IVYSPRING INTERNATIONAL PUBLISHER

Journal of Cancer

2018; 9(19): 3634-3639. doi: 10.7150/jca.26791

Research Paper

Risk of upgrading from prostate biopsy to radical prostatectomy pathology: Is magnetic resonance imaging-guided biopsy more accurate?

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Received: 2018.04.20; Accepted: 2018.07.25; Published: 2018.09.08

Abstract

Background: This study compared magnetic resonance imaging-guided biopsy (MRI-GB) and transrectal ultrasound guided biopsy (TRUS-GB) with the final histology of the radical prostatectomy (RP) specimen.

Methods: Our subjects were 229 patients with prostate cancer (PCa), proven histopathologically using MRI-GB or TRUS-GB, who underwent RP at our center between December 2015 and December 2016. The main group included 92 patients who underwent MRI-GB and the control group included 137 patients who underwent 12-core TRUS-GB. Histological findings for RP specimens were compared with those from biopsies. We also evaluated predictors of upgraded Gleason score (GS), using uni- and multivariate analyses.

Results: Upgraded GS between biopsy and RP specimen occurred to 22.7% (52/229) of the cohort overall. In univariate analysis, prostate-specific antigen density (PSAD) (P<0.001), prostate volume (PV) < 30 ml (P<0.001), biopsy modality (P=0.027), biopsy GS (P=0.032) and measured MRI lymph node metastasis (P=0.018) were prognostic factors. Multivariate logistic regression analysis showed PV < 30 ml (P<0.001) and biopsy modality (P=0.001) were independent predictors of upgraded GS.

Conclusions: MRI-GB may enhance the diagnostic accuracy of prostate cancer detection in final histopathology with lower rate of upgraded GS than TRUS-GB. Also, PV < 30 ml and biopsy modality were independent predictors of upgraded GS.

Key words: MRI; prostate biopsy; prostatectomy specimen; systematic biopsy; Gleason score upgrading.

Introduction

Clinicians depend heavily on the prostate biopsy Gleason score (GS) to predict tumor aggressiveness and counsel patients for further treatment [1]. Accurate assessment of tumor aggressiveness is essential in diagnosing PCa. Although active surveillance (AS) is often recommended to patients with low-risk PCa to avoid overtreatment [2], GS between prostate biopsy and radical prostatectomy (RP) specimens is occasionally discordant, with GS assessed by surgical specimen often lower than that of biopsy specimen [3]. As a result, PCa risk may be underestimated and patients might not obtain adequate medical care [4]. Reportedly, GS is underestimated in up to 43% of patients, compared with their radical prostatectomy (RP) specimens [5-7].

Inaccuracy of biopsy-based GS is associated with interobserver variability by different pathologists [8-10], and more significantly, with random error

from 12 core transrectal ultrasound guided biopsy (TRUS-GB) [10]. Current practice trends suggest that the use of magnetic resonance imaging-guided biopsy (MRI−GB) has been rapidly increasing worldwide and has become a more important diagnostic tool for PCa. MRI-GB is a promising method for accurate assessment of GS, enabling better tumor visualization and targeting of PCa. In-bore MRI prostate biopsy can be used for targeted biopsies. Numerous studies suggest that targeted biopsies reveal significantly greater percentages of cancer involvement in biopsy cores [5, 11-15].

The relationship between MRI-GB and final RP specimen histopathology has not been widely studied [13, 16]. This study compared outcomes from MRI-GB with histological results from RP specimens, and evaluated independent predictive factors for upgraded GS.

