REPEAT TRANSRECTAL PROSTATE BIOPSIES IN DIAGNOSING PROSTATE CANCER

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ABSTRACT
Patients with negative prostate biopsy and persistent suspicion of prostate cancer (PCa) can pose a serious diagnostic problem.

The aim of our study was to determine the frequency of PCa found on repeat prostate biopsy and the factors leading to higher possibility of cancer positive histological result.

Patients and Methods: We studied retrospectively 113 patients (82 from University Clinic, Jena, Germany and 31 from Department of Urology, Plovdiv, Bulgaria) with initial negative biopsy for cancer who underwent repeat biopsies. The patients were examined between January 1999 and May 2010. The target group included patients with Prostate Specific Antigen (PSA) level lower than 12.5 ng/ml and without suspicious finding on digital rectal examination (DRE). Different biopsy schemes were used in the initial and the following biopsies, depending on patient age and total prostate volume.

Results: Overall PCa detection rate was 22.1% (25 of 113). The repeat biopsy found PCa in 15.9% (18 of 113). In patients with 3 biopsies the PCa detection rate was considerably lower – only 8.6% (3 of 35). PCa was found in only 1 patient of 18 (5.5%) who underwent four or more biopsies. Transurethral resection of the prostate (TURP) was performed in 15 patients with at least two previously negative biopsies. The pathohistological examination of the resected tissue showed PCa in 3 of the patients (20%).

Conclusion: The interval between biopsies is not a significant predictive factor for positive prostate biopsy. The chance for detecting PCa after the second negative transrectal biopsy procedure is low. Therefore, TURP can be used as an alternative procedure to harvest adequate tissue material for pathologic examination, especially in patients with obstructive voiding symptoms.

Key words: biopsy interval, prostate cancer, repeat biopsy, TURP

INTRODUCTION
Biopsy of the prostate, mostly performed under ultrasound guidance, is the most common method for detecting PCa. In clinical practice there are frequently cases that yield cancer negative initial prostate biopsy but are persistently highly suspicious for PCa. Quite often such patients undergo a lot of unnecessary biopsies without detecting PCa. The decision to perform a repeat biopsy can be difficult for both patient and clinician. It is difficult to analyze a single factor or group of isolated factors and use them to stratify which individual is more likely to have cancer discovered on subsequent biopsy. Even with low incidence, prostate biopsy causes sepsis in 1%, moderate to severe haemorrhage in 1.5% and urinary tract infection in 5% of patients. As morbidity rate in such cases is high and there is significant initial false-negative biopsy rate, there are a lot of studies dedicated to decrease the number of negative prostate biopsies. The parameters we analysed in order to predict PCa were DRE, PSA serum level, transrectal ultrasonography (TRUS) finding and interval between the biopsies.

The interval between biopsies considered as a factor has attracted great interest recently. Urologists are very often faced with the problem of making multiple biopsies within a short period of time that may not be tolerated by patients both physically and mentally, whereas a too long course of observation without repeat biopsies may lead to cancer progression. Patients with impalpable prostate nodule that are indicated for repeat bi-
opsies only by the elevated serum level of PSA are a serious diagnostic problem, especially in cases with moderately increased PSA in the “gray zone” (2.5 - 12.5 ng/ml).

**AIM**

We determined the frequency of PCa finding in repeat prostate biopsies as well as the factors that contributed to higher likelihood of cancer positive histological result with a view to the interval between biopsies and the serum PSA level. We describe our experience with extensive TRUS guided prostate needle biopsy in patients with previously negative biopsy.

**PATIENTS AND METHODS**

We studied retrospectively 113 patients with an initial PCa negative biopsy who underwent repeat biopsies between January 2002 and May 2011 in an outpatient surgical setting. TRUS guided multisite needle prostate biopsies were performed in all patients. Specimens were separated for specific location identification. Histopathological features of biopsy samples were categorized as benign prostatic tissue or PCa. Biopsies were performed in 31 patients at Medical University, Plovdiv, Bulgaria and in 82 at the Clinic of Urology in the Medical University in Jena, Germany.

Patients were excluded from the study if they had an initial serum level of total PSA greater than 12.5 ng/ml, renal failure and were suspected for PCa on palpation. The number of biopsy cores taken was 6–10 for the initial biopsy based on total prostate volume, age and the finding of the TRUS investigation. For the subsequent biopsy we used an extended biopsy scheme with 10-14 biopsy cores. Three patients in whom the second biopsy samples were negative for PCa underwent saturation biopsy with 20-26 cores. TURP was performed in 15 patients with at least two PCa negative biopsies.

Data for patients’ age at the first biopsy, the total serum PSA level before each biopsy, the time interval between the biopsies and histological results were recorded. Continuous variables were presented as mean ± standard error. Comparisons of the parameters between the positive result group and the negative result group were performed using independent and paired samples t-test. A p < 0.05 was considered statistically significant. All statistical analyses were conducted using SPSS version 17 (SPSS Inc. Chicago, II, USA) for Windows.

**RESULTS**

The mean age of patients was 65 ± 0.62 years (range 48-82) at the initial biopsy.

Overall PCa detection rate was 22.12% (25 of 113). The second biopsy detected PCa in 15.93% (18 of 113). The patients that had 3 biopsies the detection rate was even lower – only 8.57% (3 of 35). At the fourth biopsy cancer was found in only one of the patients – 5.5% (1 of 18). Of the 113 patients, 15 (13.30%) with at least two negative biopsies underwent TURP. Three patients (20%) were found to have PCa by the histological examination of the resected tissues (Fig. 1). No cancer was detected by the saturation biopsy performed as a result of two previously negative results.

