ORIGINAL RESEARCH

Histopathological Correlation Between Transrectal Ultrasound-Guided Biopsy and Radical Prostatectomy Specimen of Filipino Men with Localized Prostate Cancer: A Local Experience

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Background: Prostate cancer is the most common malignant tumor among adult men worldwide and the second most common cause of cancer death. Gleason grading system is a powerful predictor in the prognosis and treatment outcome of prostate carcinoma.
Objective: This retrospective study aims to evaluate the accuracy of transrectal ultrasound (TRUS)-guided biopsy of the prostate compared to radical prostatectomy specimen in predicting the pathological grading of prostate adenocarcinoma using the Gleason scores between specimens.
Methods: This is a review of 69 patients who underwent radical prostatectomy due to prostate cancer in 2010-2015. The Gleason scores of the transrectal ultrasound biopsies were compared with the surgical specimen.
Results: The biopsy Gleason scores obtained from the TRUS biopsy and the radical prostatectomy specimens were similar in 79.7% of the cases. In patients with moderately differentiated tumors on biopsy (Gleason score of 5 to 7), the concordance rate was 83% with upgrading after surgery in 16% of the cases. In poorly-differentiated tumors on biopsy (Gleason score of 8 to 10), 74% revealed the same score on histopathological examination after radical prostatectomy, while 25% of the cases were given lower Gleason scores after operation. Overall, 20.3% cases were discrepant by 1 or more Gleason scores after radical prostatectomy. There was a good histopathological correlation between TRUS biopsy and prostatectomy specimen {AUC =0.787(p=0.001)}.
Conclusion: The overall accuracy of Gleason score on transrectal ultrasound-guided biopsies in predicting prostatectomy specimen grade is favorable. It plays a significant role in clinical decision making of patients with prostate carcinoma.

Keywords: prostate cancer, Gleason score, prostatectomy, biopsy, transrectal ultrasonography

Introduction

Prostate cancer is the most common solid organ malignancy among adult men worldwide. Three percent of men with prostate cancer die from the disease.[1] The most common location of prostate cancer is the peripheral zone which comprises 80% of cases.[2] The increase in the risk of prostate cancer when a first or second degree relative has cancer is proportional to the degree of consanguinity. It is higher if the relative was diagnosed at a younger age, and when the number of relatives with cancer is greater. Other risk factors are age greater than 65 years old and African descent.[1]

Transrectal ultrasound (TRUS)-guided prostate needle biopsy is the recommended diagnostic tool in most cases with suspicion of prostate cancer.[3] Among the histopathological information, the Gleason grading system is the most widely used parameter to grade adenocarcinoma of the prostate.[4] The Gleason score is incorporated in the prognostic and treatment algorithms predicting risk of recurrence following radical surgery thus plays a significant role in decision making.[5]

Bulbul, et al. reviewed the records of 100 patients with localized carcinoma of the prostate which were diagnosed by TRUS-guided prostate biopsy and treated with radical retropubic prostatectomy. They compared the Gleason scores and tumor laterality between core biopsies and surgical specimens and found that 66% of patients with unilateral disease on needle biopsy had bilateral disease on final pathology and the median Gleason score on final pathology was upgraded to 7, from a median score of 6 on biopsies ($p<0.001$).[6] In a similar study by Cam, et al. the results showed that in 28.7% of cases, the biopsy score was the same as that of the radical prostatectomy specimen. The most significant discordance was the upgrading of well-differentiated tumors after surgery in 71.7% of cases. In 81.8% of cases with high Gleason score on transrectal ultrasound, there was poor correlation with degree of cellular differentiation in the prostatectomy specimen.[7] There was no correlation between the location in the whole mount pathology specimen and the TRUS biopsy specimen.

In a blinded review by Danziger, et al., TRUS biopsy correctly predicted prostatectomy histology in 88% of men with lesions scored as Gleason 5 to 7 and 41% of men with well-differentiated (Gleason score of 2 to 4) or poorly-differentiated lesions ($p<0.01$). The sensitivity of 90% and specificity of 97% were observed for transrectal ultrasound-guided prostate biopsy with a Gleason sum of 7.[8] According to Koksal, et al., grading error was greatest with well-differentiated tumors. The accuracy of needle biopsy was 15% with Gleason score of 2-4 (well-differentiated) and 97% with Gleason score 5-7 (moderately differentiated). All of the tumors with Gleason score 8-10 (poorly differentiated) on needle biopsy were graded correctly.[9] In study by Cookson, et al. the biopsy Gleason score was identical to the specimen Gleason score in 31% of cases, and discrepant by 2 or more Gleason scores in 26% of cases. Overall, 54% of biopsies were undergraded, while 15% were overgraded.[10] It is important to note that there is a lack of studies correlating the cancers from the TRUS biopsy specimen versus the actual whole mount radical prostatectomy specimen in terms of tumor location.