Patients and methods

Patients

We initially included 245 patients who underwent laparoscopic RP at First Affiliated Hospital of Fujian Medical University in the period from December 2015 to December 2016, after being diagnosed with PCa by MRI-GB or TRUS-GB without distant metastasis at our center, in this retrospective study. We excluded the 16 patients who received neoadjuvant androgen deprivation, chemotherapy radiotherapy, previous prostate surgery, or treatment with 5-alpha reductase inhibitors that could interfere with the histological interpretation of the RP specimen. Finally, 229 cases were included in this study. We prospectively collected data on age, digital rectal exam (DRE), prostate-specific antigen (PSA), prostate volume (PV), prostate-specific antigen density (PSAD), potential lesions and preoperative lymph node metastasis detected by mpMRI, Prostate Imaging Reporting and Data System (PI-RADS) score, biopsy GS, final pathological GS after RP, biopsy cores, positive biopsy cores, tumor-involved positive biopsy cores, clinical stage, and invasion of seminal vesicles.

Multiparametric magnetic resonance imaging

MpMRI of the prostate was performed on a 3-T MRI scanner (Siemens, Munich, Germany). All patients underwent mpMRI before surgery. The MRI protocol was designed according to recommendations of the European Consensus Meeting (ESUR) on standardization of prostate MRI [17]. To characterize lesions, we calculated the PI-RADS score from the sum of the scores of each sequence (T1-weighted [T1WI], T2-weighted [T2WI], diffusion-weighted [DWI], dynamic contrast-enhanced MRI [DCE] and magnetic resonance spectroscopy [MRS]) [18]. A PI-RADS≥2 lesion on MRI was defined as biopsy target. The complete mpMRI data set was analyzed by 2 radiologists, each with at least 4 years of experience with prostate MRIs.

Multiparametric magnetic resonance imaging targeted biopsy

A total of 92 patients underwent mpMRI, all under local anesthesia, to locate their potential prostate lesions. After that, patients were placed in the decubitus position in a 3.0-T MRI scanner (Siemens, Munich, Germany), and underwent transperineal biopsy with an MRI-compatible, 18-gauge, semi-automatic biopsy gun (model: TZ 18/16 18 G×16 cm, i-MED, Suzhou, China), in which two targeted biopsy cores were taken from potential prostate lesion. Urethra, bladder and rectal injury and hemorrhage were reevaluated after biopsy. All mpMRI-GBs were performed by the same expert urologist.

Transrectal ultrasound guided biopsy

A total of 137 patients underwent TRUS-GB using color Doppler ultrasonography (Siemens-Acuson, Aspen, USA). With a 18-gauge, fully automatic biopsy gun (Max-Core, Bard, America), all 137 patients underwent 12-core TRUS-GB, including 6 sextant biopsy cores with 6 additional biopsy cores taken at the base, mid gland and apex of the prostate on the right and left sides[19]. Patients received 500 mg oral ciprofloxacin on the night before, as standard antibiotic prophylaxis. All TRUS-GBs were performed by the same urologist [20].

Radical prostatectomy

All patients underwent RP, which were performed by the same experienced urologist.

Pathological analysis

Specimens from needle biopsies and RP were assessed by the same expert pathologist from Department of Pathology in our center. We followed the recommendations of the 2005 International Society of Urological Pathology consensus for GS [21]. The highest-grade pattern was recorded. Upgraded GS was defined as any increased total sum in the pathological GS compared with that of the biopsy GS [11]. In addition, increased main structure score without changing the total sum was also defined as an upgraded GS.

Statistical analysis

Normally distributed parameters were compared between the TRUS-GB and MRI-GB

groups, using Student's *t*-test for independent groups. Nonparametric data were tested using the Mann–Whitney U test. Normally distributed data are shown as the mean ± standard deviation (SD), and other data are shown as the median and interquartile range (IQR). Clinical and pathologic parameters were analyzed by univariate (chi-square test) and multivariate (logistic regression model) methods. The statistical program SPSS, version 19, (SPSS, Chicago, I) was used. P <0.05 was considered significant [22].

