Extended Sampling at First Biopsy Improves Cancer Detection Rate: Results of a Prospective, Randomized Trial Comparing 12 Versus 18-Core Prostate Biopsy

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Purpose: We determined whether increasing the number of cores at first prostate biopsy would improve the cancer detection rate without increasing the detection of clinically insignificant tumors.

Materials and Methods: From January 2009 to January 2010 patients scheduled for prostate biopsy were randomized to 12 or 18-core sampling. Study inclusion criteria were 1) age 45 to 75 years, 2) abnormal digital rectal examination and/or prostate specific antigen 4 to 20 ng/ml, and 3) no previous biopsy. The primary end point was the cancer detection rate. Secondary end points were clinically insignificant cancer detection and morbidity.

Results: A total of 150 patients were enrolled in the study. Preoperative variables were similar in the 2 groups of 75 patients each. Cancer was detected in 23 patients (30.7%) in group 1 and in 36 (48%) in group 2 (p = 0.02). More cases of insignificant cancer were detected in group 2 (p not significant). In men with prostate volume 65 cc or less the detection rate was 30.9% in group 1 and 52.8% in group 2 (p = 0.02). In men with prostate specific antigen 10 ng/ml or less the detection rate was 19.6% in group 1 and 38.4% in group 2 (p = 0.03). Two group 2 patients (5.5%) were diagnosed based on additional samples but the diagnosis corresponded to insignificant cancer. There was no statistically significant difference in morbidity.

Conclusions: The 18-core protocol improves prostate cancer detection without increasing morbidity. Results suggest that the 12-core biopsy protocol is adequate for prostate cancer detection at first biopsy.

Key Words: prostate; prostatic neoplasms; biopsy, needle; ultrasonography; diagnosis

SINCE the advent of PSA, transrectal ultrasound guided prostate biopsy has become the cornerstone for the early diagnosis of PCa. For many years the sextant technique (6 cores) was used until it was noted that this technique underestimates CDR by 10% to 30% and additional, far lateral peripheral zone samples were needed to improve detection.[1,2] Also, some groups have investigated whether biopsying the transition zone increases diagnostic accuracy at first biopsy. However, this strategy only improves CDR in 0.5% to 3.0% of cases and is not recommended in the initial setting.[3]

The refinement in prostate biopsy techniques along with widespread PSA measurement has led to significant

stage migration. However, PCa diagnosis continues to be a challenge since almost 50% of patients have Gleason 7 disease and up to 10% have high grade PCa, ie Gleason 8 or higher, in large prostatectomy series.[4,5]

The optimal number of cores is still controversial. In recent years with the aim of standardizing this issue several studies have been published. Nevertheless, only a few series have a prospective, randomized design and most included patients with previous biopsies.[6] Currently groups at a significant number of centers perform the extended sextant technique, comprising 6 samples of the medial peripheral zone plus 6 of the far lateral peripheral zone. Despite technical modifications the rate of false-negative results is still substantial.

Some factors, including patient age, PSA and PV, have an important role in CDR. For example, there is a significant inverse relationship between PV and PCa detection. These issues motivated the development of nomograms to establish the optimal number of samples according to PV and patient age.[7,8]

We prospectively determined whether increasing the number of cores at first prostate biopsy by incorporating additional samples from the far lateral peripheral zone would improve the diagnostic accuracy of the extended sextant technique without increasing the detection of clinically insignificant tumors in a nonscreened cohort of patients.

MATERIALS AND METHODS

After obtaining approval from the institutional committee of biomedical investigation in humans at our institution we started a prospective, randomized trial to determine the PCa detection rate of 12 vs 18-core sampling at initial prostate biopsy (International Standard Randomized Controlled Trial No. 65812524). Men undergoing a first transrectal ultrasound guided prostate biopsy from January 2009 to January 2010 were enrolled in this study. All participants read and provided signed informed consent before enrolling.

Study inclusion criteria were 1) age 45 to 75 years, 2) abnormal digital rectal examination and/or PSA 4 to 20 ng/ml, and 3) no previous prostate biopsy. Exclusion criteria were 1) previous PCa diagnosis, 2) PSA greater than 20 ng/ml, 3) clinical stage T3 or T4 and 4) previous 5α-reductase inhibitor use (finasteride or dutasteride) or androgen deprivation therapy. A total of 75 patients each who met study inclusion criteria were randomly assigned to group 1 with a 12-core biopsy protocol and group 2 with an 18-core biopsy protocol. Randomization was based on closed envelopes created before the trial started with each protocol equally represented. Anticoagulant use was interrupted before the procedure according to institutional anticoagulant clinic guidelines.

The preoperative preparation used at our department was previously reported.[9] Briefly, a cleansing enema was indicated 12 and 3 hours before the procedure. Antibiotic

prophylaxis with a single intravenous dose of piperacillin/tazobactam (4/0.5 gm) was administered 15 minutes before biopsy. All procedures were done with the patient under mild intravenous sedation on an outpatient basis.

After PV was calculated using the ellipsoid formula an 18 gauge needle with an automatic biopsy gun was used to obtain the prostatic tissue. Initial sampling consisted of 6 cores from each lateral lobe in standard fashion in each study group. In group 2 another 3 samples were obtained from the far lateral peripheral zone of each lobe (see figure). Each tissue sample was placed in a separate container that identified the corresponding site to facilitate pathologist interpretation.

Our primary end point was CDR. As a secondary end point we evaluated PCa in additional samples (group 2). We also compared pain and the complication rate. Pain was evaluated by a visual analog scale and complications were assessed by a questionnaire completed 7 days after the procedure by all participants. We used the Clavien system to report complications.[10] On post hoc analysis we evaluated the detection rate of clinically insignificant PCa using the updated Epstein criteria.[11]

The total number of patients was estimated to be 150 to achieve 80.0% power, assuming a 30% PCa detection rate in group 1 and a 10% difference in the detection rate between the groups. For statistical analysis we used the chi-square and Student t tests to compare means and proportions. All analysis was done with StatView® for Windows® with results considered significant at p <0.05.

RESULTS

A total of 150 patients met study inclusion criteria and were enrolled in the study. Table 1 lists demographic characteristics. Preoperative variables were similar between the groups. Cancer was detected in 39.3% of participants. PCa was diagnosed in 23
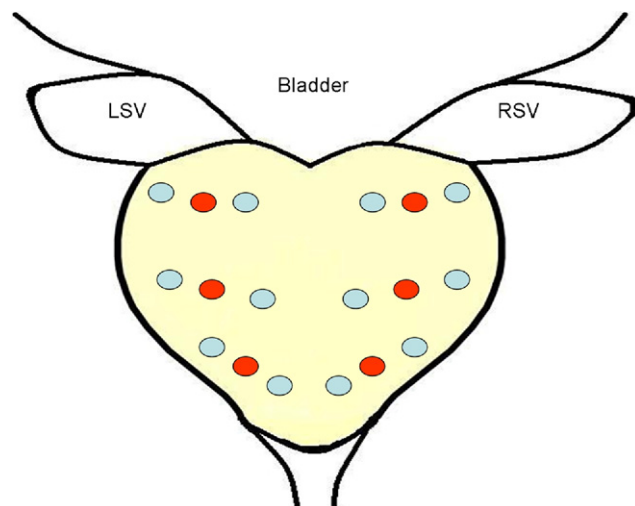
Peripheral zone sampling in 12-core (blue areas) and 18-core (blue and red areas) biopsy protocols. *LSV*, left seminal vesicle. *RSV*, right seminal vesicle.