available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Prostate Cancer

Prospective Evaluation of an Extended 21-Core Biopsy Scheme as Initial Prostate Cancer Diagnostic Strategy

Guillaume Ploussard [†,*], *Nathalie Nicolaiew* [†], *Charles Marchand, Stéphane Terry, Francis Vacherot, Dimitri Vordos, Yves Allory, Claude-Clément Abbou, Laurent Salomon, Alexandre de la Taille*

INSERM U955 Equipe 7, Departments of Urology and Pathology, CHU Henri Mondor, APHP, Créteil, France

Article info

Article history:
Accepted May 28, 2012
Published online ahead of print on June 9, 2012

Keywords:
Prostate cancer
Biopsy
Detection rate
Core number
Low risk
Insignificant

Abstract

Background: The debate on the optimal number of prostate biopsy core samples that should be taken as an initial strategy is open.
Objective: To prospectively evaluate the diagnostic yield of a 21-core biopsy protocol as an initial strategy for prostate cancer (PCa) detection.
Design, setting, and participants: During 10 yr, 2753 consecutive patients underwent a 21-core biopsy scheme for their first set of biopsy specimens.
Intervention: All patients underwent a standardized 21-core protocol with cores mapped for location.
Outcome measurements and statistical analysis: The PCa detection rate of each biopsy scheme (6, 12, or 21 cores) was compared using a McNemar test. Predictive factors of the diagnostic yield achieved by a 21-core scheme were studied using logistic regression analyses.
Results and limitations: PCa detection rates using 6 sextant biopsies, 12 cores, and 21 cores were 32.5%, 40.4%, and 43.3%, respectively. The 12-core procedure improved the cancer detection rate by 19.4% ($p = 0.004$), and the 21-biopsy scheme improved the rate by 6.7% overall ($p < 0.001$). The six far lateral cores were the most efficient in terms of detection rate. The diagnostic yield of the 21-core protocol was >10% in prostates with volume >70 ml, in men with a prostate-specific antigen level < 4 ng/ml, with a prostate-specific antigen density (PSAD) <0.20 ng/ml per gram. A PSAD <0.20 ng/ml per gram was the strongest independent predictive factor of the diagnostic yield offered by the 21-core scheme ($p < 0.001$). The 21-core protocol significantly increased the rate of PCa eligible for active surveillance (62.5% vs 48.4%; $p = 0.036$) than those detected by a 12-core scheme without statistically increasing the rate of insignificant PCa ($p = 0.503$).
Conclusions: A 21-core biopsy scheme improves significantly the PCa detection rate compared with a 12-core protocol. We identified a cut-off PSAD (0.20 ng/ml per gram) below which an extended 21-core scheme might be systematically proposed to significantly improve the overall detection rate without increasing the rate of detected insignificant PCa.

[†] These authors contributed equally to this article.
[*] Corresponding author. INSERM U955 Eq07, Department of Urology, CHU Mondor, 51 avenue du Maréchal de Lattre de Tassigny, 94000 Créteil, France. Tel. +33 149812254; Fax: +33 149812568.
E-mail address: g.ploussard@gmail.com (G. Ploussard).

0302-2838/$ – see back matter
http://dx.doi.org/10.1016/j.eururo.2012.05.049

1. Introduction

The optimal number of biopsy cores that should be taken as an initial biopsy strategy remains a controversial topic in the diagnosis of prostate cancer (PCa). Since its introduction by Hodge et al, random systematic ultrasound-guided transrectal needle biopsy has significantly improved the diagnosis of PCa in terms of detection rate and pathologic characterization of PCa before treatment decision making [1]. Studies have demonstrated that a traditional sextant technique may miss substantial numbers of PCas and that additional sampling of the lateral peripheral zone may increase the diagnostic yield [2–4]. To date, extended biopsy as defined by the National Comprehensive Cancer Network (sextant biopsies with at least four additional cores from the lateral peripheral zones) is clearly recommended at first biopsy [5,6]. However, the false-negative rate remains substantial. Several authors have already shown the benefit of saturation biopsies as an initial strategy [5,7–9], whereas other teams did not recommend saturation biopsies for cancer detection improvement [10–12]. One possible reason for these conflicting results is that accuracy of biopsy schemes depends on different parameters such as prostate volume, prostate-specific antigen (PSA) level, and digital rectal examination (DRE), suggesting the adaptation of the biopsy scheme to each individual patient [3]. The location of targeted cores (eg, far lateral peripheral zone) also must be taken into account.

