ORIGINAL RESEARCH

Concordance of Trans Rectal Ultrasound Guided Prostate Needle Biopsy and Post Radical Prostatectomy Final Histopathology

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Background: The Gleason Sum derived from transrectal ultrasound guided prostate needle biopsy (TRUS-PNB) is critical in the selection of an appropriate treatment and also important in predicting the possible outcome. Scoring is therefore critical in the selection of a proper management. The concordance between prostate needle biopsy and radical prostatectomy histopathology in terms of the Gleason Sum was here in evaluated.
Methods: This is a retrospective cohort where a review and analysis of 28 charts were made. All patients who underwent TRUS-PNB and subsequently radical prostatectomy were included in the study. The concordance rates between prostate needle biopsy and radical prostatectomy histopathology were elucidated.
Results: With the Gleason Sum 6 upon TRUS-PNB (n=17), 9 (53.9%) matched their postoperative pathological findings, while 8 (47.0%) were upgraded to Gleason Sum 7. No finding of downgrading was observed postoperatively. Tumors graded GS7 on TRUS-PNB upon biopsy (n=11) had the best concordance; with 11 (100%) matched at radical prostatectomy. No over grading or downgrading was observed.
Conclusion: GS6 tumors being upgraded to GS7 tumors are still being observed. Owing the diagnosis of prostate cancer relying heavily on biopsy may still yield discordance. Though improvements with regards to biopsy technique may evolve, the usual 12 core biopsy is still being applied. With this, different factors that may predict discordance and strategies to minimize discordance still remain important for the appropriate treatment of prostate cancer.

Key words: transrectal ultrasound-guided prostate needle biopsy

Introduction

Transrectal ultrasound guided prostate needle biopsy has become a mainstay in the clinical diagnosis of prostate cancer.[1] In addition to notable DRE and elevated PSA value, a positive TRUS-PNB increases the sensitivity to detect the presence of prostate cancer. In the evaluation of prostate needle biopsy, multiple grading systems have been made; however, the Gleason grading system is the most widely-accepted.

The Gleason Sum derived from such biopsy specimens is critical in the selection of an appropriate treatment and is also important in predicting the possible outcome. However, Gleason Sum may over grade or under grade the diagnosis of prostate cancer. One example is the gray area between Gleason Sum 6 and Gleason

Sum 7 tumors. Men classified as to having a low risk tumor with scores equal to or less than 6 may be eligible for active surveillance; while men classified as to having an intermediate risk tumor, are more prospective to undergo a radical prostatectomy.[2] Scoring is therefore critical in the selection of a proper management. These findings thus emphasize the need to accurately stratify men by risk, as active surveillance continues to gain support.[4]

The objective of this study was to determine the concordance between prostate needle biopsy and radical prostatectomy histopathology in terms of the Gleason Sum.

Review of Literature

Cancer of the prostate is now recognized as one of the principal medical problems facing the male population. The disease accounts for 9% of all cancer deaths among men.[3] Unlike most cancers, which have a peak age of incidence, the incidence of prostate cancer increases with advancing age. The lifetime risk of a 50-year-old man is 40%, for those detected as an incidental finding at autopsy, 9.5% for those clinically apparent; and for death from 2.9%. Thus, many prostate cancers are indolent and inconsequential to the patient and many are virulent, and if detected too late or left untreated, they result in the patient's death. This broad spectrum of biologic activity can make decision making for individual patients difficult.[5]

Clinically localized prostate cancer generally causes no symptoms. Slowing of the urinary stream, arising at night to void, and increased urinary frequency are common symptoms associated with aging but often are unrelated to the presence of prostate cancer. It is for this reason that early detection tests have been developed in order to identify prostate cancer while it remains confined to the prostate. The two most commonly used tests are serum PSA level and digital rectal examination (DRE).[6]

PSA is a serine protease inhibitor that lyses the coagulum in the ejaculate. It is produced by cells within the prostate and in men, PSA can be measured in the blood. While higher blood PSA levels often are noted in men with prostate cancer, PSA elevation is not specific for prostate cancer. Noting that PSA is more organ-specific and not cancer-specific. Although not absolute, at present, a higher PSA test value is the most common reason why prostate cancer is detected.[6]