Results

The MRI-GB group (n=92) and the TRUS-GB group (n=137) did not significantly differ in baseline characteristics, including age, DRE results, PSA level, PSAD, mean tumor involvement positive biopsy cores, or PI-RADS score (P>0.05, Table 1), but did differ with respect to PV, biopsy cores and proportion of cancer involvement (P<0.05, Table 1). Percentage distribution of the highest GS is shown in Table 2. MRI-GB detected 10 (10.9%) GS 6, 43 (46.7%) GS 7 (3+4), 11 (12.0%) GS 7 (4+3), and 28 (30.4%) GS ≥ 8 tumors. TRUS-GB detected 23 (16.8%) GS 6, 32 (23.4%) GS 7 (3+4), 39 (28.5%) GS 7 (4+3) and 43 (31.4%) GS ≥ 8 tumors.

Table 1. Baseline characteristics of included patients

Variable	TRUS-GB	MpMRI-TB	P value
Case, n	137	92	
Age, year (rang)	66(53.0-77.0)	67.5(53.0-78.0)	0.754
DRE, n (%)			0.205
Normal	81 (59.1%)	62 (67.4%)	
Abnormal	56 (40.9%)	30 (32.6%)	
PSA, ng/ml (rang)	15.5(0.4-156.0)	14.6(4.0-114.0)	0.199
Prostate volume, ml (rang)	31.5(10.6-91.1)	39.9(13.5-85.0)	<0.001*
PSAD, ng/ml/ml (rang)	0.5(0.0-14.8)	0.4(0.1-2.7)	0.278
Average PI-RADS score (rang)	3(3.0-5.0)	4(3.0-5.0)	0.717
Biopsy cores/case, n (rang)	12(1.0-12.0)	2(0.6-12.0)	<0.001*
Positive biopsy cores, (rang)	6(1.0-15.0)	6(1.0-19.0)	0.064
Proportion of cancer involvement, % (rang)	26.8(4.6-100.0)	31.8(7.5-100.0)	<0.001*

*P<0.05; MpMRI-TB: multiparametric magnetic resonance imaging targeted biopsy, TRUS-GB: transrectal ultrasound guided biopsy, DRE: digital rectal examination, PSA: prostate specific antigen, PSAD: prostate-specific antigen density, PI-RADS: Prostate Imaging Reporting and Data System.

Table 2. Overview of highest Gleason scores from the mpMRI-TB and TRUS-GB groups.

Highest Gleason score	TRUS-GB		MpMRI-TB		Total	
3 + 3 = 6	23	10.0%	10	4.4%	33	14.4%
3 + 4 = 7	32	14.0%	43	18.8%	75	32.8%
4 + 3 = 7	39	17.0%	11	4.8%	50	21.8%
≥8	43	18.8%	28	12.2%	71	31.0%
Total	137	59.8%	92	40.2%	229	100.0%

MpMRI-TB: multiparametric magnetic resonance imaging targeted biopsy, TRUS-GB: transrectal ultrasound guided biopsy.

Concordance of GS between biopsy specimens and final pathological specimens after RP is shown in Table 3. All cases were divided into an upgraded subgroup (n=52) and a non-upgraded subgroup (n=177). Independent risk factors associated with upgraded GS were subsequently analyzed. Univariate analysis demonstrated that age, PSA, PI-RADS score, clinical stage, final pathological GS, invasion of seminal vesicles, invasion of capsule and positive cores did not significantly differ between the two subgroups (P > 0.05, Table 4); but they did differ in PSAD (P<0.001), PV (P<0.001), biopsy modality (P=0.027), biopsy GS (P=0.032) and lymph node metastasis (P=0.018). In multivariate logistic regression analysis, only PV (P<0.001) and biopsy modality (P=0.001) were independent predictors of GSU after RP (Table 5).

Table 3. Concordance of Gleason score between biopsies and radical prostatectomy specimen in the mpMRI-TB and TRUS-GB groups

	Radical prostatectomy				
	GS 3+3=6	GS 3+4=7	GS 4+3=7	GS ≥ 8	Total
mpMRI-TB					
GS 3+3=6	8	1	1	0	10
GS 3+4=7	0	33	10	0	43
GS 4+3=7	0	0	9	2	11
GS ≥ 8	0	0	0	28	28
Total	8	34	20	30	92
TRUS-GB					
GS 3+3=6	6	8	9	0	23
GS 3+4=7	0	28	0	4	32
GS 4+3=7	0	4	26	9	39
GS ≥ 8	0	4	10	29	43
Total	6	44	45	42	137

MpMRI-TB: multiparametric magnetic resonance imaging targeted biopsy, TRUS-GB: transrectal ultrasound guided biopsy.

