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Comparison of Cognitive-targeted Biopsy and Systematic Prostate Biopsy for Predicting Radical Prostatectomy Pathology: Upgrading-downgrading and Concordance Rates

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Abstract

Objective: This purpose of this study is to compare the concordance, upgrading and downgrading rates of multiparametric magnetic resonance imaging cognitive-targeted prostate biopsy [COG-targeted biopsy (TB)] and a 12-core systematic prostate biopsy (SB) in order to assess the value of COG-TB in predicting final surgical pathology.

Materials and Methods: In this retrospective study, the medical records of 152 consecutive patients who had undergone 12-core SB (n=105) or 12-core SB and COG-TB of suspicious lesions (n=47) and corresponding radical prostatectomy (RP) at our institution were evaluated. Biopsy and RP pathologies of the two methods were compared for downgrading, upgrading and concordance rates based on the 2014 International Society of Urological Pathology grade groups (GG).

Results: For COG-TB and SB cohorts, total upgrading rates were 21.3% and 26.7%, total downgrading 10.6% and 21.9% and concordance 68.1% and 51.4%, respectively, but the differences were not statistically significant. For GG 1, 2, 3, 4 and 5, the concordance rates at COG-TB and SB were 69.6% versus 52.8%, 68.7% versus 83.1%, 75% versus 30.8%, 50% versus 9.1% and 50% versus 62.5%, respectively. There was no statistically significant difference in concordance rates regarding GG between COG-TB and SB groups. According to GG, there was also no significant difference in the rates of upgrading and downgrading of COG-TB and SB.

Conclusion: Although COG-TB outperforms SB in terms of pathological upgrading, downgrading and concordance rates, COG-TB has no statistically significant advantage over SB in terms of predicting final RP pathology.

Keywords: Prostate biopsy, prostate cancer, radical prostatectomy, upgrading

Introduction

The pathologic grading of prostate cancer (PCa) is based on the Gleason scoring system, and accurate determination of the Gleason score (GS) improves risk prediction, decision-making on treatment alternatives and selection of candidates for active surveillance (AS) (1,2,3,4). The most commonly used method for diagnosing PCs is transrectal ultrasonography (TRUS)-guided systematic biopsy (SB) of the prostate, but nearly one-third of patients are known to have GS upgrading between SB and radical prostatectomy (RP) pathology (5,6,7). Some authors reported that the SB method underestimated the final surgical pathology in 30-43% of cases (7,8). Multiparametric magnetic resonance imaging (mpMRI) is a valuable modality for detecting PCa, and this ability has resulted in the development of various MRI-guided targeted biopsy (TB) methods (1). Furthermore, the most commonly used TB methods are fusion-TB (FUS-TB) and cognitive-targeted biopsy (COG-TB). Previous studies found that TB methods resulted in significantly lower pathologic upgrading or downgrading rates than SB methods (9,10). However, the majority of these studies compared the rates of upgrading and downgrading of SB with FUS-TB (1,10,11). Moreover, the purpose of this study was to compare the concordance, upgrading and downgrading rates of COG-TB and SB in order to assess the value of COG-TB in predicting the final surgical pathology.

Materials and Methods

Before the mpMRI examination and TRUS-guided biopsies, all patients provided written informed consent. All procedures were carried out in accordance with the 1964 Helsinki Declaration

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and its subsequent amendments. In addition, the study was approved by our Institutional Ethics Committee. The registration number for the local ethics committee is I4-219-20.

Patients and Study Design

In this retrospective study, the medical records of 181 consecutive patients who had a prostate biopsy and a corresponding RP at our institution between 2015 and 2019 were evaluated. All of the patients were diagnosed with clinically significant PCa following a prostate biopsy and underwent RP surgery within 3 months of the biopsy procedure. Patients who had prostate mpMRI at other hospitals or who had previously been diagnosed with PCa were excluded from the study. Thus, the study population included 152 patients. They were divided into two groups: those who had only 12-core SB (n=105) and those who had 12-core SB and COG-TBs of suspicious lesions (n=47). All of the patients in the COG-TB group were scanned using a 3T MRI scanner at our institution. The prostate lesions in each patient's mpMRI were described by using a standardised method known as the Prostate Imaging Reporting and Data System (PIRADSv2) (12,13). Patients in the SB group either did not have mpMRI examinations or had only PIRADSv2 score 1 or 2 lesions in mpMRI.

