Original article

Histopathologic discrepancy between prostatic core biopsy and open radical prostatectomy specimens in clinically localized prostatic cancer

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Abstract

Objective: 1. To assess the histopathologic discrepancy between prostatic needle biopsy and open radical prostatectomy specimens in terms of Gleason score upgrading and bilaterality

2. To evaluate the impact of this discrepancy on the surgical margin status of radical prostatectomy specimens

Methods: This study was conducted at Prince Hussein Urology Center, Amman, Jordan. Between May 2010 and August 2015, 74 patients underwent open radical prostatectomy for localized prostatic cancer diagnosed by prostatic needle biopsy based on high PSA level. We compared histopathologic findings regarding Gleason score and bilaterality between prostatic biopsy and radical prostatectomy specimens, and then we evaluated the impact discrepancy between them on the surgical margin status of radical prostatectomy specimens.

Results: 52 patients (70%) had upgrade in Gleason score with mean increase by one. All 34 patients who had bilateral disease on prostatic biopsy had bilateral disease on radical prostatectomy, but of the remaining 40 patients with unilateral disease 18 patients (45%) had bilateral disease on radical prostatectomy specimen. Surgical margin was involved in 3 patients (4%), all of them had Gleason score > 7 and bilateral disease on both biopsy and surgical specimens.

Conclusion: In spite of the significant histopathologic discrepancy between prostatic needle biopsy and open radical prostatectomy specimens, however in clinically localized prostatic cancer this discrepancy has no impact on surgical margin status.

Keywords: *Histopathologic , radical prostatectomy ,cancer.*

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Introduction

Prostate cancer is the most common cancer and the second leading cause of cancer related death in the male (1,2,3). As with other types of malignancy, early detection and treatment is the key to achieve best outcomes including cure. At early stages, prostate cancer rarely produces clinical symptoms. The presence of symptoms usually suggests locally advanced and/or distant disease. Digital rectal exam, PSA and prostate ultrasound findings usually give useful information about the extent of the prostatic cancer.

Digital rectal examination has low reproducibility in the hands of experienced urologists (Smith and Catalona, 1995) and can miss a significant proportion of early organ confined cancers (Ellis et al, 1994). In one study, 565 men with a presumed organ localized prostate cancer based upon digital rectal exam alone, the sensitivity and specificity were 51% and 82% for prediction of organ confined cancer, respectively (Partin et al, 1993). However, digital rectal exam can be used in conjunction with other tools to aid in prediction of disease extent.

Between 1992 and 2003, with the onset of widely spread PSA testing, the mortality rate from prostate cancer decreased by 32.5% (Surveillance, Epidemiology, and End Results Program). A 75% decline in the proportion of high stage disease at diagnosis was also noted.

It was found that when digital rectal exam and PSA were used for prostate cancer screening, detection rates were higher for PSA than with digital rectal exam but were highest when both tests were used together (Catalona et al, 1991). As digital rectal exam and PSA do not always detect the same cancers (Okotie et al, 2007), these tests are best

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used in combination for predicting prostate cancer risk.

Diagnosis of prostate cancer is usually made by histological confirmation of malignant prostatic cells in prostatic specimen derived mainly from prostatic biopsy but occasionally by transurethral resection of prostate (TURP) done for management of bladder outlet obstruction due to prostatic enlargement in the context of normal PSA value and absence on digital rectal examination of any signs of prostate malignancy. Tow important histopathologic findings derived from prostatic biopsy revealing prostatic cancer are the Gleason score and whether one or both lobes are involved (unilateral or bilateral).

Localized prostate cancer is defined as prostate cancer that doesn't breach outside prostatic capsule and this confinement is confirmed by imaging studies of the pelvis including CT scan and MRI. Radical prostatectomy is the mainstay of treatment of localized prostate cancer in patient with good life expectancy (more than 10 years in most series).

Radical prostatectomy was the first established surgery for prostate cancer treatment that has been used for more than 150 years (Kuchler er al, 1866) and it still the gold standard treatment because of the fact that hormonal therapy and chemotherapy are not curative, and not all malignant cells can be eradicated primarily by radiotherapy whether by external beam radiation or in the form of brachytherapy, even if the tumor is localized to the prostate gland. The major benefit of radical prostatectomy is that when it is done by experienced hands, it provides the best chance for cure while risking minimal collateral damage to nearby structures (Hull et al, 2002). Moreover, it gives more precise tumor grading and staging by histopathologic examination of the surgical specimen. In addition, failure of treatment can be more readily identified, as chemical failure based on PSA values are well agreed upon post radical prostatectomy in contrast to the controversy encountered for other options of treatment.

The most important prognostic pathologic criteria after radical prostatectomy are grade (Gleason score) , surgical margin status, extracapsular extension, seminal vesicle invasion, and pelvic lymph node involvement (Partin et al, 1993; Pound et al, 1997).

Here we compare the histopathologic difference regarding Gleason score and bilaterality between prostatic biopsy and radical prostatectomy in patients with localized prostatic cancer and the impact of this difference on the surgical margin status of radical prostatectomy specimen.

Methods

At our urology center we reviewed retrospectively the medical records of 74 patients who underwent open radical prostatectomy between May 2010 and August 2015 including histopathologic reports for both prostatic biopsy and radical prostatectomy. The age of patients ranged from 54 to 73 years. All patients had localized prostate cancer confirmed by imaging studies (CT and/or MRI) of the pelvis and abdomen. PSA levels ranged 9 - 26. All patients were diagnosed by prostatic biopsy under transrectal US guidance with 10 cores after receiving prophylactic antibiotics and with bowel preparation. For prophylaxis we give oral fluoroquinolone and metronidazole one day before biopsy and continue therapy for 2 to 3 days after wards. To decrease bacterial load from site of biopsy and so minimizing the risk of urinary tract infection we advise patients to self-administer a rectal enema at home in the morning of the day of biopsy. Using transrectal ultrasound probe, the prostate volume is initially assessed, and examination of the prostate in both the sagittal and transverse planes is done identifying the location and criteria of any abnormality (e.g., heterogeneous, hypoechoic or hyperechoic, calcifications, cysts and nodules). We begin the examination almost always at the base of the gland and then move toward the apex.