This study was undertaken to show the significance of evaluating the accuracy of biopsy in predicting pathological grading and extent of the disease compared with the final surgical pathological specimen in the National Kidney and Transplant Institute (NKTI) setting.

This study aims to compare prostate adenocarcinoma Gleason scores between specimens of transrectal ultrasound guided prostate biopsy and surgical specimen who underwent prostatectomy.

Patients and Methods

This was a retrospective cohort study of patients, 40 years and older, seen at NKTI from January 2010 to December 2015. A minimum of 49 cases was estimated at 95% confidence level and 10% confidence interval.

A comparison was made between the Gleason scores of the needle biopsy and prostatectomy specimens. Overall accuracy was evaluated using sensitivity, specificity, and positive and negative predictive values. The accuracy of needle biopsy in predicting prostatectomy specimen grading was also assessed using receiver operating characteristic (ROC). The area under the curve (AUC) should be higher than 0.50 to be considered a significant predictor of the outcome.

Included in the study were patients who underwent TRUS-guided prostate biopsy and then radical prostatectomy. The authors excluded patients who underwent TRUS-guided prostate biopsy or radical prostatectomy in another hospital, patients who have metastatic clinical disease and histopathological reports done in another institution.

Biopsies were done in the NKTI operating room and in the ultrasound section by a urologist together with a radiologist. The indications for biopsy was based on clinical (digital rectal examination) and Prostate Specific Antigen (PSA) result. All TRUS-guided biopsies were done using a Bard disposable core biopsy instrument with a gauge 18 needle and a Hitachi ultrasound diagnostic scanner (Tokyo, Japan) with a 6.5MHz endosonic transducer. Following biopsy, the specimens were routinely processed and subjected to histological evaluation by a board-certified pathologists. Prostatectomy was likewise done in this institution by the same urologist who performed the biopsy. However, the pathologist who examined the radical prostatectomy specimen was not the same one who read the TRUS-guided biopsy report. The hospital's electronic database was used to retrieve the name and age of the patients and histopathological results. Patient data were kept strictly confidential using codes and access was restricted only to authors of this study.

A well-differentiated prostate cancer was defined as a lesion with a Gleason score of 2 to 4. A moderately-differentiated prostate cancer was defined as a lesion with a Gleason score of 5 to 7. Lastly, a poorly-differentiated prostate cancer was defined as a lesion with a Gleason score of 8 to 10.

This study was approved by the NKTI Research Ethics Committee.

Results

The authors compared the Gleason score assigned to the tumor on needle biopsy specimens to that assigned to the radical prostatectomy specimen in 69 patients. Patient ages ranged from 54 to 80 years old.

The biopsy Gleason scores obtained from the TRUS biopsy and the radical prostatectomy specimens were similar in 79.7% of the cases (Table I). In patients with moderately differentiated tumors on biopsy (Gleason score 5-7), the concordance rate was 83% (35/42) with upgrading after surgery in 16% (7/42) of the cases. In poorly-differentiated tumors on biopsy (Gleason score 8-10), 74% (20/27) revealed the same score in histopathological examination after radical prostatectomy, while 25% (7/27) of the cases were given a lower Gleason scores after operation. In general, 20.3% (14/69) cases were discrepant by 1 or more Gleason scores after radical prostatectomy (Table 1).

Transrectal ultrasound guided biopsy has a 74% sensitivity and 83% specificity with a negative and positive predictive value of 83% and 74%, respectively (Table 2).

Lastly, Figure 1 shows that the area under the curve (AUC) is 0.787 (p=0.001) which denotes that the transrectal ultrasound-guided prostate needle biopsy is a significant predictor in the

Table 2. Accuracy measure of transrectal ultrasound-guided biopsy

Summary Measures	Point estimate	95% confidence interval
Sensitivity	74.07%	53.72 - 88.89
Specificity	83.33%	68.64 - 93.03
PPV	74.07%	53.72 - 88.89
NPPV	83.33%	68.64 - 93.03
Likelihood ratio (+)	4.44	2.18 - 9.06
Likelihood ratio (-)	0.31	0.16 - 0.60
Prevalence	39.13%	27.60 - 51.63

Table 1. Comparison of Gleason grades of transrectal ultrasound biopsy and radical prostatectomy specimens.

Transrectal Ultrasound-Guided Biopsy Gleason Score	Prostatectomy Biopsy Gleason Score (%) 8 - 10 (Poorly differentiated)	5-7 (Moderately differentiated)	Total
8 - 10 (Poorly differentiated)	20 (74.1)	7 (25.9)	27
5-7 (Moderately differentiated)	7 (16.7)	35 (83.3)	42
Total	27	42	69

histopathological outcome of radical prostatectomy specimens, as well as it can discriminate poorly-differentiated from moderately-differentiated tumors.