Histopathology

Biopsy and RP pathology specimens were examined at our institution's Department of Pathology by an experienced uropathologist. Biopsy specimens were evaluated using the modified Gleason system developed by the 2014 International Society of Urological Pathology (ISUP) (14). GS and grade groups (GG) were reported separately for each biopsy site. For downgrading, upgrading and concordance rates, the highest GG of biopsy and RP were compared. As a reference standard, histopathological GG from RP sections was used. The patients were divided into five groups labelled GG 1-5 according to the biopsy results. Upgrading and downgrading were defined as an increase or decrease in prognostic GG from one to another.

Multiparametric MRI

Multiparametric MR images were obtained using a 3.0 Tesla system (MAGNETOM Verio; Siemens Medical Solutions, Erlangen, Germany). For signal reception from the patients' prostate, a standard body matrix coil was used. The sequences used in the study were T2-weighted, diffusion-weighted and dynamic contrast-enhanced imaging. Before the biopsy, all patients had mpMRI, and no endorectal coils were used.

Prostate Biopsy

TRUS was performed with a GE P5 ultrasound scanner (GE Healthcare, Tokyo, Japan) and a biplanar convex/convex transrectal probe (BE9CS). The biopsies were performed transrectally, using a full automatic core biopsy device with an 18-gauge, 25-cm Tru-Cut-type needle and the same operator (E.O) with 20 years of TRUS-SB experience. For SB, all of the patients underwent the same 12-core systematic prostate biopsy procedure. For COG-TB procedure, prior to biopsy, the operator (E.O) reviewed each patient's mpMRI and the locations of suspicious lesions. Following a 12-core SB, the regions of lesions with PIRADS 3, 4 or 5 scores were cognitively sampled by taking three extra cores from each lesion location. All biopsy specimens were placed in separate containers labelled with the location of the prostate biopsied and sent for histopathologic evaluation.

Statistical Analysis

For statistical analysis, IBM SPSS® Statistics version 25 was used. Moreover, the Kolmogorov-Smirnov test was used to determine whether variables were suitable for normal distribution. For non-normally distributed variables, descriptive statistics were expressed as median + interquartile range. The chi-square test of independence for categorical variables and Mann-Whitney U test for continuous variables were used to compare cohort demographics and characteristics. As appropriate, the chi-square test was used to determine the significance of differences. In the 95% confidence interval, p-values of <0.05 were considered statistically significant.

Results

Table 1 shows the preoperative clinical and pathological characteristics of the patients, which were similar in both groups. According to biopsy results, GG 1 was the most commonly observed pathology in both the SB and COG-TB groups (52.4%, 48.9%). According to RP, the most common pathology observed was GG 2 for both groups (48.6%, 40.4%). In COG-TB group, total upgrading and downgrading rates were 21.3% and 10.6%, while in the SB group, total upgrading and downgrading rates were 26.7% and 21.9%, respectively. There was no statistically significant difference between the two groups in terms of total upgrading and downgrading rates

Table 1. Clinical and pathological information of the two patients' cohorts

Characteristics	**SB (105) COG-TB (47) p-value* (n=105) (n=47)**
Median age (yr) (IQR)	67 (59-71) 65 (58-9) 0.490
Median PSA (ng/mL) (IQR)	6.10 (5.10-10.20) 5.90 (4.90-8.60) 0.116
Median TRUS Volume mL (IQR)	42 (35-58.5) 45 (33-65) 0.774
Median MRI volume (IQR)	-50 (37-73)
Biopsy ISUP Grade	0.114
Grade 1 Grade 2 Grade 3 Grade 4 Grade 5	55 (52.4%) 23 (48.9%) 18 (17.1%) 16 (33.9%) 13 (12,4%) 4 (8.6%) 11 (10,4%) 2 (4.3%) 8 (7.7%) 2 (4.3%)
Pathologic ISUP Grade	0.330
Grade 1 Grade 2 Grade 3 Grade 4 Grade 5	31 (29.5%) 18 (38.3%) 51 (48.5%) 19 (40.4%) 13 (12.4%) 7 (14.9%) 3 (2.9%) 2 (4.3%) 7 (6.7%) 1 (2.1%)

