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Retrospective Analysis of 5379 Cases of Template-Guided Transperineal Prostate Biopsy (Post-Print)

Authors: Du Jianhui, Yan Weigang, Mai Zhipeng, Zhou Yi, Zhou Zhi' en, Ji Zhigang

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Abstract

To investigate the accuracy and safety of template-guided transperineal prostate biopsy.

Methods A retrospective analysis was performed on clinical data from 5379 patients who underwent prostate biopsy at our center from November 2004 to January 2018. The patients' ages ranged from 14 to 89 years (mean 68.1 years). Serum tPSA levels ranged from 0.03 to 5000.00 ng/ml (mean 11.2 ng/ml). All patients underwent transrectal ultrasound-guided transperineal template-localized 11-zone prostate biopsy. The prostate biopsy positive rate and complications were analyzed.

Results Each patient received 1–4 cores per zone, with a total of 11–44 cores (mean 19 cores). The overall prostate cancer detection rate was 39.9%. Stratified by serum tPSA level, detection rates were 16.6% (46/277) for 0–4.0 ng/ml, 25.2% (525/2057) for 4.1–10.0 ng/ml, 34.1% (573/1680) for 10.1–20.0 ng/ml, 65.9% (673/1022) for 20.1–100 ng/ml, and 95.3% (327/343) for >100 ng/ml. Postoperative complications included hematuria in 42.1% of patients, acute urinary retention in 2.2%, and one case of septic shock. There were no deaths.

Conclusion Transrectal ultrasound-guided transperineal template-localized prostate biopsy is accurate and safe.

Full Text

Preamble

Title: Template-Guided Transperineal Prostate Biopsy: A Retrospective Analysis of 5,379 Cases

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Authors: Du Jian-hui, Yan Wei-gang, Mai Zhi-peng, Zhou Yi, Zhou Zhi-en, Ji Zhi-gang

Affiliation: Department of Urology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100730, China

Corresponding Author: Yan Wei-gang
Tel: 010-69152520, E-mail: yanwg111@126.com

Abstract

Objective: To investigate the accuracy and safety of transperineal template-guided prostate biopsy.

Methods: We retrospectively analyzed clinical data from 5,379 patients who underwent prostate biopsy at our center between November 2004 and January 2018. Patient age ranged from 14 to 89 years (mean 68.1 years), and serum total prostate-specific antigen (tPSA) levels ranged from 0.03 to 5,000.00 ng/ml (mean 11.2 ng/ml). All patients underwent transrectal ultrasound-guided transperineal template localization for 11-region prostate biopsy. Prostate cancer detection rates and biopsy-related complications were analyzed.

Results: Each patient received 1–4 cores per region, totaling 11–44 cores (mean 19 cores). The overall prostate cancer detection rate was 39.9%. Stratified by tPSA level, detection rates were 16.6% (46/277) for 0–4.0 ng/ml, 25.2% (525/2,057) for 4.1–10.0 ng/ml, 34.1% (573/1,680) for 10.1–20.0 ng/ml, 65.9% (673/1,022) for 20.1–100 ng/ml, and 95.3% (327/343) for >100 ng/ml. Postoperative complications included hematuria in 42.1% of patients, acute urinary retention in 2.2%, and one case of septic shock; no deaths occurred.

Conclusion: Transrectal ultrasound-guided transperineal template-guided prostate biopsy is an accurate and safe technique.

Keywords: prostate cancer; biopsy, transperineal; template

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1. Materials and Methods

1.1 Patient Data

A total of 5,379 patients were enrolled, with ages ranging from 14 to 89 years (mean 68.1 years). Total prostate-specific antigen (tPSA) levels ranged from 0.03 to 5,000.00 ng/ml (mean 11.2 ng/ml), and prostate volume ranged from 14 to 450 ml (mean 45 ml). Biopsy was indicated if patients met any of the following criteria: (1) tPSA >4 ng/ml; (2) palpable prostate nodule on digital rectal examination (DRE); or (3) suspicious nodule detected on ultrasound or MRI.

Exclusion criteria included: (1) prior prostate biopsy; (2) confirmed history of prostate cancer; (3) prior endocrine therapy for suspected prostate cancer; and (4) urinary tract infection, bleeding disorders, or severe cardiovascular disease.