Prostatic tissues provided were examined by senior histopathologists. Open retropubic radical prostatectomy (non-nerve sparing) was done for all patients. We compared the Gleason score and bilateral involvement between prostatic biopsy and final pathology and checked the margin status of the radical prostatectomy specimen to assess for any increase in the chance of getting positive margin when upgrading in these parameters was encountered.

Result

Two patients developed urinary tract infection and fever post biopsy and were admitted to the hospital. Both patients developed urinary retention that mandated suprapubic cystostomy insertion. Gleason scores ranged from 5 to 7 on biopsy and 5 to 8 on radical prostatectomy. There was an upgrade in Gleason score in 52 patients (70%); in 3 patients the upgrade was by 3, in 8 patients the increase was by 2 and in 41 patients by 1. The increase was disproportional, so highest increase was seen for prostatic biopsy Gleason score 5 compared to scores 6 and 7. Thirty four Patients had bilateral disease in both biopsy and prostatectomy. In contrast, 40 patients reported to have unilateral disease on biopsy, yet 18 patients of them (45%) turned to have bilateral disease on final pathological report. Surgical margin was involved

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in 3 patients (4%), all of them had Gleason score 7-8 and bilateral disease on both biopsy and prostatectomy Histopathology.

Table 1 Increasing prostate cancer detection rates with extended core biopsy protocols

STUDY	NO. OF CORES	CANCER DETECTION RATE
Eskew et al, 1997	6 13	26.1% 40.3%
Naughton et al, 2000	6 12	26% 27%
Presti et al, 2000	6 8 10	33.5% 39.7% 40.2%
Babaian et al, 2000	6 11	20% 30%

Discussion

Transrectal ultrasound guided prostate biopsy is important diagnostic tool for prostatic cancer. The indications for this procedure are many but mainly for high PSA level and/or abnormal prostate on digital rectal exam. During sampling of the peripheral zone, the needle tip must be placed at least 0.5 cm posterior to the prostatic capsule before firing; more advancement of the needle tip to or through the capsule may result in sampling of more anteriorly located tissue, and accordingly missing sampling of the most common and probable location of tumors and/or leading to misinterpretation of biopsy pathological findings.

Modifications of the previously standard sextant prostate biopsy system have put into consideration the importance of laterally located tumors (Terris et al, 1992). Currently, six cores are widely considered to be inadequate for routine prostatic biopsy for cancer detection and interpretation. Many studies have confirmed the improved cancer detection rates by providing additional laterally directed samples into the systematic sextant technique, taking at least anywhere from 8 to 12 cores. Table 1 compares different extended biopsy studies based on number of cores taken during sampling.

Gleason Score is the most widely used pathological grading system of prostate cancer (4). It is the sum of a grade (from 1 to 5) assigned to the most predominant pattern (involving the largest volume of the tumor in the specimen) and the second predominant pattern to produce a scoring system ranging from 2 to 10. It is being implemented in many prognostic indices created to establish a measurement of the possibility of presence of malignant cells in distant places outside the prostate and accordingly the probability of the failure of treatment modalities addressing complete local tumor control. The most popular index is the one established by D'Amico, who demonstrated that the stratification of prostate cancer into low risk (clinical stage T1 to 2a, PSA 10 ng/mL or less, and Gleason score 6 or less), intermediate-risk (stage T2b, PSA greater than 10 but less than 20 ng/mL, or Gleason score 7), and high-risk disease (stage T2c, PSA greater than 20 ng/mL, or Gleason score 8 to 10) (D'Amico et al, 1998) could predict 10 years disease free survival after radical prostatectomy; 83% for low-risk, 46% for intermediate-risk, and 29% for high-risk disease (D'Amico et al, 2001).

Unfortunately, Gleason Score is commonly higher on radical prostatectomy compared to prostatic biopsy(5,6,7,8,9), and this inaccuracy is related mainly to low tissue volume provided by the biopsy and to pathologist's tendency to report a lower score on biopsy (10,11) but not related to cancer volume within the core or the needle gauge (12,13,14). In our study we found that the increase in score is significantly more if the score on biopsy is 6 or less, an observation that has also been noted on earlier study (15).

Prostate cancer is often multifocal and commonly bilateral on prostatectomy specimens, but can be misinterpreted as unilateral on biopsy. This misinterpretation is also related to sampling error as the biopsy needle could miss small volume cancer located laterally (16,17). So increasing number and distribution of cores taken will probably sample a greater fraction of cancer (18,19).

One of the most important parameters to look at by the pathologist on radical prostatectomy specimen is the surgical margin of the specimen, as any presence of positive surgical margin indicates incomplete resection and so further management is required to control malignant cells left behind by the surgeon in prostatic bed. in our study we found that neither increase in Gleason score nor discrepancy in bilaterality affects surgical margin status. As in a previous study we noticed that a unilateral positive biopsy, comparerd with a bilateral positive one, is associated with a negative surgical margin, most likely because a unilateral positive biopsy reflects a small volume disease and organ confinement (20).

Conclusion

We found a significant upgrading in both Gleason score and bilaterality in final pathology compared to prostatic biopsy. This is most probably caused by missing small volume of tumors by the needle and by tendency of the pathologists toward interpreting lower grades of tumor on biopsy.

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Fortunately, this upgrading is not associated with increased positivity in surgical margin.

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