1st group, 18 (46.2%) - 2nd group, in 33 (61.1%) - 3rd. In patients of group 1, the number of “positive” biopsies obtained of 74 lesions (average target lesion volume 3.23 ± 0.86 cm³), subject to targeted biopsy, was 39 (7.6%), in patients of group 2 - 53 (5.1%), 3rd – 187 (13.6%). Number of biopsies taken using a random perineal biopsy technique, in patients of group 3 – 1182 (86.4%). Adenocarcinoma was detected in 114 biopsies, which amounted to 8.3% from the number of all biopsies. Number of biopsies, obtained by targeted biopsy - 75 (65.8% of the total number of “positive” biopsies), with random – 39 (34.2% of the total "positive" biopsies).

Distribution of patient groups depending on the number of previously performed biopsies, n (%)

Number of biopsies in medical history	1st group (n = 49)	2nd group (n = 39)	3rd group (n = 54)
0	---	5 (12,8)	12 (22,3)
1	34 (79,1)	21 (53,8)	22 (40,7)
2-3	9 (20,9)	10 (25,6)	16 (29,6)
≥4	–	3 (7,8)	4 (7,4)

Diagnosis and treatment of tumors of the genitourinary system. Prostate cancer obtained “positive” biopsy samples using random and targeted techniques in patients of group 3 are statistically significant ($p < 0.01$; Spearman correlation coefficient 0.8). When analyzing data mpMRI and morphological report detects adenocarcinoma corresponding to PIRADS 3, was 33.3% (n = 13), PIRADS 4 – 75.0% (n = 9), PIRADS 5 – 77.8% (n = 7). Patients of group 1 underwent biopsy on an outpatient basis. The observation time for the patient after the procedure was 2–4 hours. If there were no pronounced complaints and indications for inpatient treatment, patients could leave clinic with recommendations for taking antibacterial drugs, alpha blockers, oral and rectal nonsteroidal anti-inflammatory drugs funds.



Postoperative course in patients 2nd and 3rd groups was 1–2 days. The urethral catheter after the biopsy was removed approximately after 8–12 hours. Antibacterial therapy was not carried out in the postoperative period; it was recommended use of alpha blockers, oral and rectal non-steroidal anti-inflammatory drugs funds.

The total number of complications identified during the analysis of medical records was 72 (in group 1 - 21, in the 2nd – 23, in the 3rd – 28). Complication severity assessed according to the Clavien–Dindo classification.

In group 1, complications of degrees II and IIIa developed in 14 (28.6%) and 2 (4.7%) cases, respectively, in Group 2 – in 11 (28.2%) and 1 (2.6%) cases. In group 3, the most significant complications were grade II - 6 (11.1%) cases; grade IIIa complications were not recorded. Complications IIIb – V in none group was not detected (Fig. 1).

Most patients had hematuria varying degrees of severity (in group 1 – 14 (33.3%) patients, in the 2nd – in 20 (42.5%), in the 3rd – in 27 (42.2%)), which in most cases was self-limited and did not require additional treatment. Presence of slight blood admixture in urine that persists for 2–3 days after pancreatic biopsy, or in seminal fluid that persists for 1–2 months is considered expected after this manipulation, and all patients were informed about this. Treatment for hematuria was required 5 (11.9%) patients from group 1, 8 (17.0%) –from the 2nd and 5 (7.8%) from the 3rd. Hemotamponade developed 1 (2.4%) patient was in group 1 and 2 (4.2%) were in group 2.

Additional manipulations (bladder washing) were required in 1 patient from 1st group and 2 from the 2nd group, and hemostatic therapy was prescribed to 4 patients from the 1st group, 6 –from the 2nd and 5 – from the 3rd. As a rule, there was a short course (2–3 days), after which the hematuria stopped fully.

Additional inpatient treatment and additional medications were required 8 (16.3%) patients in group 1 and 1 (2.5%) in group 2. Of these, in patients of group 1 – 2 (4.7%) cases severe rectal bleeding and 2 (4.7%) cases of acute urinary retention, in patients of the 2nd and group 3 – 1 (2.1 and 1.6%) case each. During development acute urinary retention (in the 1st group – in 2 (4.7%) patients, in the 2nd – in 1 (2.1%) patients, in the 3rd – in 1 (1.6%) patients) drainage of the lower urinary tract with a urethral Foley catheter was used (no more than 2 days) with a course drug therapy, including the use alpha-blockers, an tibacterial, anti-inflammatory drugs. Due to the ineffectiveness of conservative methods for resolving acute urinary retention required epicystostomy in 2 (4.7%) patients of group 1 and 1 (2.1%) - 2nd. Long-term hospital treatment and change of antibacterial therapy to the carbopenem series, due to the phase of acute post-biopsy inflammation of the pancreas, 2 (4.7%) patients required 1st group. When analyzing the medical records, it turned out that both patients had previously undergone 3 consecutive standard transrectal biopsies and in all cases they were previously prescribed chemoprophylaxis with antibacterial drugs of the fluoroquinolone series. These facts, in our opinion, became predictors of the development of septic conditions in these 2 patients. Development of purulent-septic no complications were registered in patients of groups 2 and



3, which is associated with aseptic conditions performing biopsies and adequately selected antibacterial and anti-inflammatory therapy. Complication rate of standard transrectal biopsy, perineal mapping biopsy and targeted fusion biopsy under MRI/TRUS navigation was statistically insignificant ($p > 0.05$).

Patient survey data are grouped and presented in the form of diagrams (Fig. 2). In the majority cases, the consequences of the biopsy were unexpressed character, did not require additional treatment and resolved independently.

From the data presented in the diagrams it follows that patients after a standard transrectal biopsy most often experienced severe pain syndrome, and that in these patients in the postbiopsy period, impurity was significantly more often noted blood in urine and stool. In groups 2 and 3 (estimate subjective attitude of the patient and clinical manifestations) incidence of gross hematuria comparable with literature data, which directly associated with the extended biopsy technique.

During the survey, patients Group 1 more frequently reported symptoms lower urinary tract – in 79.6% ($n = 39$) of cases, patients of groups 2 and 3 – in 28.2% ($n = 11$) and 29.6% ($n = 16$) cases, respectively. Symptoms of inflammatory diseases of the testicles and appendages after biopsy were more often noted by patients of group 1 – in 16.3% ($n = 8$) cases, while patients of groups 2 and 3 – in 5.1% ($n = 2$) and 1.9% ($n = 1$) of cases, respectively.

Conclusion

The results of the study allow us to conclude that the use of perineal mapping and transperineal fusion biopsy under MRI/TRUS navigation allows to identify malignant changes in a significantly larger number of biopsies and these diagnostic methods are safe and invasive. The undeniable advantage of transperineal extended and targeted biopsy compared to transrectal blind biopsy – significantly fewer infectious diseases complications.

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