1.2 Methods

Equipment: The AccuSeed localizer with targeting guidance, localization frame, and puncture template (part of a prostate brachytherapy system) was provided by Computerised Medical System (CMS), USA. SONOLINE Adara SLC digital enhanced ultrasound with a transrectal biplane probe was provided by Siemens, Germany. Bard 18G disposable automatic biopsy devices (USA) were used.

Biopsy Procedure: All 5,379 procedures were performed in outpatient operating rooms. Patients were placed in lithotomy position, and DRE was performed to assess prostate consistency and detect nodules. Among all cases, 803 (14.9%) received intravenous anesthesia, while 4,576 (85.1%) received local anesthesia with 1% lidocaine infiltrated from the perineum to beneath the prostate capsule. Transrectal ultrasound (TRUS) was used to identify suspicious prostate lesions and measure prostate volume, calculated as height $\times$ width $\times$ length $\times$ 0.52 (ml). Transperineal template-guided 11-region prostate biopsy was performed using our previously reported method [Figure 1: see original paper]. Biopsy specimens from different locations were sent for pathological examination separately.

Based on prostate anatomy, we defined the area anterior to the urethra as the anterior prostate zone and the area posterior to the urethra as the posterior prostate zone. In our 11-region biopsy scheme, positivity in any of regions 1, 2, 9, or 10 indicated anterior zone involvement; positivity in regions 4, 5, 6, or 7 indicated posterior zone involvement. Regions 3 and 8 are adjacent to the urethra, and region 11 represents the prostate apex; these were not classified into anterior or posterior zones [4].

Definitions: DRE positivity was defined as detection of a palpable prostate nodule. Prostate cancer Gleason scores and prognostic grade groups were determined according to the 2014 International Society of Urological Pathology (ISUP) Consensus Conference: Grade 1 (Gleason score 6), Grade 2 (Gleason score 3+4=7), Grade 3 (Gleason score 4+3=7), Grade 4 (Gleason score 8), and Grade 5 (Gleason score >9) [5]. Clinically insignificant prostate cancer was defined as Gleason 3+3 (Grade 1), while clinically significant prostate cancer was defined as Gleason 3+4 (Grade 2) or higher [6].

Perioperative Management: None of the 5,379 patients received bowel preparation or preoperative antibiotics. Postoperatively, all patients received oral levofloxacin 0.5 g daily for three days. Anticoagulant and antiplatelet medications (warfarin, clopidogrel, aspirin, etc.) were not discontinued before or after the procedure.

Statistical Analysis: SPSS 19.0 software was used for data analysis. Chi-

square tests compared rates, and multivariate logistic regression analyzed correlations between risk factors and biopsy positivity, calculating odds ratios (OR), 95% confidence intervals (CI), and P-values. P<0.05 was considered statistically significant.

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2. Results

Among 5,379 patients, 1,585 (29.5%) had abnormal DRE. Each patient received 1–4 cores per region, totaling 11–44 cores (mean 19 cores). Mean procedure duration was 32 minutes. Pathological results revealed prostate cancer in 2,144 cases (39.9%), benign prostatic tissue or hyperplasia in 2,664 (49.5%), chronic prostatitis in 362 (6.7%), atypical small acinar proliferation in 118 (2.2%), high-grade prostatic intraepithelial neoplasia in 73 (1.4%), and other pathologies in 18 (0.3%, including 5 cases of urothelial carcinoma, 3 rhabdomyosarcomas, 2 schwannomas, 2 small cell carcinomas, 2 fibroblastomas, 1 tuberculosis, and 3 metastatic cancers).

Prostate biopsy positivity rates stratified by tPSA level, prostate volume, age, and DRE results are shown in . The detection rate of clinically significant prostate cancer (Grade 2 or higher) across different volume intervals was 66.9% (91/136), 65.9% (778/1,181), 68.1% (410/602), and 61.3% (138/225), respectively, with no significant difference (^{2}=3.429, P=0.330). In DRE-positive patients, biopsy positivity rates across tPSA intervals (0–4, 4.1–10, 10.1–20, 20.1–100, >100 ng/ml) were 21.7% (18/83), 52.6% (159/302), 67.3% (222/330), 88.2% (488/553), and 96.2% (305/317), respectively. In DRE-negative patients, corresponding rates were 14.4% (28/194), 20.9% (366/1,752), 25.9% (351/1,353), 39.4% (185/469), and 84.6% (22/26).

