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ORIGINAL ARTICLE

Can transrectal ultrasound-guided biopsy of the prostate with extended 14-core scheme improve the predictive accuracy of Gleason score and tumor site in prostate cancer treatment?

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Summary

Purpose: *Several studies have reported upgrading of patients with Gleason score (GS) at the time of prostate biopsy to GS following radical prostatectomy (RP). We reviewed the predictive accuracy of extended 14-core prostate biopsies, in terms of GS and tumor location in patients with prostate cancer (PCa) treated by RP.*

Methods: *We retrospectively reviewed 163 patients who underwent RP for clinically localized PCa. Preoperatively, all patients underwent a transrectal ultrasound-guided biopsy of the prostate (TRUSBP) with 14-core scheme for suspected PCa. According to GS, patients were categorized as low (GS 2-6), moderate (GS 7), and high (GS 8-10). A comparison between GS and tumor laterality of the needle biopsy and RP specimens was carried out.*

Results: *Bioptic GS was low (≤ 6) in 55.9%, moderate (7) in 34.9%, and high (≥8) in 9.2% of the patients. Pathological GS was 40.5, 46.6, and 12.9%, respectively. Of the 66 patients with low GS by RP, 41 (62.1%) were in agreement with TRUSBP, whereas 25 (37.9%) were underestimated by TRUSBP. Of the 76 patients with moderate GS by RP, 47 were in agreement with TRUSBP (61.8%), and 4 were underestimated by TRUSBP (5.3%). In the assessment of tumor laterality, TRUSBP falsely showed 51 cases as unilateral tumors, whereas RP diagnosed that both sides had PCa ($p<0.001$).*

Conclusion: *These data are in line with those of the literature, although the group of low-risk tumors remained the same only in 40.5% of the cases. Therefore, we conclude that this type of biopsy (14-core TRUSBP) should not be used alone to guide therapy in PCa.*

Key words: *Gleason score, prostate biopsy, prostate cancer, radical prostatectomy, upgrading*

Introduction

PCa is the most common malignant disease in males and the second cause of cancer-related deaths after lung cancer in developed countries [1]. The diagnosis of PCa is performed by digital rectal examination (DRE), serum prostate-specific antigen (PSA) test and TRUSBP. The role of prostate biopsy has changed. Its importance has evolved from pure cancer detection to assisting clinical patient management [2]. Therefore, TRUSBP provides data, such as histologic grade and tumor laterality, that can guide the therapeutic approach of PCa [3]. The histologic grade of PCa, usually assessed using the Gleason score (GS), is an important marker for this disease progression and cancer-specific survival [4,5]. A high RP Gleason score is associated with higher rate of biochemical recurrence and worse prostate cancer-specific survival [6,7]. Several studies have reported upgrading patients with Gleason sum 6 at the time of biopsy to Gleason sum 7 following RP in up to 30-60% of the cases. However, many of these studies differ in their prostate biopsy (PBx) meth-

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odologies [8-10]. In this study we reviewed the predictive accuracy of extended 14-core TRUSBP, in terms of Gleason score and tumor location in patients with PCa treated by RP.

Methods

Clinical and pathological studies

Between July 2007 and December 2014, we retrospectively reviewed the medical records of 163 patients who underwent RP (47 with laparoscopic technique and 116 with open technique) for clinically localized PCa (stage cT1 to cT2N0M0) at our Department of Urology. All patients preoperatively underwent an initial TRUSBP with 14-cores scheme for abnormal DRE, high PSA levels (≥4 ng/mL), or both. Patients with a history of biopsy, surgical treatment of prostatic disease, neoadjuvant therapy or incomplete clinical data were excluded from the study. Preoperative data (age, PSA, prostate volume (PV), clinical stage, laterality of the needle biopsy, and prostate biopsy Gleason grade) and pathological data (postoperative GS, pathological stage, and margin status) were collected retrospectively for analysis. TRUSBP was performed with the patient in left lateral decubitus position, using a General Electric Logiq 7 (GE Ultraschall, Solingen, Germany) machine equipped with a 5-9MHz multi-frequency convex probe "end-fire". Each transrectal ultrasound performed included an assessment of the prostatic diameter, the volume of the whole prostate, the transition zone, capsular and seminal vesicle characteristics, as well as morphological description of potential pathological features. After having imaged the prostate, sampling was carried out with a 18-Gauge Tru-Cut needle powered by an automatic spring-loaded biopsy disposable gun. Three experienced urologists of our Department performed a 14-core biopsy, as first intention, including 2 lateral peripheral (1 basal and 1 apical), the 3 conventional parasagittal, and 2 midline peripheral samples (1 basal and 1 apical) on each side. Each patient was treated under local anaesthesia with Lidocaine spray (10 g/100 ml), applied 2 min before the procedure [11]. The transrectal ultrasound-derived prostate volume was invariably calculated using prostate ellipse formula (0.52 × length × width × height). Clinical and pathological stages were assigned based on the 2002 tumor-node-metastasis (TNM) system. The Gleason grading was based on the recommendations of the 2005 International Society of Urological Pathology Consensus conference. All biopsy cores were analysed by pathologists of our Pathology Department specialized in genitourinary pathology. The overwhelming majority (91.5%) of the patients were operated on within 4 months from biopsy, so potential grade progression between procedures was not an issue. RP was performed by three experienced surgeons. All RP specimens were submitted in their entirety for histological examination. Cases were not reviewed for the purposes of this study. Patients were then categorized into the following GS according to the biopsy and prostatectomy: low (Gleason 2-6), moderate (Gleason 7), and high (Gleason 8-10) categories. In cases in which different GS were found in multiple samples of the same prostate biopsy, the highest GS was assumed for that patient. Moreover, we performed a comparison between GS and tumor laterality of the needle biopsy and RP specimens. The definitive GS and tumor laterality of the PCa was defined at the prostatectomy specimens.