A digital rectal examination (DRE) is an examination by a physician using a gloved finger placed into the rectum to feel the surface of the prostate. The region examined is adjacent to the rectal wall where the tumors commonly develop; hard regions, presence of nodules, induration or asymmetry may indicate the presence of prostate cancer.[6]

Although a higher PSA value or abnormal DRE may raise the suspicion of prostate cancer, detection requires confirmation with a prostate biopsy. At the time of biopsy, several small cores of tissue are removed from the prostate and are then examined by a pathologist to determine if cancer is present.[6]

In terms of evaluation of tissue biopsy, the most commonly used system for grading is the Gleason Scoring system. It is a system that relies upon the low-power appearance of the glandular architecture under the microscope. In assigning a grade to a given tumor, pathologists assign a primary grade to the pattern of cancer that is commonly observed and a secondary grade to the second most commonly observed pattern in the specimen. If the entire specimen has only one pattern present, then both the primary and secondary grades are reported as the same grade. The Gleason score or the Gleason sum is obtained by adding the primary and secondary grade together.[5] Gleason scores or sums thus range from 2 to 10. One important point that needs to be clarified is that the primary Gleason Grade is perhaps the most important with respect to placing the patients in prognostic groups. This is most important in assessing the patients with a sum of 7. Patients who have a sum of 7 and a primary grade of 4 (4+3) tend to have a worse prognosis than those having a primary grade of 3 (3+4).[5]

Despite the fact that prostate cancer is so prevalent, many aspects of its management still remain controversial.[4] Issues in the management of a patient with a newly-diagnosed, clinically localized prostate cancer is whether or not any

treatment should be recommended. If treatment is advised, choice of which of the available treatments is best for a particular patient. Specifically, with respect to surgery, it is debated as to whether or not radical prostatectomy offers a survival advantage over expectant management, also referred to as watchful waiting. If effective diagnostic procedures are used unselectively in elderly men with a short life expectancy, a problem of over-diagnosis and over-treatment might occur. Thus the same stage of prostate cancer may need different treatment strategies depending on a patient's life expectancy.[4]

Watchful waiting is based on the premise that some patients will not benefit from definitive treatment of the primary prostate cancer. The decision is made at the outset to forego definitive treatment and to instead provide palliative treatment for local or metastatic progression if and when it occurs. Options for local palliation could include transurethral resection of the prostate or other procedures for the management of urinary tract obstruction, and hormonal therapy or radiotherapy for palliation of metastatic lesions.[8]

In contrast to watchful waiting, a program of "Active Surveillance" is based on the premise that some, but not all, patients may benefit from treatment of their primary prostate cancer. It involves active monitoring of the course of the disease with the expectation to deliver curative therapy if the cancer progresses. This is mainly applicable in younger men with seemingly indolent cancer. This has two goals: 1) provide definitive treatment for men with localized cancers that are likely to progress and 2) reduce the risk of treatment-related complications for men with cancers that are not likely to progress.[8]

An ideal regimen for active surveillance has not been defined but could include periodic physical examination and PSA testing or periodic repeat prostate biopsies to assess for sampling error of the initial biopsy as well as for subsequent progression of tumor grade and/or volume. Suitable candidates for active surveillance are those with lower risk tumors (Gleason Sum less than 6, presence of disease fewer than 3 biopsy cores, PSA density <0.15 ng/mL/g, and clinical stage T1c) could be candidates for this treatment strategy. Several studies have shown that patients with lower grade, localized prostate cancer have a low risk for clinical progression within the first 10 to 15 years after the diagnosis.[8,9]

Under special conditions, some patients with a longer life expectancy may opt for active surveillance as their primary management. This may include patients with very small areas of cancer in their biopsy or patients who, at the time of diagnosis, are reluctant to accept the side effects of potentially curative therapies. If the tumor shows evidence of progression (e.g., increased grade, volume, or stage) while the patient still has a reasonable life expectancy, curative treatments (e.g., surgery or radiation) can be initiated.[10] This can be a difficult clinical decision since signs of progression must be identified before the cancer evolves to a stage (or grade) where therapy is no longer curative. Currently, providing evidence-based recommendations for when to intervene in patients with a long life expectancy are not possible since markers of disease progression are poorly validated. Clinically, follow up strategies includes regular PSA level measurement and DRE with a periodic repeat prostate biopsy along with an option of more active therapy if biochemical (increasing PSA) or histopathologic (increased tumor grade or volume) progression occurs.[11,12]

