Risk of prostate cancer at first saturation re-biopsy in a patient with previous diagnosis of HGPIN.

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Introduction: It is advisable to submit a patient with isolated HGPIN to re-biopsy every 3-6 months, performing an increasing number of samples in order to increase the detection rate. The aim of this study is to evaluate if the use of saturation needle biopsy technique may increase this rate.

Materials and methods: From January 2004 to June 2006, 780 patients with hypoechoic nodule at TRUS and/or PSA values between 2.5 and 10 ng/ml underwent TRUS 10-core prostate needle biopsy, performed by the same operator. Isolated HGPIN was detected in 26 cases (3.3%). Within a year all these patients underwent saturation needle re-biopsy. This procedure consisted of 24 samples obtained using a tru-cut needle 18 G under soft anesthesia by a major opiate. All the patients received a single dose of Levofloxacin per os before the biopsy and for the following 2 days.

Results: Prostate cancer was found in 8 (33.3%) of the 24 eligible patients: 40% showed a Gleason Score 6 and 60% > 7. Concerning PSA, we observed 35% of neoplasms for values between 2.5 and 3.9 ng/ml and the remaining 65.0% for values between 4.0 and 9.9 ng/ml.

Conclusions: The use of saturation needle biopsy allowed to detect 30.8% of prostatic cancer performing the first re-biopsy within a year. This result does not differ from others obtained with 8-10 cores techniques, therefore the indication of the 24-cores procedure should be limited to carefully selected patients with a high risk of developing cancer after that techniques had not been successful.

KEY WORDS: Prostate cancer; Ultrasound guided transrectal core biopsy; Re-biopsy; Saturation biopsy; PCA detection rate; HGPIN.

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INTRODUCTION
Since the advent of Prostatic Specific Antigen (PSA) screening there was a considerable prostate cancer migration versus the diagnosis of lower risk disease (1). The challenge now is to differentiate high risk patients avoiding clinically indolent disease overtreatment. The lack of consistently reliable radiological features in staging adenocarcinoma of the prostate resulted in the study of clinical variables such as PSA, Gleason Score, grade, clinical stage and, lately, biopsies (2). During the last decade a considerable number of modifications have been made to improve the technique of prostate cancer (PCa) biopsy. Studies showed that increasing the number of biopsy cores increased PCa detection rates (3). Total prostate volume too is an important factor: higher PCa detection rate was reported in men with smaller prostates (4). Recent prospective (4) and retrospective (5) studies showed a PCa detection rate from 10% to 27% on repeated biopsies. Several studies identified biopsy characteristics, including percent of positive biopsies and number of positive biopsies as strong independent risk category of pathological stage (6) and outcome after treatment such as radical prostatectomy or radiotherapy (7). Extended biopsy scheme and saturation biopsy strategy resulted in a greater than 30% PCa detection rate in men with previous negative sextant biopsies (8). Since the description
of High Grade Prostatic Intraepithelial Neoplasia (HGPIN) by McNeal and Bostwick in 1986, several studies reported about the positive predictive value of isolated HGPIN on repeated prostate needle biopsy, which ranged from 2.3% to 100% (6).

**Material and Methods**

In this study, 780 patients (age range 38-79 years) were enrolled from January 2004 to January 2006. Inclusion criteria were: PSA values > 2.5 ng/ml and < 10 ng/ml, a suspicious digital rectal examination (DRE) or TRUS hypoechoic nodule. Exclusion criteria were: history of PCa, acute or chronic prostatitis, histological evidence of PIN (prostatic intraepithelial neoplasia), urinary retention, indwelling urinary catheter or confirmed urinary tract infection. All patients discontinued anti-coagulants 5 days before biopsy and received a single dose of fluoroquinolone (levofloxacin) before biopsy and the following two days after the procedure. Patients were fully informed and consented the procedure. TRUS guided biopsies were performed by the same surgeon (G.V.) using a tru cut 18 gauge needle in left lateral supine decubitus without local anesthesia. We performed 10-cores biopsies as described by Gore et al. (9) plus, if present, 2-cores biopsies on the hypoechoic nodule. Of all these patients, 176 (22.6%) showed PCA and 540 patients (69.2%) were PCA free: 26 HGPIN (3.3%), 12 atypical small acinar proliferation (ASAP) (1.5%) and 502 (64.4%) benign prostatic hyperplasia. For a year all the 26 HGPIN patients were included in a follow-up protocol consisting in PSA determination every 3 months, DRE every 6 months and, in the case of a modification of one of these parameters, a repeated ultrasound guided transrectal core biopsy of the prostate with saturation biopsy technique. Prior to saturation biopsy clinical evaluation excluded acute or chronic prostatitis, urinary tract infection or lower urinary tract endoscopic procedures. Patients were fully informed and consented the procedure. All patients discontinued anti-coagulants 5 days before biopsy and received antibiotic prophylaxis with a single dose of Levofloxacin.

