ELSEVIER

Urologic Oncology: Seminars and Original Investigations 31 (2013) 1060–1066

UROLOGIC ONCOLOGY

Original article

Detailed biopsy pathologic features as predictive factors for initial reclassification in prostate cancer patients eligible for active surveillance

Guillaume Ploussard, M.D., Ph.D.*, Alexandre de la Taille, M.D., Ph.D., Stéphane Terry, Ph.D., Yves Allory, M.D., Ph.D., Idir Ouzaïd, M.D., Francis Vacherot, Ph.D., Claude-Clément Abbou, M.D., Ph.D., Laurent Salomon, M.D., Ph.D.

INSERM U955 eq07 Departments of Urology and Pathology, APHP, CHU Henri Mondor, Créteil, France

Received 19 October 2011; received in revised form 21 December 2011; accepted 23 December 2011

Abstract

Objective: To evaluate the impact of detailed biopsy characteristics such as positive cores location or multifocality on the risk of initial reclassification in prostate cancer (CaP) patients eligible for active surveillance (AS).

Materials and methods: We reviewed data from 300 consecutive men eligible for AS (PSA ≤ 10 ng/ml, clinical stage T1c, Gleason score ≤6, <3 positive cores, extent of cancer in any core < 50%) who have undergone a radical prostatectomy (RP). Reclassification was defined as upstaged disease and/or upgraded disease in RP specimens.

Results: Biopsy features showed 36% of CaP involving 2 cores and a mean total tumor length of 2.63 mm. The 2 most frequently positive sites were base and apex. Mean total tumor length was significantly associated with upgraded disease ($P = 0.025$). In a multivariate model taking into account PSA, PSAD, number of positive cores and total tumor length, a total tumor length > 5 mm were independently predictor for a upgraded disease (OR 1.93, $P = 0.046$). The number, the multifocality and the bilaterality of positive cores were not associated with reclassification. Upgraded disease was significantly less reported in case of positivity at midline zone compared with positivity at base, apex, or transition zone ($P = 0.013$).

Conclusions: Detailed biopsy data provide additional information on the initial risk of reclassification in AS patients. Patients having a total tumor length < 5 mm and positive cores at midline zone are more likely to have favorable pathologic characteristics at diagnosis. These variables can be used for selection and monitoring improvement in AS programs.

Keywords: Prostate cancer; Radical prostatectomy; Active surveillance; Low risk; Criteria; Reclassification; Upstaging; Upgrading

1. Introduction

Active surveillance (AS) entails a strategy by which selected men are managed expectantly with the intention to apply potentially curative treatment in case of progression signs [1–4]. Patients eligible for AS are identified by Gleason score, PSA, clinical stage, and tumor extent of biopsy involvement [5–10]. Whatever the pathologic criterion used, there is a risk of initial reclassification and, thus, missing window of curability if AS is preferred [11,12]. Current results show a risk of reclassification on repeat biopsy ranging from 20% to 30 % [13–15]. The fact that most progression in AS series occurs 1–2 year after diagnosis suggests that the tumors have not truly progressed but were understaged and/or undergraded at diagnosis. Thus, assessment of factors predicting reclassification to higher risk at diagnosis and during follow-up in men participating in AS program appears clinically relevant. In the Johns Hopkins program, PSA density (PSAD), year of diagnosis, and PSA at the time of diagnosis were significantly different in men who eventually underwent treatment compared with those who did not [2]. PSAD as baseline predictor of reclassification has previously been highlighted in various studies [13,16–19]. Biological and clinical criteria have thus been studied but no series has thoroughly assessed the impact of detailed biopsy parameters such as bilaterality, multifocality, or location of positive cores.

* Corresponding author. Tel.: +33149812254; fax: +33149812568.
E-mail address: g.ploussard@gmail.com (G. Ploussard).

1078-1439/$ – see front matter
doi:10.1016/j.urolonc.2011.12.018

Thus, from a large series of RP patients eligible for AS who had undergone a standardized biopsy scheme with cores mapped for location, we decided to assess the impact of biopsy parameters on the risk of reclassification.