Radical prostatectomy is a surgical procedure in which the entire prostate gland and attached seminal vesicles plus the ampulla of the vas deferens are removed. Radical prostatectomy may be performed using a retropubic or perineal incision or by using a laparoscopic or robotic-assisted technique. Depending on tumor characteristics and the patient's sexual function, either nerve-sparing (to preserve erectile function) or non-nerve-sparing radical prostatectomy is commonly performed. Pelvic lymphadenectomy can be performed concurrently with radical prostatectomy and is generally reserved for patients with higher risk of nodal involvement.[8]

Since the entire prostate gland is removed with radical prostatectomy, the major potential benefit of this procedure is a cancer cure in patients whose prostate cancer is truly localized. In cases where the prostate cancer is of a high grade, when

the tumor has spread outside of the prostate gland, or when the tumor is not completely excised, removing the prostate may not ensure that all the cancer is eliminated, putting the patient at risk for recurrence.[8]

Significance of the Study

Overgrading and undergrading in terms of Gleason sum in prostate needle biopsy, pose a risk to men who may then receive inappropriate treatment. Therefore, documentation of the concordance between prostate needle biopsy and radical prostatectomy histopathology would help in terms of decision making. It would elucidate how recent events; specifically, the advent of active surveillance and the update in the Gleason grading system, have influenced the discordance rates over time.

Methods

Research Design

The study is a retrospective cohort design. It elucidated the concordance rates between prostate needle biopsy and radical prostatectomy histopathology.

Study Setting and Population

Abstracted records of patients from Veterans Memorial Medical Center who were treated with Radical Prostatectomy from January 2011 to October 2014 were included in the study. Prior to doing Radical Prostatectomy, all patients should have undergone transrectal ultrasound guided prostate needle biopsy (TRUS-PNB).

The Gleason Score, PSA at the time of diagnosis on TRUS-PNB, patient age at surgery, pathological stage, and tumor margins were considered.

Study Sample Selection

The following selection criteria were used to identify studies for inclusion in this research:

Inclusion criteria:

- Prostate biopsy performed within two years prior to radical prostatectomy
- Presence of an existing pathology report for prostate needle biopsy and radical prostatectomy specimen

Exclusion criteria:

- Patients who underwent adjuvant or neoadjuvant treatment as to this can affect both the Gleason score and the PSA value
- Patients having a Gleason score less than 6 or more than 7 on TRUS-PNB

Informed consent

The study is a retrospective cohort. No informed consent was involved in this study

Statistical Analysis

Data were extracted from abstracted records in a cohort. TRUS-PNB Gleason score and radical prostatectomy histopathology Gleason scores were compared and tested for concordance. Following a previous study by Walker and colleagues[2], patients were categorized in 3 patient groups: Gleason score 6/6, Gleason score 6/7 and Gleason score 7/7, where the score preceding the dash belongs to the TRUS-PNB and the subsequent sum to that of radical prostatectomy.

One-way ANOVA was used for continuous variables and the chi - square test for categorical variables.

Results

Preoperative clinical and post-operative pathological characteristics

The cohort analysis yielded 28 charts reviewed. Eighteen RPV (Retired Philippine Veteran) and 10 CP (Civilian) patients who underwent radical prostatectomy from January 2011 to October 2014. All of the data included for analysis fit the inclusion criteria. The records

were then divided into 3 groups: 1). 9/28 (32.14%) men were Gleason 6 on both biopsy and histopathology post RP (GS6/6), 2). 8/28 (28.57) were upgraded from Gleason 6 to Gleason 7 (GS6/7) and 3). 11/28 (39.29%) were Gleason 7 on both (GS7/7). Their respective preoperative and post-operative characteristics were tallied in tables 1 and 2. With respect to their preoperative characteristics, the age, PSA upon diagnosis, TRUS volume yielded no difference in between groups with the p-values of 0.549 and 0. 856 respectively. Mean ages were 67.88, 68.78, 63.66 for GS 6/6, 6/7, 7/7 correspondingly (p=0.276). On their postoperative characteristics, it can be noted on table 2 that the GS 7/7 group has a higher frequency, 10 (90.9%), in terms of postoperative stage (T3/4) compared to the other 2 groups; however, the pathological stage, including the margins yielded no difference in between groups. Conversely, Gleason pattern at RP for GS6/7 and GS7/7 was noted to be statistically significant (p<0.0001).