SB: Systematic prostate biopsy, COG-TB: Cognitive-targeted prostate biopsy, IQR: Interquartile range, PSA: Prostate specific antigen, TRUS: Transrectal ultrasound, MRI: Magnetic resonance imaging, ISUP: International society of urological pathology, *Mann-Whitney U test and chi-square test

(p=0.478, p=0.098) (Table 2). For the COG-TB and SB groups, the overall concordance rates between biopsy and RP pathology were 68.1% and 51.4%, respectively. There was no statistically significant difference between the two groups (p=0.056).

When the results were analysed by GG, the highest concordance was observed in the GG 2 (83.1%) for SB and the GG 3 (75%) for COG-TB groups. The lowest concordance was found in the GG 4 (9.1%) for SB and the GG 4 and 5 (50% for both) for COG-TB groups. Table 2 shows the concordance rates according to GG. Moreover, concordance rates did not differ significantly between the SB and COG-TB groups. SB was upgraded at a higher rate than COG-TB in GG 1 and GG 3 (47.2% versus 30.4% and 7.7% versus 0%, respectively) but at a lower rate in GG 2 (5.8% versus 18.8%). In both groups, no upgrading was noted in GG 4. In terms of different GG, no significant difference in upgrading rates of COG-TB and SB was observed (Table 2). SB has a higher downgrading rate than COG-TB in GG 3, GG 4 and GG 5 but a lower rate than COG-TB in GG 2 (Table 2). In terms of different GG, no significant difference in downgrading rates of COG-TB and SB was observed (Table 2).

Table 2. Upgrading, downgrading and concordance rates according to grade groups

	N (152)	Upgrading p-value* rate	Downgrading p-value* rate	Concordance p-value* rate
ISUP grade 1		0.081	-	0/084
Systematic biopsy COG-TB	55 23	6 (47.2%) 7 (30.4%)	- -	29 (52.8%) 16 (69.6%)
ISUP grade 2		0.231	0.772	0.089
Systematic biopsy COG-TB	18 16	1 (5.8%) 3 (18.8%)	2 (11.1%) 2 (12.5%)	15 (83.1%) 11 (68.7%)
ISUP grade 3		0.567	0.134	0.115
Systematic biopsy COG-TB	13 4	1 (7.7%) 1 -	8 (61.5%) 1 (25%)	4 (30.8%) 3 (75%)
ISUP grade 4		-	0.125	0.165
Systematic biopsy COG-TB	11 2	- -	10 (90.9%) 1 (50%)	1 (9.1%) 1 (50%)
ISUP grade 5		-	0.647	0.567
Systematic biopsy COG-TB	8 2	- -	3 (37.5%) 1 (50%)	5 (62.5%) 1 (50%)
Total		0478	0098	0.056
Systematic biopsy COG-TB	105 47	28 (26.7%) 10 (21.3%)	23 (21.9%) 5 (10.6%)	54 (51.4%) 32 (68.1%)

ISUP: International society of urological pathology, COG-TB: Cognitive-targeted prostate biopsy, *According to chi-square and Fisher's Exact test

Discussion

Classically, GS at RP is regarded as the gold standard and final indicator of cancer severity. On the other hand, preoperative treatment options depend on biopsy GS (3,9). In this regard, biopsy GS is one of the most important criteria for selecting therapeutic approaches such as AS, focal therapy, androgen deprivation therapy, radiotherapy or RP (9,10,15). One of the most important inclusion criteria in AS is GS determined at biopsy, that is, GS less than 7 which equals to ISUP GG 1 (16). On the other hand, definitive treatment is required for patients with clinically localised PCa with GG >1, and these patients generally are typically excluded from AS protocols (16). However, biopsy GS is frequently incongruent with RP GS. Many researchers examined the concordance between biopsy GS to RP GS, and it has been reported that when SB was used, 25-30% of low-grade cancers were upgraded to high-grade cancers at RP (5,6,7,8).