2. Materials and methods

Between January 2001 and March 2011, we identified patients who have undergone a RP for low-risk prostate cancer (CaP) after a 21-core biopsy scheme and who were eligible for active surveillance at diagnosis according to the following criteria: PSA ≤ 10 ng/ml, clinical stage T1c disease, Gleason score ≤6, <3 positive cores, an extent of cancer in any core < 50%, and a life-expectancy > 10 years. The study included 300 men. All patients underwent digital rectal examinations, serum PSA, and transrectal ultrasound. All the patients had undergone a 21-core biopsy protocol as previously described [20]. The biopsy regimen consisted of first 6 sextant medial biopsies at a standard 45° angle, then 3 biopsies in each lateral zone from base to apex at an 80° angle (Fig. 1). Next, 3 biopsies were taken in each transitional zone (TZ) from base to apex. Finally, 3 biopsies were sampled in the periurethral zone. Each core was mapped for location and was evaluated separately by a senior uropathologist. Prostate volume and PSAD was calculated during the prostate ultrasound examination by using the prostate ellipsoid formula. All radical prostatectomies were also performed in our department, and specimens were evaluated by senior uropathologists. Tumor volume was not measured routinely. Data from clinical evaluation, biopsy and RP specimens, and follow-up were recorded in a prospective database. PSA recurrence was defined as PSA > 0.2 ng/ml after RP.

Biopsy pathologic parameters were studied as follows: 1 vs. 2 positive cores; bilaterality or not; multifocality or not; location of positive core (base, median, apex, transition zone); total tumor length and tumor length at each location. Bilaterality was defined by 1 positive core in each prostate lobe. Multifocality was defined by 1 positive core in 2 separate locations as follows: right base, right midline zone, right apex, right TZ, left base, left midline zone, left apex, left TZ. Correlations between pathologic RP features and biopsy characteristics at diagnosis were assessed. Reclassification was defined as non-organ-confined disease (pathologic stage > pT2) and/or upgraded disease (Gleason score 7 or more; primary Gleason pattern 4) in RP specimens. The qualitative data were tested using a χ^2 test or Fisher's exact test as appropriate and the quantitative data were tested using Student's *t*-test. The Mann-Whitney test was used in case of no normal distribution. A logistic regression was used to test qualitative factors correlated with the risk of reclassification. Variables associated with a P value < 0.20 in univariate analysis were included in the multivariate model. Biochemical recurrence-free survival was established using the Kaplan-Meier method. Curves were tested by log-rank test. The limit of statistical significance was defined as $P < 0.05$. The SPSS ver. 13.0 (SPSS Inc., Chicago, IL) software was used for analysis.

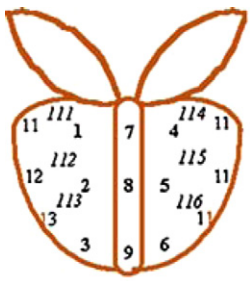
3. Results

Patient cohort characteristics are shown in Table 1.

Biopsy features showed 36% of CaPs involving 2 cores and a mean total tumor length of 2.63 mm. In RP specimens, a Gleason score 7 or 8 was found in 42.7% of cases. Extraprostatic extension was reported in 13.7% of cases. Only 2 cases of seminal vesicle invasion were reported. Mean follow-up after surgery was 25.3 months. Fifteen biochemical recurrences (5.0%) after surgery were reported during follow-up.

Table 2 shows the repartition of positive biopsies in function of the mapped location. The 2 most frequently positive sites were the base and the apex that were involved in 44% and 45% of cases, respectively. The largest tumor lengths per site were also reported in these 2 regions (2.18 and 2.27 mm). The midline and transition zones were involved in 33% and 27.7% of cases, respectively. The most frequently positive cores were the far lateral cores. Thus, cores 11, 13, and 14 were positive in >10% of cases. All others cores were positive in <10% of cases.

Total tumor length was significantly different according to the number of positive cores: 1.79 mm in case of a single



C

	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. Standardized 21-core biopsy scheme. The biopsy regimen consisted of first 6 sextant medial biopsies at a standard 45° angle, then 3 biopsies in each lateral zone from base to apex at an 80° angle. Next, 3 biopsies were taken in each transitional zone (TZ) from base to apex. Finally, 3 biopsies were sampled in the periurethral zone. Each core was mapped for location as shown. (Color version of figure is available online.)