The main end point of our long-term prospective trial was to study the detection rate of PCa according to the biopsy-core number. An intermediate analysis based on the first 1000 consecutive patients was published in 2007 [7]. We aimed to confirm, or not, these findings after a 10-yr follow-up and to perform subgroup analyses.

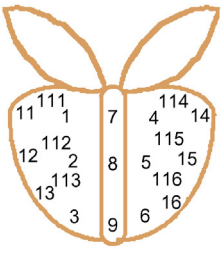
2. Materials and methods

Between December 2001 and December 2011, 2753 consecutive patients suspicious for PCa prospectively underwent an extended 21-core biopsy protocol as a first set of biopsies. Indications for prostate biopsy were (1) abnormal DRE, regardless of PSA level; (2) a PSA level >4 ng/ml (or 3 ng/ml in patients <60 yr); and (3) a free:total PSA ratio (%fPSA) <10%. All patients had undergone a standardized 21-core biopsy protocol as previously described [9]. Clinical stage was determined prior to biopsy by the same three experienced urologists who subsequently performed the biopsy procedure. Patients were given a fluoroquinolone antibiotic as prophylaxis and were prescribed enemas at 1 d and again at 3 h before the procedure. Three dedicated surgeons performed all biopsies. The 21-sample biopsy protocol included prostate ultrasound examination to evaluate the prostate volume using the prolate ellipsoid formula. All patients received local anesthesia by injection of 5 ml 2% lidocaine into each neurovascular bundle through a 22-G spinal needle. A 18-G biopsy needle and a spring-loaded biopsy gun that could collect 17-mm-long tissue cores were used. The biopsies were performed in the following order: six sextant biopsies (standard 45° angle), then three biopsies in each peripheral zone (80° angle), then three biopsies in each transition zone (TZ), and finally three biopsies in the midline peripheral zone (Fig. 1). Thus the six-core scheme included the sextant biopsies. The 12-core scheme added the six additional lateral peripheral biopsies. The 21-core scheme added the three midline cores and the six TZ cores. Each prostate core was given a specific number according to the biopsy protocol and mapped for location. Each core was placed in its own container and analyzed separately. Two senior uropathologists reviewed the cores.

Prebiopsy clinical and biologic data were abstracted from a computerized prospective database. Findings from pathologic assessment included the length of cores, the number of positive cores and their location, the percentage of cancer involvement in any positive core, and the biopsy Gleason score. Insignificant PCa was defined according to the Epstein criteria: PSA density (PSAD) ≤0.15 ng/ml per gram, Gleason score ≤6, fewer than three positive cores, and <50% cancer involvement in any core [13,14]. PCa eligible for active surveillance was defined according to two common definitions: (1) PSA <10 ng/ml, Gleason score ≤6, clinical T1c stage, and fewer than three positive cores; and (2) PSA <10 ng/ml, Gleason score ≤6, PSAD <0.20 ng/ml per gram, clinical T1c–T2a stage, and fewer than three positive cores.

The main end point of this trial was to study the detection rate of PCa according to the biopsy-core number. The PCa detection rate of the 21-core protocol was compared with the rate from 6- and 12-core biopsy schemes. Results were also shown as percentage improvement in cancer detection rate. Due to the dependence of these cohorts, the McNemar test was used. Statistical significances were confirmed by the Cochran Q, W Kendall, and Friedman tests. Predictive factors of the diagnostic yield achieved by the 12-core scheme (PCa detected in the six far lateral cores, but not in the six sextant biopsy specimens) and 21-core scheme (PCa detected by the three midline biopsies or the six TZ cores, but not by the 12-core protocol) were studied using logistic regression taking into account PSA, PSAD, age, and clinical stage.

Clinicopathologic characteristics of PCa diagnosed or missed by each biopsy scheme were also assessed and compared. The normal distribution of continuous variables was confirmed prior to analysis, and continuous variables were reported as mean and standard deviation. For independent parameters, the Student t test was used for quantitative variables and the chi-square test (or a Fisher exact test, as appropriate) was used for qualitative variables. Statistical analyses were performed using SPSS software (IBM Corp, Armonk, NY, USA). The limit of statistical significance was defined as $p < 0.05$.



	Right				Left		
	Lat	TZ	Sext	Mid	Sext	TZ	Lat
Base	11	111	1	7	4	114	14
Midline	12	112	2	8	5	115	15
Apex	13	113	3	9	6	116	16

Fig. 1 – The 21-core biopsy scheme: six sextant biopsies (Sext) (standard 45° angle), three biopsies in each peripheral zone (Lat) (80° angle), three biopsies in each transition zone (TZ), and three biopsies in the midline (Mid) peripheral zone.