In the relevant literature, some authors evaluated the performance of saturation biopsies, considering that increased sampling would improve the GS concordance, but even saturation biopsy protocols still misclassified GS in 27% to one-third of cases (17,18). This highlights the significance of sampling error in the correlation of biopsy and RP pathology (18). Inaccurate grading is reported to be caused by the sampling error of untargeted SB (19,20). Fortunately, mpMRI allows for the detection and localisation of suspicious prostate lesions, and it has been reported that mpMRI TB predicts the final pathology at RP better than SB (1,9,10,21,22). It was indicated by the PRECISION Trial that TB better detects clinically significant GG 2 and higher PCa than SB (23). The suggested explanation for the lower level of upgrading with TB is that TB may contain a higher percentage of cancer per core due to preferential tumour sampling (11,24,25). TB can be performed using direct MR guidance, with COG-TB or FUS-TB methods (26). Technically, COG-TB is an appealing option because it is not time-consuming and is inexpensive; thus, many centres around the world continue to perform mpMRI-targeted biopsies using the cognitive method (27). However, COG-TB lacks the inherent advantage of FUS-TB in terms of visualising suspicious lesions on the monitor during biopsy. Many studies comparing SB and FUS-TB for upgrading biopsy pathology found that FUS-TB has lower rates of upgrading than SB (1,10,11). However, the purpose of this study was to compare pathology upgrading and downgrading rates of SB and COG-TB, as well as to assess the impact of COG-TB on predicting the final pathology following RP.

In our study group, the rate of total upgrading was 26.7% for SB and 21.3% for COG-TB, but the difference was not statistically significant (p=0.478). Porpiglia et al. (10) reported that the rate of pathological upgrading with SB was significantly higher than with FUS-TB (7.8% for FUS-TB and 39.3% for SB). In a meta-analysis, Goel et al. (9) determined a 23.3% upgrading rate for TB versus 42.7% for SB (p=0.001). The significantly lower upgrading rate of FUS-TB than SB reported in previous studies and the lower but not statistically significant upgrading rate of COG-TB than SB noted in our study can be explained as follows: inaccurate grading is reported to be caused by the sampling error of untargeted biopsy, FUS-TB has the advantage of visualising suspicious lesions on the ultrasound monitor during biopsy, but during COG-TB, the operator is unable to visualise the lesions directly and can only take samples from the suspicious regions (9,10,26). Our results may imply that COG-TB does not have the advantage of FUS-TB when it comes to precise sampling of suspicious lesions.

According to Porpiglia et al. (10), FUS-TB reduced the risk of upgrading at RP for all histopathological categories. In a report

by Epstein et al. (18), a number of SB series were analysed for the incidence of upgrading from biopsy GS 6 to RP GS ≥7, and it was discovered that the mean upgrading was 35%. When we analysed our results by GG, the upgrading rates in GG 1 were 47.2% and 30.4% (p=0.081) for SB and COG-TB, respectively. Here it is important to note that higher upgrading rates from GG 1 to GG 2 will have a significant negative impact on the selection of AS patients. For GG 2, upgrading rate of COG-TB was higher than SB (18.8% versus 5.8%), though the difference was not statistically significant (p=0.231). Within the COG-TB group, no patient was upgraded from GG 3, and only ones (7.7%) was upgraded by SB. Moreover, there were no upgradings noted in both biopsy methods for GG 4 pathology. These findings suggest that, despite not being statistically different, COG-TB may be more valuable than SB for upgrading from GG 1 to GG 2 with lower upgrading rates, thus allowing for more precise selection of patients for AS.