The mean interval between the initial biopsy and the final cancer diagnosis was 32.12 ± 6.37 months and that between the first and last biopsy for the group with benign prostatic tissue was 32.88 ± 2.84 months. The interval between the initial biopsy and the last biopsy for the patients in the positive result group was longer than that in the negative result group, but the difference failed to reach statistical significance (t = 0.12, p = 0.90) (Fig. 2).

Mean serum total PSA level was significantly lower in patients showing no PCa (6.15 ± 0.23 ng/ml) than in those harboring PCa (8.74 ± 1.12 ng/ml) (t = 3.54, p = 0.0006). Stratifying by number and order of negative biopsies, we found that the mean level of serum total PSA before the initial biopsy was 5.29 ± 0.20 ng/ml, 6.78 ± 0.44 ng/ml at the second biopsy and stably elevated (p = 0.04 for trend) at the next biopsies (7.70 ± 0.55 ng/ml) (Fig. 3).

![Figure 1. Distribution of patients by histological result.](Unauthenticated Download Date | 7/2/17 1:36 AM)
Repeat biopsies of the prostate are often indicated in patients with a negative initial biopsy because of persistent abnormal PSA and/or digital rectal findings. In the present study – detection rate of 15.93% for the second biopsy and 8.57% for the third biopsy – is lower than those reported in other studies, even after the extended repeat prostate biopsy scheme with 10-14 cores. These results could be explained by the specific target group – patients without palpable suspicion for PCa and with total PSA in the “gray zone” (2.5-12.5 ng/ml). Even PCa detection rate after repeat prostate biopsy is high, there is a relevant question: when should biopsies cease to be performed and what alternative can be advised to the patient? Several studies reported increasing detection rate of PCa after TURP in comparison with prostate needle biopsy. This might have been affected by the greater likelihood for PCa developed in the transitional zone in patients with negative previous biopsies. According to Katto et al. additional biopsy cores taken from transitional zone and anterior apex of the prostate, performed as a repeat biopsy, are more likely to give positive histological result. In general, our data suggest that the detection rate for the target group of subsequent biopsies is lower and TURP has a greater detection rate of PCa in patients with previously negative biopsies. We strongly recommend TURP in patients with persistently increased or increasing serum PSA level in the “gray zone” and without palpable suspicion for PCa. A moderately increased prostate volume (up to 80 ml) allows a radical removal of prostatic tissue by transurethral surgery (to the prostatic capsule), which may be necessary after negative biopsies. At the same time this diagnostic and therapeutic action allows radical prostatectomy at a second stage if there are positive histological results. If there is an obstructive comorbidity with moderate or severe elevated International Prostatic Symptom Score (IPSS), TURP has to be diagnostic and treatment tool of choice for patients with previously negative biopsies. In addition, biopsies were performed by different urologists and there is likely to have been some variations in the indications for biopsy and the exact techniques used for biopsy. In the present study, the patients in the positive result group and those in the negative group had an equally long interval between the initial biopsy and the last biopsy. Moreover, our results demonstrated that the interval between the biopsies was not a significant predictor of prostate cancer at repeat biopsies. Only PSA is an important parameter for accurate prediction of cancer at repeat biopsies. These data suggest that biopsy interval cannot be recommended and it should be considered
individually, depending on PSA-related variables, previous biopsy results and TRUS finding. Complex assessment of the risk for positive result in each patient should be performed to increase accuracy in diagnosing PCa.

CONCLUSIONS

The likelihood for detecting PCa after the second negative biopsy is low and alternative for the patients is TURP, especially in patients with obstructive voiding symptoms. The procedure should be considered when findings are suspicious for PCa despite previously negative second biopsy to optimize cancer detection and avoid unnecessary biopsies.

REFERENCES

Повторные трансректальные биопсии простаты при диагностике рака простаты

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Резюме

Введение: Пациенты с негативной для рака биопсией простаты и персистирующей суспекцией для рака простаты (РИП) могут быть серьезной диагностической проблемой.

Цель: Исследование ставит себе целью определить частоту РИП, обнаруженного при повторных биопсиях простаты, а также и факторы, приводящие к более высокой вероятности позитивного патогистологического результата.

Пациенты и методы: Ретроспективно обследована группа, состоящая из 113 пациентов (82 пациента из Университетской клиники урологии, г. Йена, Германия и 31 пациент из Университетской клиники урологии, г. Пловдив, Болгария) с негативной для РИП первоначальной биопсией и которым проведены повторные биопсии (январь 1999 - май 2010 г.). В группу включены пациенты с сывороточным уровнем простатоспецифического антитела (ПСА) ниже 12.5 ng/ml и без суспектией находкой от ректального туширования. При инициальной и при последующих биопсиях использованы различные биопсические схемы в зависимости от возраста и от тотального объема простаты.

Результаты: РИП обнаружен у 25 из 113 пациентов (22.1%). При повторной биопсии РИП выявлен у 18 из 113 (15.9%). В группе пациентов с 3 проведенными биопсиями результат значительно ниже — у 3 из 35 (8.6%). РИП доказан только у одного пациента из 18 с проведенными 4 или более биопсиями. Трансуретральная резекция простаты (ТУРП) проведена только 15 пациентам с неменее двух негативными для РИП биопсиями. У трех из этих пациентов (20%) патогистологическое исследование резецированной ткани доказывает наличие РП.

Заключение: Интервал между биопсиями не является значимым фактором для позитивного гистологического результата. Шанс обнаружить РП после повторной негативной трансректальной биопсии простаты очень низок. Альтернативой может быть ТУРП, обеспечивающая адекватный материал ткани для патогистологического исследования особенно у пациентов с обструктивными симптомами нижних мочевых путей.