Multivariate logistic regression identified significant correlations with biopsy positivity: tPSA (OR=1.016, 95% CI 1.013–1.018, P<0.01), prostate volume (OR=0.964, 95% CI 0.960–0.968, P<0.01), age (OR=1.070, 95% CI 1.062–1.079, P<0.01), number of cores (OR=1.056, 95% CI 1.040–1.073, P<0.01), and DRE positivity (OR=0.227, 95% CI 0.194–0.266, P<0.01). Higher tPSA, smaller prostate volume, older age, more biopsy cores, and positive DRE were associated with higher detection rates.

All 2,144 biopsy-positive patients underwent Gleason scoring. Distribution was: Gleason 6 in 33.9% (727/2,144), Gleason 7 (3+4) in 19.6% (420/2,144), Gleason 7 (4+3) in 17.7% (379/2,144), Gleason 8 in 11.9% (256/2,144), Gleason 9 in 14.9% (319/2,144), and Gleason 10 in 2.0% (43/2,144). Mean Gleason score was 7.5 in DRE-positive patients (n=1,192) versus 6.7 in DRE-negative patients (n=952). Among all positive cases, 727 (33.9%) had clinically insignificant prostate cancer, while 1,417 (66.1%) had clinically significant disease.

Region-specific positivity rates were: region 1: 46.8% (1,003/2,144), region 2: 46.2% (991/2,144), region 3: 48.9% (1,048/2,144), region 4: 50.7% (1,086/2,144),

region 5: 52.1% (1,116/2,144), region 6: 52.4% (1,124/2,144), region 7: 50.7% (1,088/2,144), region 8: 49.2% (1,055/2,144), region 9: 48.9% (1,048/2,144), region 10: 49.7% (1,066/2,144), and region 11: 58.6% (1,257/2,144).

Complications occurred as follows: mild gross hematuria in 2,262 patients (42.1%), resolving within 3-7 days with increased fluid intake; severe gross hematuria in 48 (0.9%), requiring catheterization or continuous bladder irrigation. Acute urinary retention occurred in 115 patients (2.2%): 92 (1.7%) were managed successfully with 1-week catheterization, while 23 (0.4%) required transurethral resection of the prostate (BPH diagnosis) and 1 required 2-month catheterization (prostate cancer diagnosis). Hematospermia occurred in 312 patients (5.8%) and perineal hematoma in 22 (0.4%), both resolving without intervention. One elderly patient with chronic indwelling catheter developed septic shock (E. coli infection) and recovered with aggressive treatment. No rectal bleeding or deaths occurred.

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3. Discussion

Since Hodge et al. [7] introduced TRUS-guided transrectal 6-core biopsy in 1989, this approach has remained the mainstream method for prostate biopsy. Both the American and European Urological Associations recommend transrectal biopsy as the standard technique, with transperineal biopsy as a useful alternative [8]. Studies by Taira et al. [9] and Ding et al. [10] demonstrated that transperineal template-guided biopsy effectively improves early prostate cancer detection compared to conventional methods.

The comparative detection rates between transperineal and transrectal approaches remain a hot topic. Ex vivo simulations [11] and in vivo comparisons of simultaneous transperineal and transrectal 6-core biopsies [12] have shown significantly higher positivity rates with the transperineal approach, suggesting superior accuracy. However, other studies report similar detection rates between the two methods [13-16]. Our transperineal template-guided biopsy achieved a 39.9% detection rate, higher than our center' s 28.0% (68/243) rate with transrectal 6-core biopsy from 2002–2003 and higher than the 29.8% reported for transrectal approaches internationally [17]. Our findings also confirm that higher tPSA, smaller prostate volume, older age, more biopsy cores, and positive DRE correlate with higher detection rates, consistent with our previous studies and international literature [18-20].

