Morbidity and Discomfort of Ten-Core Biopsy of the Prostate Evaluated by Questionnaire

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Key Words

Prostate cancer · Transition zone biopsy · Transrectal ultrasound · Morbidity · Prophylactic antibiotic treatment · Questionnaire

Abstract

Transition zone biopsies have been found to increase the detection rates of cancer of the prostate in patients with negative digital rectal examination. There are however no data available whether the higher biopsy rate is associated with greater morbidity. The present study was therefore designed to evaluate the complication rate of extended sextant biopsy. In this prospective study, 162 consecutive patients who presented for prostatic evaluation were included. After starting prophylactic antibiotic treatment 48 h prior to the procedure, transrectal ultrasound-guided core biopsies were obtained from each lobe: three each from the peripheral zone (apex, mid-zone and base) and two from the transition zone of each prostatic lobe. In all patients a questionnaire was obtained 10–12 days after the procedure. Major complications occurred in 3 patients. In 2 of the 3 cases major macroscopic hematuria was treated by an indwelling catheter for 1 or 2 days and 1 patient developed fever $>38.5^{\circ}\text{C}$ for 1 day. Minor macroscopic hematuria was

present in 68.5% of the patients. In 17.9% of these cases, the hematuria lasted for more than 3 days. Hematospermia was observed in 19.8% and minor rectal bleeding occurred in 4.9%. Ten-core biopsies did not lead to an increase in adverse effects or complications when compared to the results of sextant biopsies reported in the literature.

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Introduction

The diagnosis and treatment of prostate cancer (CaP) requires histological proof. Ultrasound-guided systematic sextant biopsy of the prostate became the standard procedure for the histological confirmation of CaP. However, in PSA screening studies there is a high rate of patients without the confirmation of a CaP (65.6–82.1% [1, 2]). In these patients a second set of sextant biopsies may be performed to rule out CaP. Keetch et al. [3] could show that in serial prostatic biopsies, 79% of CaP are detected with the first set of biopsies, another 16.6% with the second and only 4.4% with further prostatic biopsies. According to Keetch et al. [3], a total of 95.6% of CaP can be detected with two sets of prostatic biopsies. For these reasons, some authors [4, 5] advocate a higher number of

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biopsy cores expecting an improvement in the detection rate especially in large prostate glands. Different propositions have been made such as a five-region biopsy, taking far lateral biopsies or taking an individualized number of biopsy cores depending on the patient's age and the size of his prostate. Also, the concept of taking additional transition zone biopsies has been discussed, as McNeal et al. [6] could show that more than 20% of CaP originate in the transition zone only. Reissigl et al. [7] recently confirmed the data of McNeal et al. [6] (28% tumors originated in the transition zone only and would not have been detected by standard sextant biopsy). However, the rate of complications by performing additional biopsies has to be taken into consideration, as the biopsy procedure is performed in 65.6–82.1% on healthy men. In the following study, a ten-core biopsy protocol, including four biopsies from the transition zone – taken as a model for an extended biopsy protocol – was therefore evaluated regarding the complication rate. In all patients, a questionnaire was obtained relating to complications and personal discomfort.

Materials and Methods

Between September 1997 and June 1998, men who were referred for prostate biopsy were admitted to this prospective study after informed consent. Indications for prostate biopsy were an elevation in the serum PSA and/or a digital rectal examination (DRE) suspicious for CaP. A total of 162 consecutive men was evaluated. None of the patients had a history of open or transurethral prostate surgery or prior radiation therapy. In all cases, DRE was performed and classified as benign, benign enlargement or suspicious. For prophylactic

antibiotic treatment, ciprofloxacin (2×250 mg b.d.) was administered for 5 days, beginning 2 days before the procedure. Men with a known bleeding tendency were prepared according to the underlying disorder. Patients with urinary tract infections had their procedure postponed and received antibiotics corresponding to urinary culture and sensitivity testing. Careful counseling relative to the possible complications was carried out with special emphasis on the clinical importance of infectious side effects and the need for immediate treatment. Both oral and written consent was obtained. All men underwent real time transrectal ultrasound using a 7.5-MHz biplanar ultrasound probe (Siemens Versa®). Core biopsies were obtained by an automatic biopsy device (BiopsyGun®). From each lobe, five cores were taken: three ultrasound-guided cores from the peripheral zone (apex, mid-zone and base) and two from the transition zone. All tumors were classified according to the TNM classification of 1997 [8].

