Indications for Extended 14-Core Transrectal Ultrasound-Guided Prostate Biopsy

Hiromi Uno, Masahiro Nakano, Hidetoshi Ehara, and Takashi Deguchi

OBJECTIVES We compared the cancer detection rate of extended 14-core biopsy with that of sextant biopsy to assess whether additional biopsy cores are useful for detection of prostate cancer and to clarify the indications for obtaining additional cores.

METHODS Study subjects were 313 patients who underwent transrectal ultrasound-guided 14-core biopsy because of a prostate-specific antigen (PSA) level greater than 4.0 ng/mL and/or abnormalities found on digital rectal examination (DRE). In addition to the standard 6 biopsy cores, 6 lateral cores were obtained as well as 2 transition zone cores. PSA density (PSAD) was determined as the total PSA level divided by the prostate volume as estimated by transrectal ultrasound.

RESULTS Prostate cancer was diagnosed in 127 patients (40.6%). In 28 (22%) patients, the cancer would not have been detected by the sextant method alone. Among 211 patients with normal DRE findings, the cancer detection rate with 14-core biopsy was statistically higher than that with 6-core biopsy in the 141 patients with a PSA level of 4.01 ng/mL to 10.0 ng/mL, and 14 (38.9%) of 36 cancers were diagnosed in additional cores only, not in the standard sextant biopsy cores. Among the 141 patients with a gray-zone PSA level, the cancer detection rate with extended biopsy was statistically higher in those with PSAD greater than 0.13 ng/mL.

CONCLUSIONS Lateral biopsy should be used in conjunction with sextant biopsy in patients with a PSA level of 4.01 ng/mL to 10.0 ng/mL with normal DRE findings, especially in those with PSAD greater than 0.13 ng/mL. UROLOGY 71: 23–27, 2008. © 2008 Elsevier Inc.

Prostate cancer can be diagnosed only by histologic confirmation of cancer in prostate tissues. Several investigators have argued that the sextant method reported by Hodge *et al.*[1] in 1989, i.e., obtaining prostate specimens from the base, midgland, and apex bilaterally in the midlobar parasagittal planes, misses 20% to 30% of clinically important prostate cancers.[2–5] Various biopsy strategies have been devised to improve the cancer detection rate, including sampling of additional cores from other areas of the prostate, especially the lateral regions.[6,7]

Although increasing the number of cores increases the cancer detection rate, concerns exist regarding the potential for increased pain and morbidity. Horninger *et al.*[8] noted increased pain with 14 versus 10 cores.

Patients with cancer who have a high prostate-specific antigen (PSA) level probably have a greater cancer volume, so extended biopsy specimens would not be needed in such cases. We obtained biopsy specimens from lateral regions of the prostate and the transition zone in addition to the sextant biopsy cores, and we analyzed the cancer detection rate to clarify the indications for obtaining additional biopsy specimens.

MATERIAL AND METHODS

Our prospective study involved 313 men who underwent transrectal 14-core ultrasound-guided biopsy at Hirano General Hospital or Gifu University Graduate School of Medicine in Japan between January 2002 and April 2005. The patients ranged in age from 45 to 88 years, with an average of 69.9 years. The numbers of patients aged 59 years or younger, 60 to 69 years, 70 to79 years, and 80 years or older were 30, 108, 142, and 33, respectively. The indication for biopsy was a PSA level greater than 4.0 ng/mL on Tandem-R assay and/or abnormal digital rectal examination (DRE) findings. We recommended biopsy for patients younger than 60 years with a PSA level between 2.5 ng/mL and 4.0 ng/mL or for patients with PSA velocity 0.75 ng/mL or greater per year. None of the patients had previously undergone prostate biopsy. Men who had clinical prostatitis develop within 1 month of biopsy or who had an active urinary tract infection were excluded from the study, as were those unable to tolerate the 14-core biopsy procedure. Internal review board approval was obtained, and all participants provided written informed consent.

From the Department of Urology, Hirano General Hospital, Gifu, and Department of Urology, Graduate School of Medicine, Gifu University, Gifu, Japan

Reprint requests: Hiromi Uno, M.D., Department of Urology, Hirano General Hospital, 176-5 Kurono, Gifu-city, Gifu 501-1192, Japan. E-mail: hgp-naik@jupiter.plala.or.jp

Submitted: December 21, 2006, accepted (with revisions): September 13, 2007

0090-4295/08/$34.00
doi:10.1016/j.urology.2007.09.020

Table 1. Patient characteristics

	Overall n = 313	With Cancer n = 127 (40.6%)	Without Cancer n = 186 (59.4%)	*P* Value
Mean age (yr)	69.9 (45–88)	71.8 (51–88)	68.7 (45–88)	0.00071
Mean PSA (ng/mL)	23.8 (0.477–2000)	47.2 (2.03–2000)	7.7 (0.477–28.59)	0.00385
Mean prostate volume (mL)	40.4 (7.9–353)	32.1 (7.9–87.9)	46.1 (13.7–353)	<0.0001
Mean PSAD	0.57 (0.026–28.82)	1.13 (0.079–28.82)	0.19 (0.026–0.993)	<0.0001
No. DRE abnormalities	102 (32.6%)	65 (51.2%)	37 (19.9%)	—

PSA = prostate-specific antigen; PSAD = prostate-specific antigen density; DRE = digital rectal examination.