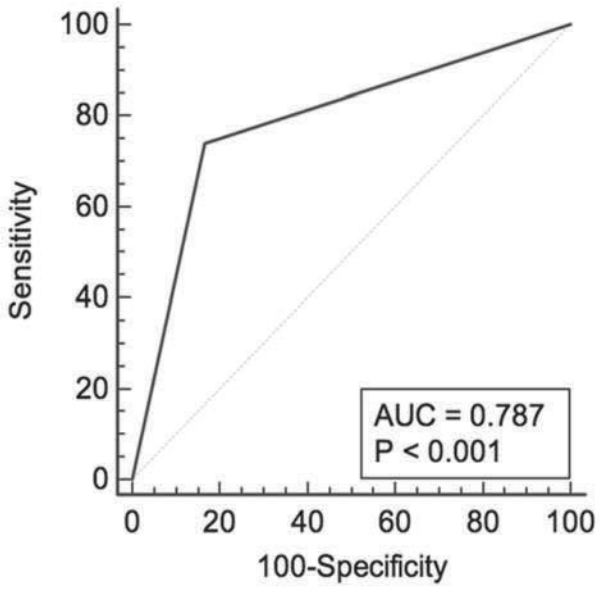

Figure 1. Receiver operating characteristic of transrectal ultrasound-guided prostate needle biopsy

Discussion

The Gleason grading system has been widely used worldwide by urologists as a tool in therapeutic decision-making for prostate cancer. Gleason grade from transrectal ultrasound-guided biopsy may differ from the grade of the prostatectomy specimens. Several studies showed different discordance rates.

In this study, there were no well-differentiated tumors obtained on biopsy. Majority of cases showed identical Gleason scores between needle biopsy and radical prostatectomy specimens with a concordance rate of 79.7%. Epstein, et al. reported a 69% correlation of TRUS biopsy grade with radical prostatectomy grade in their cases.[11] Carlson, et al. proposed that 68% of biopsy and prostatectomy specimen have the same Gleason score while Cecchi, et al. showed that only 47% of Gleason scores were identical in the biopsy and prostatectomy specimens.[12-13]

Furthermore, patients with moderately-differentiated tumors on biopsy (Gleason score 5-7), the concordance rate was 83% with upgrading after surgery in 16% of the cases. In poorly-differentiated tumors on biopsy (Gleason score 8-10), 74% revealed the same score on histopathological examination after radical prostatectomy, while 25% of the cases were given lower Gleason scores after operation. In general, 20.3% cases were discrepant by 1 or more Gleason scores after radical prostatectomy. Cookson, et al. proposed that the biopsy score was identical to prostatectomy specimen score in 31% of cases, while 26% were discrepant by 2 or more Gleason scores. Overall,15% of biopsy specimen were over graded while 54% were undergraded after radical prostatectomy.[10] According to Koksal, et al. grading error was greatest with well-differentiated (Gleason 2-4) tumors. All those with Gleason score of 8-10 (poorly-differentiated) on needle biopsy was graded correctly.[9]

The discordance between Gleason score of TRUS biopsy and prostatectomy specimens can be attributed to the limited amount of tissue obtained by the biopsy. Insufficient samples may miss the higher grade tissue obtained in the final histopathologic specimen. It is very important to do a 12-core biopsy rather than a 6-core biopsy to lessen the chances of under sampling. The ultrasound machine is user-dependent, thus the skill and experience of the urologist are also factors to consider. Tumor heterogeneity of prostate cancer can also be a possible explanation for inconsistencies in grading. In the radical prostatectomy specimen, the whole mount specimen was not used to correlate with the biopsy specimen. Therefore, the actual volume and location of cancer was not included in this correlation study. It is highly emphasized that the correlation in this study did not use whole mount prostatectomy specimen, and the biopsy done is a 12-core TRUS biopsy which may miss anterior zone cancers. These factors could explain the dissimilarities in Gleason grading between TRUS biopsy and the prostatectomy specimen.

In this study, the histopathological correlation between transrectal ultrasound-guided biopsy and radical prostatectomy specimens in terms of Gleason scores {(AUC) is 0.787 (p=0.001)}.

Transrectal ultrasound-guided biopsy has a 74 % sensitivity and 83 % specificity with a negative and positive predictive value of 83% and 74% respectively.

Conclusion

The overall accuracy of Gleason score on transrectal ultrasound guided biopsies in predicting prostatectomy specimen grade is favorable. However, there are small percentages of discordance between biopsy and radical prostatectomy specimen. Therefore, it is still very important to compare biopsy Gleason scores with the final prostatectomy specimen in the prognosis and treatment options of prostate cancer.

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