In our study group, the rate of total downgrading was 21.9% for SB and 10.6% for COG-TB, but the difference was not significant (p=0.098). In our cohort, 11.1% of SB and 12.5% of COG-TB pathology were downgraded from GG 2 to GG 1. According to Moussa et al. (28), there is a 7.3% chance of downgrading from GS 3 + 4 to GS 6 for SB. In Epstein's study, 12% of cases diagnosed with GS 3+4 on SB biopsy also had GS 6 at RP (18). Our results support these findings, as we have determined that 12.5% of COG-TB and 11.1% of SB were downgraded from ISUP GG 2 to GG 1. Porpiglia et al. (10) reported that one-third of SB patients with GS 8 in their study group were downgraded to a lesser disease, whereas none were downgraded in the FUS-TB group, and downgrading was significantly higher in SB than in FUS-TB. According to a recent study, it was found that 49% of patients with biopsy GG 4 were downgraded at RP pathology (29). Epstein et al. (18) also reported a similar rate of downgrade from GS 8 as. Another study reported a higher (80.4%) downgrading for single-core GS 8 biopsy pathology (30). According to our results, downgrading of GG 4 was noted at 50% of COG-TB and 90.9% of SB patients (p=0.125). According to Altok et al. (30), the high downgrading rates for biopsy GS 8 may be explained by the ease of finding additional areas of pattern 3 in the predominant foci to downgrade it to GS 4+3 or 3+4 biopsy during histopathological evaluation. They have also proposed that GS 8 patients may have that finding in isolation, with other positive cores showing lower grade (30). Downgrading rate of COG-TB GG 4 pathology in our study group is generally consistent with the literature, but the downgrading of SB GG 4 pathology we have determined is higher than the rates reported in previous studies (10,29,30). This could be due to the relatively lower number of patients with GG 4 biopsy pathology in our study group, which would have an impact on statistical analysis.

According to our findings for the two biopsy methods shows that the overall concordance rate of biopsy and RP pathology was 68.1% for COG-TB and 51.4% for SB (p=0.056). Although COG-TB performed better than SB for concordance with final pathology in all GGs except GG 2, the differences were not statistically significant (Table 2). By using the highest Gleason pattern, Le et al. (11) reported a concordance rate of 54% for SB and 81% for FUS-TB pattern. Our results support the advantage of TB over SB regarding biopsy and RP pathology concordance. However, the overall concordance rate of COG-TB (68.1%) observed in our study is lower than the rate of 81% reported by Le at al. (11) reported using FUS-TB method (17). As previously stated, the reported higher concordance rate of FUS-TB is possibly due to the visualisation of suspicious lesions on the monitor during FUS-TB, as mentioned earlier.

Study Limitations

It is critical to note that our study has some limitations. This is a retrospective study conducted at a single institution. Because the study is focused on GG concordance, upgrading and downgrading of two different biopsy methods, core length or percentage of cancer-positive cores were not included in the definitions. The population size of COG-TB group may be relatively small to show a difference between COG-TB and SB techniques. Because of the limited number of patients in the COG-TB group, no univariate or multivariate analysis for predicting of concordance rates for variables such as prostate volume, prostate specific antigen or prostate specific antigen density. On the other hand, all biopsies in or study group were performed by a single experienced operator, and which is a strength of our study, but the operators with varying levels of experience may achieve different results.

Conclusion

Despite not being significantly different, COG-TB may be more valuable than SB for upgrading from GG 1 to GG 2 with lower upgrading rates, thus allowing more precise selection of patients for AS. Although COG-TB outperforms SB in terms of overall pathological upgrading, downgrading and concordance rates, our results indicate that COG-TB has no statistically significant advantage over SB for predicting the final RP pathology.

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Ethics

Ethics Committee Approval: All procedures were carried out in accordance with the 1964 Helsinki Declaration and its subsequent amendments. In addition, the study was approved by our Institutional Ethics Committee. The registration number for the local ethics committee is I4-219-20.

Informed Consent: Before the mpMRI examination and TRUS-guided biopsies, all patients provided written informed consent.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: E.Ö., Design: E.Ö., A.İ., Data Collection or Processing: A.İ., Ç.A., E.K., Analysis or Interpretation: Ç.A., E.K., Ç.G., Literature Search: Ç.G., S.B., D.K., Writing: Ç.G., S.B.

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