All patients were given fluoroquinolone antibiotics for 3 days, starting on the day of biopsy. A cleansing enema was administered before the biopsy. Biopsy specimens were obtained with patients in the lithotomy position under sacral anesthesia (10 mL of 1% lidocaine). Procedures were well tolerated, and there was no need for intravenous sedation. After DRE, transrectal ultrasound was performed, and prostate volume was calculated according to the formula for the volume of a prostate spheroid: $\pi/6 \times (\text{major axis}^2 \times \text{minor axis})$.[9] PSA density (PSAD) was determined as the ratio of the total PSA level to the ultrasonographically estimated prostate volume.

Prostate cores were obtained with an automatic spring-loaded 18-gauge needle driven by a Magnum Biopsy gun (CR Bard, Inc, Covington, Ga) under transrectal ultrasound guidance. We obtained 6 cores from the prostate in the midlobar parasagittal planes, halfway between the lateral edge and midline of the prostate gland, at the apex, mid-gland, and base, bilaterally.[1] Lateral biopsy was performed by obtaining 6 prostate cores from the lateral apex, mid-gland, and base, bilaterally, and bilateral transition zone biopsy was then performed. All prostate needle biopsy specimens were examined by the same pathologist. Tumor grade was assigned according to the Gleason grading system, and the number of cancer-positive cores was determined. Significant cancer was defined as a PSAD of 0.15 ng/mL or more, a Gleason score of 7 or greater, or 3 or more cancer-positive cores.[10] Clinical stage was determined according to the 2002 tumor-node-metastasis (TNM) classification system.[11]

Morbidity associated with 14-core biopsy was assessed. Major complication was defined as a complication requiring treatment; all other complications such as hematospermia, hematuria, and rectal bleeding were considered minor complications.

Differences in variables between patients with cancer and those without cancer were analyzed by unpaired *t* test. Difference in the cancer detection rate between biopsy methods was analyzed by chi-squared test. Statistical analyses were performed with Statview-J 5.0 for Windows (Abacus Concepts, Berkeley, Calif). A *P* value of less than 0.05 was considered statistically significant.

RESULTS

Of the 313 patients included in the study, 127 (40.6%) were found to have prostate cancer. Characteristics of patients with and without cancer are shown in Table 1. Patients with prostate cancer were significantly older than those with benign disease ($P = 0.00071$). Patients with prostate cancer had a significantly higher PSA level (47.2 ng/mL versus 7.7 ng/mL, $P = 0.00385$), greater PSAD (1.13 versus 0.19 ng/mL, $P < 0.0001$), and smaller prostate volume (32.1 versus 46.1 cm^3, $P < 0.001$) than patients with benign disease.

The cancer detection rates, clinicopathologic findings, and biopsy sites are shown according to PSA levels in Table 2. Biopsy positivity rates in patients with a PSA level 4.0 ng/mL or less, 4.01 to 10.0 ng/mL, 10.01 to 20.0 ng/mL and greater than 20.0 ng/mL were 17.2%, 30.4%, 50.9%, and 82.6%, respectively. The incidences of localized disease (T2 or less) in relation to these PSA levels were 100%, 98.2%, 86.2%, and 39.5%, respectively. Distant metastases were found in 2 patients with a gray-zone PSA level and in 7 patients with a PSA level greater than 20.0 ng/mL. Sites of cancers detected by 14-core biopsy are shown in Table 2. If the sextant method had been used without obtaining prostate cores from the far lateral region or transition zone, 24 cancers in the far lateral region, 3 cancers in the far lateral region and transition zone, and 1 cancer in the transition zone would not have been detected. That is, 28 (22%) cancers would not have been detected if only sextant biopsy had been performed. Gleason scores in these 28 cases were as follows: 8 in 3 cases, 7 in 7 cases, 6 in 12 cases, 5 in 2 cases, and 4 in 4 cases. Twenty-three (82.1%) of the 28 patients were shown to have significant cancer. Cancer detection rates of 14-core biopsy and those of sextant biopsy are shown according to DRE findings in Table 3. Among 211 patients with normal DRE findings, cancer detection rates in relation to the various PSA levels with 14-core biopsy were higher than those with 6-core biopsy. Among the 141 patients with a PSA level of 4.01 ng/mL to 10.0 ng/mL, 36 (25.5%) cancers were detected, and 14 (38.9%) cancers were diagnosed in additional cores only, not in the standard sextant biopsy cores. The cancer detection rate with 14-core biopsy in patients with a gray-zone PSA level was statistically higher than that with 6-core biopsy. Eighteen patients with PSA 4.0 or less underwent biopsy, 12 patients aged 69 or younger, and 6 patients aged 70 or older with a PSA velocity of 0.75 ng/mL or greater per year. Among the 22 cancer patients with a PSA level greater than 10 ng/mL, 17 (77.3%) cancers were diagnosed by the standard sextant biopsy method. We compared cancer detection rates according to PSAD among the 141 patients with a PSA level of 4.01 ng/mL to 10.0 ng/mL, and the cancer detection rate of extended biopsy was statistically higher in those with PSAD greater than 0.13 ng/mL. Among the 102 patients with abnormal DRE findings, cancer detection rates of 14-core biopsy and those of sextant biopsy according to the various PSA