The clinical intra- and perioperative complications were documented. All patients were followed until complications disappeared. Ten to 12 days after the procedure a urinalysis was done. At the same time, a questionnaire was given to all the patients. The questionnaire related to clinical hematuria, hematospermia, rectal bleeding, fever, pain during the procedure and later discomfort. One of the objectives of the questionnaire was to determine the length of post-procedural discomfort following transrectal biopsy. The distribution of parameters was assessed using the Mann-Whitney test.

Results

Patient age ranged from 37 to 79 years (mean 63.4). Serum PSA levels were elevated in 141 patients (PSA ≥ 4 ng/ml; Abbott AxSym enzyme immunoassay). The mean PSA level was 13.5 ng/ml with a range from 0.4 to 210.0 ng/ml. DRE was suspicious for CaP in 66 patients.

Table 1. Influence of the number of biopsies in bleeding complications after transrectal biopsy of the prostate

Author, year	Patients	Cores	Hematuria %	Rectal bleeding, %	Hematospermia, %
Hodge et al. [15], 1989	251	mean 6.2	NR	1.2	NR
Vallencien et al. [16], 1989	167	1–2	25	12	3
Torp-Pedersen et al. [17], 1989	138	2–3	37	9.4	5
Gustafsson et al. [18], 1990	145	2–4	39.3	NR	46
Collins et al. [11], 1993	89	≥ 6	58	37.1	28.1
Aus et al. [13], 1993	391	1–5	13	2.8	9
Clements et al. [19], 1993	80	≤ 5	20	7.5	11.3
Hammerer and Huland [20], 1994	651	6	14	2	6
Niesel et al. [10], 1995	76	6	48	4	28
Enlund and Varenhorst [12], 1997	415	1–8 (mean 4)	49.6	21.7	NR
Rietbergen et al. [2], 1997	1,687	6–7	23.6 ^a	1.7	45.3
Present series, 2000	162	10	17.9 ^a	4.9	19.8

NR = Not reported.

^a Hematuria for more than 3 days.

From each of the 162 patients, ten-core biopsies were obtained. In all but 1 patient, the biopsies were performed without general anesthesia on an outpatient procedure. The patients reported no or only minimal discomfort during the procedure. Histological examination revealed the diagnosis of CaP in 52 of the 162 patients (32.1%). Tumor stages were classified as T1c (n = 10), T2 (n = 24), T3 (n = 15), and T4 (n = 3) according to the 1997 TNM classification [8]. Of the T2 cancers (according to the TNM classification) 15 had a positive DRE while 9 had a normal DRE but a suspicious lesion in TRUS.

The complications of the procedure are specified in tables 1–3. In 2 cases, severe macroscopic hematuria had to be treated by an indwelling catheter for 1 or 2 days. No bleeding necessitating blood transfusion occurred. Minor (macroscopic) hematuria was present in 68.5% of the patients; in 17.9% of these cases hematuria persisted for more than 3 days (table 2) and 4.9% of the patients had hematuria for more than 7 days. Thirty-two patients developed hematospermia (19.8%). Minimal rectal bleeding was noted in 4.9%. Surgical intervention was not required in any case. Urinary retention did not occur,

while 24 patients (14.8%) reported a temporarily obstructed micturition. Infectious complications such as septicemia (n = 0) or fever (>38.5°C; n = 1) were rare.

Ten to 12 days after this procedure, no patient had urinary tract infection (positive urine culture). The analysis of complications did not reveal significantly more complications in the group of patients with CaP than in men with a benign histology.