TRUS guided biopsies performed by the same surgeon (G.V.) using a tru cut 18 gauge needle in left lateral supine in the operating room under intravenous anesthesia by Remifentanil (Ultiva, GlaxoSmithKline). This anesthesia technique increased the procedure compliance and reduced patient's discomfort. Biopsy were obtained on each side: 1) lateral base with 2 cores, 2) lateral mid zone with 3 cores, 3) apex with 3 cores, 4) parasagittal middle zone with 2 cores and 5) parasagittal base with 2 cores. We take care to assure that the 3 apical biopsies adequately sampled the anterior horn of the peripheral zone tissue. An experienced pathologist evaluated all the slides.

For each patient we evaluated PCA detection rates according to the PSA ranges. We also evaluated clinical outcome and postoperative complication rate (total postoperative hospital stay, haemoglobin loss, catheter time, pain rate, QoL). Clinical characteristics of the patients with detected cancer were recorded: PSA levels at diagnosis, presence of palpable tumour, Gleason score of prostate biopsy, volume, localization, percentage of tumour and number of involved cores. The presence of clinically insignificant cancer (defined as tumour volume less than 0.5 cc and Gleason score < 7) was estimated following the model of Epstein et al. (10), based on clinical and biopsy criteria: non-palpable cancer, F/T ratio greater than 0.15, less than 3 biopsy cores involved with no more than 50% and Gleason score < 7.

**Results**

Of 26 patients with isolated High Grade PIN (HGPIN) only 24 (92.3%) were eligible for this study. Of these, 16 (66.7%) were cancer free and 8 (33.3%) showed adenocarcinoma of the prostate: 5 (20.8%) had Gleason score 4 or 5, 3 (12.5%) 6 or 7 and none from 8 to 10. The mean prostate volume measured by TRUS was 46.7 ± 17.8 cc and 11 of 24 patients (45.8%) presented an hypoechoic nodule in peripheral zone tissue. Suspicious digital rectal examination was present in 7 cases (29.1%). Concerning to PSA value, we observed 6 (25%) PCA patients and 2 (0.8%) disease free in the PSA range 2.5-3.9 ng/ml while in the PSA range 4.0-9.9 ng/ml we observed 10 (41.6%) PCA patients and 6 (25%) tumour free, respectively.

Sectors apical biopsies carried out in the anterior horn of the peripheral zone tissue showed over 29% (7 patients) of cancer detection rate, while cancer was detected in 8.3% (1 patients) in lateral base tissue, 4.5% (1 patients) in lateral mid zone and in no sample of the parasagittal zone. In all patients we evaluated tumour volume biopsy cores, percentage of biopsy cores involvement and number of biopsy cores involved. In 3 (12.5%) patients we observed a tumour volume < 0.5 cc, in other 3 (12.5%) volume tumour between 0.5 and 1 cc and in 2 (8.3%) volume tumour > 1 cc.

In 3 (12.5%) patients we evaluated a percentage of involvement of biopsy cores > 50%, in 5 (20.8%) < 50%. Only three (12.5%) patients presented more than 3 positive biopsies cores, and 5 (20.8%) < 3. We observed only 2 (8.3%) patients with tumour volume < 0.5 cc, < 5% of involvement and only one biopsy core involved; 2 (8.3%) patients with tumour volume < 0.5 cc, 25% of involvement and 2 biopsy cores involved; 1 (4.16%) with tumour volume > 0.5 cc, > 50% of involvement and more than 3 biopsy cores. A total of 7 (29.1%) patients underwent radical retropubic prostatectomy and only one (4.16%) was treated by external beam radiation therapy (tumour volume < 0.5 cc, 25% of involvement and 2 biopsy cores involved). Final examination of the specimen showed that cancer was clinically significant in 4 patients (16.6%) and 3 of them presenting an organ confined tumour after radical surgery. No residual cancer was identified on the final surgical specimen in one case (2%) who presented to saturation biopsy a tumour volume < 0.5 cc with 5% of involvement and one biopsy cores involved.

**Discussion**

Many papers in Literature demonstrate that HGPIN is a precursor lesion of prostate cancer (11) and several stud-
ies reported about the positive cancer predictive value of isolated HGPIN on repeated prostate needle biopsy, with rates ranging from 2.3% to 100% (8, 11-12). Recommendations about the follow-up in men with isolated HGPIN on initial biopsy vary widely from immediate re-biopsy to re-biopsy after 3 to 6 months, after 6 to 12 months, or after 3 years (13, 14). In most recent studies, PCA detection rates in HGPIN patients re-biopsies, after sextant sampling, range from 20% to 30% (8). In our saturation biopsy experience, after a first one 12-core sampling, we found a cancer detection rate of 33.3% within one year from the initial HGPIN diagnosis.

REFERENCES


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