Table 1. Demographic and clinicopathologic features of patients undergoing radical prostatectomy

Variables	*Values*
Age (years), mean ± SD	65.2 ± 5.9
PSA level (ng/mL), mean ± SD	8.34 ± 7.22
Prostate volume (mL), median (range)	43.7 (17-115)
DRE, N (%)	59 (36.2)
Clinical stage, N (%)	
T1c	79 (48.5)
T2a-b	55 (33.7)
T2c	29 (17.8)
Mean positive cores, N (range)	3.15 (1-11)
Biopsy Gleason score, N (%)	
lowgrade (≤6)	91 (55.9)
moderategrade (7)	57 (34.9)
highgrade (8-10)	15 (9.2)

SD: standard deviation, PSA: prostate-specific antigen, DRE: digital rectal examination

Statistics

Continuous variables were evaluated using mean and standard deviation or median and interquartile range, according to their distribution. The association between upgrading and upstaging and age, preoperative PSA level, PV, laterality of positive cores and margin status were evaluated using the Student's t-test or the Mann Whitney U test, depending on their distribution. Statistical analyses were performed using Microsoft Excel 2010 platform. A $p<0.05$ was considered to indicate statistical significance.

Results

The descriptive characteristics of the study cohort are shown in Table 1. The mean age of the 163 patients was 65.2±5.9 years, and the mean preoperative PSA level was 8.34±7.22 ng/mL, the median prostate volume was 43.7 mL (range 17-115) and 59 (36.2%) patients had a positive DRE. Clinical stage was cT1 in 79 (48.5%), and cT2 in 84 (51.5%) patients. Bioptic GS (ranged from 5 to 9) was: low (GS ≤6) in 91 (55.9%), moderate (GS =7) in 57 (34.9%), and high (GS ≥8) in 15 (9.2%) patients. Pathological GS was low in 66 (40.5%; $p<0.001$), moderate in 76 (46.6%; $p<0.002$), and

Table 2. Correlation between bioptic Gleason score and postoperative pathologic features of patients undergoing radical prostatectomy

Variables	*Values N (%)*
Biopsy Gleason score*	
5	9 (5.5)
3+3	82 (50.3)
3+4	37 (22.7)
4+3	20 (12.3)
8-10	15 (9.2)
Prostatectomy Gleason score*	
5	4 (2.5)
3+3	62 (38)
3+4	39 (23.9)
4+3	37 (22.7)
8-10	21 (12.9)
Same Gleason score	99 (60.7)
Upgrading after surgery	35 (21.5)
Downgrading after surgery	0 (0)
Margin-positive tumors	29 (17.8)
Lymph nodes invasion	45 (27.6)

*Biopsy Gleason score vs prostatectomy Gleason score, p<0.001

high in 21 (12.9%; p>0.05) patients. Table 2 shows the relation between bioptic and pathological GS. Of the 66 patients classified as low-grade by RP, 41 (62.1%) were in agreement with TRUSBP findings, whereas 25 (37.9%) patients were underestimated by TRUSBP. Of the 76 patients classified as moderate-grade by RP, 47 (61.8%) were in agreement with TRUSBP findings, and 4 (5.3%) were underestimated by TRUSBP. Finally, of the 21 patients classified as high-grade by RP, 11 (52.4%) were in agreement with TRUSBP findings, and 6 (28.6%) were underestimated by TRUSBP. In the assessment of tumor laterality, TRUSBP falsely showed 51 cases (31.3%) as unilateral tumors, whereas RP diagnosed that both sides of the prostate were affected by cancer (p<0.001). Overall, 37 (22.7%), 99 (60.7%), 17 (10.4%), and 10 (6.2%) patients had pT1, pT2, pT3a, pT3b PCa, respectively. With regards to stage, 51.5% of the patients were upstaged after RP (p<0.001). Moreover, 45 (27.6%) had lymph nodes invasion (pN1). The surgical margins were positive in 29 (17.8%) patients. Analysing the correlations between age, preoperative PSA level and PV and cancer upgrading, no variable showed such a correlation (p>0.05).