Discussion

PSA screening for prostate cancer led to a rapid increase in the numbers of prostate biopsies performed in the last years. For 1998, Landis et al. [9] estimated 184,500 new cases of CaP in the United States based on the Surveillance, Epidemiology and End Results data of the National Cancer Institute. Regarding the detection rate of the screening studies already mentioned above, in the United States the number of prostate biopsies performed can be estimated to be two- to threefold higher. This fact leads to the question of the morbidity of this diagnostic procedure, especially if the number of cores taken is increased. Although important improvements were made in the biopsy technique, e.g. the use of Tru-Cut needles instead of Silverman needles, spring-loaded biopsy guns instead of hand proceeded needles and ultrasound instead of digitally guided biopsies, severe complications of prostatic biopsy do occur.

In the present series, severe bleeding was found in 2 of 162 patients (1.2%) which could be resolved by a short-term indwelling catheter. Similar results were reported by Niesel et al. [10], who performed sextant biopsy and had to insert indwelling catheters in 2.6% of their patients.

Table 2. Duration of hematuria after transrectal biopsy of the prostate

Duration of hematuria	n	%
0	51	31.5
1 day	37	22.8
2–3 days	45	27.8
4–7 days	21	13.0
≥8 days	8	4.9

Table 3. Influence of prophylactic antibiotic treatment and time of first application on the rate of clinical infection in patients with six or more biopsy cores

Author, year	Patients	Prophylactic antibiotic treatment	Time of first application hours before biopsy	Fever %	Septicemia %
Kilner et al. [21], 1995	98	N	–	9	NR
Hodge et al. [15], 1989	251	Y	1	0.8	NR
Collins et al. [11], 1993	89	Y	1	4.5	0
Hammerer and Huland [20], 1994	372	Y	1	0.5	NR
Rietbergen et al. [2], 1997	1,687	Y	2	4.2	0.2
Niesel et al. [10], 1995	76	Y	24	9.0	0
Sieber et al. [14], 1997	4,439	Y	24	0.07	0
Present series, 2000	162	Y	48	0.6	0

Y = Yes; N = no; NR = not reported.

Transfusion as a result of a major bleeding complication was never necessary after ten-core biopsies were taken. However, 17.9% of the patients reported minor bleeding such as hematuria for more than 3 days. This is in accordance with other studies on sextant biopsies, where hematuria was present in 14–58% of patients biopsied (table 1).

Theoretically, the number of cores taken should influence the rate of complications, as the risk for bleeding or infection should be the same for every single core. So the complication rate should increase with each additional core taken. Table 1 shows the results of studies with different numbers of cores taken and the reported bleeding complications. In contrast to the theoretical assumption, there is no obvious recognizable trend for more complications with increasing numbers of core biopsies (table 1). Hematuria ranges from 13 to 58%, the same wide range exists for rectal bleeding (1.2–37.1%) and hematospermia (3–46%). Besides other reasons, this may be due to different study designs and ultrasound probes used. Manufacturers provide ultrasound probes of various sizes, biopsy angles and needle sleeves. The angle for the

biopsy may in so far represent a potential risk factor, as narrow angles may result in a higher rate of bladder perforations in biopsies taken near the bladder neck. Furthermore, the needle sleeves may hold a possible risk for mucosal injury of the rectum.

Other important points are the infectious complications of transrectal prostatic biopsy. In this series, clinical infections were rarely seen, which is probably due to the antibiotic regimen of 5 days beginning 2 days prior to the procedure. So the rate of patients with fever (0.6%) was rather low, and no additional risk by the extended biopsy could be found in comparison to the literature.

The questionnaire filled out by all patients showed that discomfort as well as hematuria and hematospermia may last longer than 8 days in a considerable number of patients. It is therefore important to inform the patients prior to the treatment.

In conclusion, the extension of six- to ten-core biopsies did not lead to a recognizable increase in adverse effects or complications when compared with the data of sextant biopsy reported in the literature.

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