Original Study

# A Prospective Randomized Trial Comparing the Vienna Nomogram and a Ten-Core Prostate Biopsy Protocol: Effect on Cancer Detection Rate

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## Abstract

**We performed a prospective randomized study of men undergoing prostate biopsy randomized to a Vienna nomogram protocol (group A) or a 10-core protocol (group B). The results suggest that the use of the Vienna nomogram does not significantly increase the overall cancer detection rate compared with a 10-core biopsy scheme. Further prospective randomized studies, with adequate sample sizes, are needed to definitively determine the best prostate biopsy protocol.**

**Background:** We evaluated whether the Vienna nomogram increases the detection rate of transrectal ultrasound-guided prostate biopsy compared with a 10-core biopsy protocol. **Patients and Methods:** In the present prospective randomized study, men eligible for prostate biopsy were randomized to a Vienna nomogram protocol (group A) or a 10-core protocol (group B). They were further stratified according to age ($\leq 65$, $> 65$ but $\leq 70$, and $> 70$ years) and prostate volume ($\leq 30$, $> 30$ but $\leq 50$, $> 50$ but $\leq 70$, and $> 70$ $cm^3$). The cancer detection rate (CDR) was compared between the groups by logistic regression analysis, with adjustment for age as necessary, overall and with age and prostate volume stratification. Additional statistical analysis was performed with Fisher's exact test for contingency tables and the Mann-Whitney *U* test for 2 independent samples. $P < .05$ was considered statistically significant. A subgroup analysis was performed for patients with serum prostate-specific antigen levels of 2 to 10 ng/mL. **Results:** From January 2009 to July 2010, 456 patients were enrolled, 237 to the Vienna nomogram group and 219 to the 10-core group. No significant differences were found in serum prostate-specific antigen or prostate volume between the 2 groups. Multivariate analysis with adjustment for age revealed no significant differences in CDR, with 42.6% in group A and 38.4% in group B ($P = .705$). When stratified by age and prostate volume, no statistically significant differences were found in the CDR between the groups in all subclasses. Also, in the subgroup analysis, CDR was not significantly different, 37.9% versus 34.7% for groups A and B, respectively ($P = .891$). **Conclusion:** These results study suggest that the use of the Vienna nomogram does not significantly increase the overall CDR compared with a 10-core biopsy scheme. Further prospective randomized studies, with adequate sample sizes, are needed to definitively determine the best prostate biopsy protocol.

*Clinical Genitourinary Cancer,* Vol. ■, No. ■, ■-■ 
**Keywords:** Nomograms, Prostate biopsy, Prostate cancer, Prostatic neoplasms, Ultrasonography

## Introduction

Transrectal ultrasound (TRUS)-guided prostate biopsy remains the standard for prostate cancer diagnosis. Sextant biopsy has been the standard protocol for many years, since its introduction in 1989 by Hodge et al.[1] However, these protocols miss 15% to 30% of cancers, leading to a varying number of repeat biopsies.[2]

Several studies have been addressed the question of whether we could enhance the cancer detection rate (CDR) by increasing the

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Submitted: Feb 6, 2016; Accepted: Jun 5, 2016

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1558-7673/$ - see frontmatter 
http://dx.doi.org/10.1016/j.clgc.2016.06.003

number of biopsy cores. In a systematic review, Eichler et al[3] concluded that increasing the number of biopsy cores improved cancer detection, including 12 cores, with laterally directed cores detecting 31% more cancer than the standard sextant protocol. In contrast, the CDRs decrease with an increasing prostate volume.[4] Uzzo et al[5] found that using sextant biopsies, the CDR was 23% in prostates $> 50$ cm$^3$ and 38% in prostates $< 50$ cm$^3$ ($P < .01$).[5] These conclusions led to the creation of nomograms defining the number of cores to be extracted for a specific patient according to the patient's age and prostate volume.[6,7]

In 2005, Remzi et al[7] introduced the Vienna nomogram, which defined the number of cores to be obtained in a prostate biopsy in relation to patient age and prostate volume in patients with a serum prostate-specific antigen (PSA) level of 2 to 10 ng/mL.[7] They compared a group of patients who had undergone TRUS-guided biopsies according to the Vienna nomogram in a prospective manner with a retrospective group of patients who had undergone an 8-core biopsy protocol. The Vienna nomogram increased the detection rate by 66.4% (36.7% vs. 22.0%; $P = .002$). That study had some important limitations. It was not a prospective randomized study, and the 2 groups were significantly different in terms of age, PSA level, and digital rectal examination findings.