Frequency of discordance

With the GS6 upon TRUS-PNB (n=17), 9 (53.9%) matched their postoperative pathological findings, while 8 (47.0%) were upgraded to GS7. No finding of downgrading was observed post-operatively, which is due to the limited samples included that fit the inclusion criteria. Tumors graded GS7 on TRUS-PNB upon biopsy (n=11) had the best concordance; with 11 (100%) matched at RP. No over grading or downgrading were observed. (Table 3)

Discussion

Under-grading of GS6 post biopsy prostate cancers is still seen after RP.[2] Based on Walker and colleagues' retrospective study, from May 2004 to April 2011, they found that 48.9% tumors diagnosed via TRUS-PNB as GS6 tumors that turned out to be GS7 after radical prostatectomy.

Table 1. Preoperative characteristics.

		GS 6/6 n = 28	GS 6/7 n = 28	GS 7/7 n = 28	p value
Age	Mean n	67.88 8	68.78 9	63.66 11	0.216
PSA closest to biopsy	Mean n	16.48 8	20.12 9	30.77 11	0.549
TRUS volume	Mean n	41.88 8	47.44 9	45.00 11	0.856

Table 2. Postoperative characteristics.

		GS 6/6 n = 9	GS 6/7 n = 8	GS 7/7 n = 11	p value
Margins	Positive Negative Total	3 (33.3%) 6 (66.7%) 9 (100%)	3 (37.5%) 5 (62.5%) 8 (100%)	6 (54.6%) 5 (45.5%) 11 (100%)	0.187
Pathological stage	pT2 pT3/4 Total	4 (44.4%) 5 (55.6%) 9 (100%)	2 (25.0%) 6 (75.0%) 8 (100%)	1 (9.1%) 10 (90.9%) 11 (100%)	0.918
Gleason pattern at RP	3 +4 4+3 Total	- - -	6 (75.0%) 2 (25.0%) 8 (1005)	6 (54.6%) 5 (45.5%) 11 (100%)	<0.0001
Prostate weight	Mean	42.00	53.00	41.68	0.334

Table 3. Discordance and concordance of biopsy and RP GS results.

Biopsy GS 6		Biopsy GS 7	
Difference*	Frequency (%)	Difference*	Frequency (%)
-1	0 (0.0)	-1	0 (0.0)
0	9 (53.9)	0	11 (100.0)
1	8 (47.0)	1	0 (0.0)
Total	17 (100.0)	Total	11 (100.0)

*Negative scores denote downgrading

In this institutional single center study, from January 2011 to October 2014, the analysis showed a 28.5% under-grading, however, the data on table 3 yielded only n=28 which was noted to be far less from the study of Walker and colleagues' n=356. Interestingly, a high total concordance of 71.4% was noted in predicting GS6 (53.9%) and GS7 (100%) post RP.

There were different clinical features between the 3 subgroups. Compared to GS 6/6, the GS 7/7 had a higher PSA, higher prostate volume. Post operatively, those of GS 7/7 compared to GS 6/6 had a higher pT3 and pT4 disease and a higher positive margin rate. Since this study is a single-center cohort with all patients undergoing the traditional 12 core biopsy, a correlation of larger tumors may harbor a higher grade highly likely. With the following results analyzed, the GS 6/6 subgroup was the most advantageous group. Hence an increase in active surveillance will surely have a favorable effect in this group.

Conclusion

GS6 tumors being upgraded to GS7 tumors are still being observed. Owing the diagnosis of prostate cancer relying heavily on biopsy may still yield discordance. Though improvements with regards to biopsy technique may evolve, the usual 12 core biopsy is still being applied. With this, different factors that may predict discordance and strategies to minimize discordance still remain important for the appropriate treatment of prostate cancer.

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