Although prostate volume inversely correlated with overall biopsy positivity, the detection rate of clinically significant prostate cancer showed no significant difference across volume intervals (^{2}=3.429, P=0.330). This contrasts with Zhu' s [21] findings that smaller prostates harbor higher-grade, more aggressive tumors. This discrepancy likely stems from limitations in multicenter data with relatively small case numbers and fewer biopsy cores (some using 6-core methods). Fewer cores increase the likelihood of missing clinically significant tumors

in larger prostates, artificially reducing detection rates in higher-volume glands. Digital rectal examination remains important for prostate cancer detection and significantly affects biopsy positivity. In our study, DRE positivity alone yielded a 75.2% (1,192/1,585) detection rate, higher than the 41.1% (2,098/5,102) rate for abnormal tPSA alone (>4 ng/ml). Combining DRE positivity with tPSA >4 ng/ml increased the detection rate to 78.2%. Lee et al. [22] reported similar findings: 59.2% detection with DRE positivity alone, increasing to 69.9% when combined with tPSA >4 ng/ml. Notably, DRE-positive patients had higher mean Gleason scores than DRE-negative patients (7.5 vs 6.7), suggesting that DRE-positive cancers may be more pathologically aggressive with worse prognosis.

Traditional views suggest 20–30% of prostate cancers involve the anterior zone [23], but our study found anterior zone involvement in 81.2% (1,741/2,144) of cases, indicating superior anterior zone detection with transperineal biopsy. International studies confirm that transperineal approaches improve anterior zone access [24]. Among 327 patients with anterior zone cancers, 41.6% (136/327) had clinically significant disease, significantly lower than the 49.5% (157/317) rate in the posterior zone (P=0.043). These findings align with Japanese pathological studies by Sato et al. [25] of radical prostatectomy specimens, which found clinically significant cancer rates of 15.7% (13/83) in purely anterior tumors versus 28.8% (21/73) in purely posterior tumors (P=0.048), validating the accuracy of template-guided transperineal 11-region biopsy for assessing high-grade tumors in both zones.

Most importantly, transperineal template-guided biopsy demonstrates low complication rates. Minor, self-limiting bleeding is the most common complication regardless of approach [26]. In our series, hematospermia occurred in 5.8% and mild hematuria in 42.1% of patients, all resolving without intervention. Acute urinary retention rates for transperineal biopsy (1.7–11.1%) are slightly higher than transrectal approaches [27-29]; our rate was 2.2% (115 patients), with most (92 cases, 1.7%) managed successfully with catheterization alone. Chung et al. [30] demonstrated that perioperative alpha-blockers reduce post-biopsy urinary symptoms and retention, suggesting a strategy to decrease these complications. Regarding sepsis, transperineal biopsy carries significantly lower risk than transrectal biopsy [3]. Rectal bleeding, common in transrectal biopsy (1.3-45%), was completely absent in our series, and no anticoagulant medications were discontinued preoperatively—a clear advantage of the transperineal approach. Transrectal biopsy increases infection risk by allowing enteric bacteria to enter the bloodstream during specimen acquisition [31,32].

However, transperineal template-guided biopsy under local anesthesia has limitations, including longer procedure time, specialized equipment requirements, and greater patient tolerance demands. Beyond the inherently longer procedure, unexpected patient discomfort during local anesthesia can further extend operative time. While perineal puncture pain during local anesthesia represents the most significant discomfort, international literature confirms that local anesthe-

sia is appropriate for transperineal biopsy [33], a finding supported by our study where 85.1% (4,576 cases) were completed successfully under local anesthesia. General anesthesia remains an option for less tolerant patients.

In conclusion, template-guided transperineal 11-region prostate biopsy is effective and safe. While multiparametric MRI and MRI-TRUS fusion-guided targeted biopsy are increasingly adopted, systematic saturation biopsy remains irreplaceable. Studies by Borkowetz et al. [34] and Mendhiratta et al. [35] demonstrated that combining targeted biopsy with systematic saturation biopsy increases detection of clinically significant prostate cancer by an additional 14–17%, highlighting the necessity of systematic sampling. Transperineal biopsy may ultimately replace transrectal biopsy as the new "gold standard"for prostate biopsy.

Figure 1: Puncture needle and localization template for template-guided transperineal prostate biopsy

Table 1: Prostate biopsy positivity rates by tPSA level, prostate volume, age, and digital rectal examination (DRE) results

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