Discussion

Pathological GS is considered as one of the strongest predictors of PCa control outcomes in postoperative prediction models [3,12]. The prostate biopsy remains the standard method for diagnosing early PCa [2]. Therefore, the clinician can use the information obtained from the needle biopsy in the management of this disease, which may range from an active surveillance protocol to RP or radiotherapy and various therapies. However, the needle biopsy and the corresponding RP Gleason grades may not be the same for several reasons: pathology error, borderline grades, and sampling error [13-15]. In the literature, the ability to predict the final GS has been quite poor, with a concordance rate between the biopsy and RP Gleason grades of only 25-48% [8,10,16-18]. King et al. [19] coined the term of "upgrading", defined as bioptic GS upgrading from ≤6 to ≥7, or from 7 to ≥8. The authors reported an exact match between the biopsy and RP GS in 42% of the patients on average, and the bioptic GS had undergraded the PCa in 43% of the patients on average. This study, however, consisted of patients undergoing standard sextant prostate biopsy. Few studies have suggested an improved correlation between the prostate biopsy and final Gleason grades; however, these studies lacked a clear definition of the biopsy schemes. Chun et al. [7] showed that extended biopsy schemes (≥10 cores) might affect the rate of significant bioptic GS upgrading, and the ability to predict it. These results indicated that the difference in the extent of prostate sampling resulting from the use of extended biopsy schemes is almost insignificant in the contest of bioptic GS upgrading. In fact, the rate of significant bioptic GS upgrading was 28.7 vs 28.2% in the entire cohort of patients. In a cohort of 191 patients Pereira et al. [20] reported that TRUSBP overestimated 6% and underestimated 24% of the cases in comparison with RP for GS, and overestimated 2.6% and underestimated 46% of the cases compared with RP for tumor laterality. The authors used a standard 12-core biopsy technique. Our objective was to examine the ability to predict GS upgrading in a cohort of patients with low-risk PCa, who were diagnosed using extended biopsy schemes (14 cores). Our results suggested that the GS of the prostate bioptic specimens was identical to that of the RP specimens in 60.7% of the patients undergoing TRUSBP with 14-cores scheme. Overall, 31.5% of needle biopsy specimens were undergraded, and none was upgraded in all groups of Gleason grades (Table 2).

These data are in line with those of the literature although, as regards the group of low-risk tumors, these remain in the low-risk group only in 40.5% of the cases. However, with regard to tumor laterality, TRUSBP falsely showed 51 cases (31.3%) as unilateral tumors. These results suggest that the extended biopsy scheme by 14-cores, in addition to its increased cancer detection rate, can provide clinically useful prognostic information by detecting high Gleason grades and laterality of PCa that would be missed by the sextant scheme. Recent studies have shown that if TRUSBP detects cancer in only one lobe of the prostate, these cases are good candidates for focal therapy; therefore, hemi-ablation is being used more frequently for such patients [21,22]. At present, the transperineal template-guided mapping biopsy (TTBx) prostate biopsies is an alternative to minimize the probability of underestimation of PCa diagnosed by a conventional TRUSBP. Recently, Taira et al. [23] have defined the TTBx as the best procedure for active surveillance. However, given the increased risk of complications of this technique, the first biopsy remains the standard biopsy technique for an initial diagnostic evaluation of a patient suspicious for PCa [2]. Our study is one of the largest contemporary reports analyzing the predictive accuracy of a standard biopsy scheme in terms of GS and tumor location in patients affected by PCa. This study differs from other reports in the homogeneity of patients treated and analysed at a single institution, and in the standardization of biopsy technique. However, several limitations need to be acknowledged. A first limitation of our study concerns the race: all patients were white, therefore results might not be generalizable to other races. Finally, we did not have an oncological follow-up of the patients and, therefore, cannot correlate the biopsy specimens with the patient follow-up. Additional studies with more detailed exposure measurement are warranted to evaluate questions about GS upgrading in the management of patients affected by localized PCa.

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