Since the original Vienna nomogram report, only 1 prospective randomized study addressing this issue was published in 2010.[8] That study compared the Vienna nomogram with an 8-core biopsy scheme and showed no significant difference in CDRs between the 2 groups, questioning the findings of the original validation study.[8]

In the present study, we sought to determine whether the Vienna nomogram increases the detection rate of TRUS-guided prostate biopsies by conducting a prospective randomized trial comparing the Vienna nomogram with a 10-core biopsy protocol.

## Patients and Methods

The present study was a single-center, prospective, randomized, parallel group study of men eligible for TRUS-guided prostate biopsy. The inclusion criteria were suspicious digital rectal examination findings, an elevation of serum PSA level, or TRUS imaging findings suspicious for prostate cancer. The exclusion criteria were active urinary tract infection, documented previous pathologic prostatitis, a history of urinary retention, and recent lower urinary tract surgery.

The study was performed at the Urology Department of Santa Maria Hospital (tertiary referral center), Lisbon Faculty of Medicine, Portugal, and was approved by the joint ethics committee for health for the Lisbon Faculty of Medicine and Santa Maria Hospital. The ethics committee of Santa Maria Hospital/Lisbon Faculty of Medicine approved the present study, which was authorized by the board of directors of the same institution (authorization no. 0208; ClinicalTrials.gov identifier, NCT01752140; the full protocol can be accessed at http://www.clinicaltrials.gov). The study period was defined to 18 months of enrollment because of local logistic determinants.

After appropriate written informed consent, the patients were randomized (simple randomization) by an urologist of the department, using computer-generated random numbers, to a TRUS-guided biopsy with a Vienna nomogram-defined number of cores (group A; Table 1) or a 10-core protocol (group B). In the latter group, the 10 cores were directed at the peripheral zone, 2 cores at each base, 2 at each middle third, and 1 at both apexes. In the former group, the cores were also limited to the peripheral zone.

On the day before the procedure, all patients were given a 7-day 500 mg ciprofloxacin twice-daily prophylactic antibiotic course and potassium citrate micro-enemas on the morning of the procedure. Local vascular bundle anesthesia with 2% lidocaine was performed using a 22-gauge Chiba needle. The prostate volume was measured using TRUS before biopsy, which was performed by a urologist with TRUS-guided prostate biopsy experience. A Hitachi Vision 5500 ultrasound system was used, with a biplanar 7-MHz transrectal probe.

The primary endpoint was the comparison of prostate CDRs between the 2 groups. In a secondary analysis, both groups were further stratified by age ($\leq 65$, $> 65$ but $\leq 70$, and $> 70$ years) and prostate volume ($\leq 30$, $> 30$ but $\leq 50$, $> 50$ but $\leq 70$, and $> 70$ cm$^3$) and the detection rates were compared in each subclass. Another secondary endpoint was the Gleason score concordance between the biopsy and radical prostatectomy specimens, for those who chose this treatment modality.

Because the Vienna nomogram was originally studied only for serum PSA values between 2 and 10 ng/mL, we performed a subgroup analysis of these patients using all the previously mentioned parameters.

The data were prospectively collected and registered in the study forms. Subsequently, the data were entered in a computer database. Statistical analysis was performed on using IBM SPSS, version 20, with the Mann-Whitney $U$ test for independent samples. The primary endpoint was analyzed with multivariate logistic regression after controlling for age. The secondary endpoints were analyzed using univariate logistic regression for age stratification, with multivariate logistic regression analysis with adjustment for age for volume stratification and Fisher's exact test for Gleason score concordance (significance level, 5%).

## Results

From January 2009 to July 2010, 456 patients were included in the present study, 237 (52.0%) of whom were randomized to the Vienna nomogram group (group A) and 219 (48.0%) to the 10-core group (group B). The patient characteristics and results of the study are listed in Table 2. No significant differences were found in PSA level or prostate volume between the groups, although the median age was greater for the Vienna nomogram group. The CDR was greater for the Vienna nomogram group than for the 10-core

**Table 1** Vienna Nomogram

| Prostate Volume (cm$^3$) | Age (Years) | | | |
|---|---|---|---|---|
| | <50 | 50-60 | 60-70 | >70 |
| 20-29 | 8 | 8 | 8 | 6 |
| 30-39 | 12 | 10 | 8 | 6 |
| 40-49 | 14 | 12 | 10 | 8 |
| 50-59 | 16 | 14 | 12 | 10 |
| 60-69 | – | 16 | 14 | 12 |
| >70 | – | 18 | 16 | 14 |