Table 4. Univariate analysis of possible GS predictors

Variables	Non-upgrading	Upgrading	P value
Case, n (%)	177	52	
Age, year(rang)	66.0 (53.0-77.0)	68.0 (57.0-78.0)	0.122
PSA, ng/ml(rang)	15.0 (0.7-114.0)	14.8 (0.4-156.0)	0.577
PSAD, ng/ml/ml(rang)	0.4 (0.0- 2.7)	0.5 (0.0-14.8)	<0.001 *
Prostate volume			<0.001*
<30ml	24 (13.6%)	40 (76.9%)	
≥30ml	153 (86.4%)	12 (23.1%)	
Biopsy modality, n (%)			0.027*
mpMRI-TB	78 (44.1%)	14 (26.9%)	
TRUS-GB	99 (55.9%)	38 (73.1%)	
PI-RADS score, n (%)			0.535
3	90 (50.8%)	28 (53.8%)	
4	40 (22.6%)	14 (26.9%)	
5	47 (26.6%)	10 (19.2%)	
Clinical stage, n (%)			0.148
T1c	29 (16.4%)	6 (11.5%)	
T2a	31 (17.5%)	17 (32.7%)	
T2b	24 (13.6%)	4 (7.7%)	
T2c	52 (29.4%)	11 (21.2%)	
T3a	39 (22.0%)	14 (26.9%)	
T3b	2 (1.1%)	0 (0.0%)	
Biopsy Gleason score, n (%)			0.032*
<7	17 (9.6%)	11 (21.2%)	
≥7	160 (90.4%)	41 (78.8%)	
Postoperative Gleason score, n (%)			0.201
<7	14 (7.9%)	1 (1.9%)	
≥7	163 (92.1%)	51 (98.1%)	
Invasion of seminal vesicle, n (%)			0.421
No	113 (63.8%)	30 (57.7%)	
Yes	64 (36.2%)	22 (42.3%)	

Variables	Non-upgrading	Upgrading	P value
Invasion of capsule, n (%)			0.198
No	86 (48.6%)	20 (38.5%)	
Yes	91 (51.4%)	32 (61.5%)	
Lymph node metastasis, n (%)			0.018*
No	135 (76.3%)	31 (59.6%)	
Yes	42 (23.7%)	21 (40.4%)	
Positive biopsy cores ,n (rang)	6.0 (1.0-19.0)	6.0 (1.0-16.0)	0.907

*P<0.05; PSA: Prostate specific antigen, PSAD: prostate-specific antigen density, PI-RADS: Prostate Imaging Reporting and Data System.

Table 5. Multivariate logistic regression of independent predictors of upgraded GS after radical prostatectomy

Variable	*P value*	*Odd ratio (95% confidence interval)*
PSAD	0.273	0.8 (0.6, 1.1)
PV (<30ml vs. ≥30ml)	<0.001*	0.7 (0.6, 0.8)
Biopsy modality	0.001 *	12.1 (2.6, 55.4)
Biopsy Gleason score (<7 vs.≥7)	0.367	0.4 (0.1, 3.0)
Lymph node metastasis	0.734	0.8 (0.3, 2.3)

*P<0.05; PSAD: prostate-specific antigen density, PV: prostate volume.

Discussion

Gleason scores are important for therapeutic decisions with regard to prostate cancers [23, 24]. They can predict time to development of metastatic disease for patients who undergo radiation therapy (RT) [25], and inform therapeutic strategy. Accuracy of GS is therefore very important, especially for those patients who require treatments other than RP, such as AS or RT. Underestimated GS may lead to insufficient therapy; patients may lose the opportunity for optimal treatment. Hence, correct GS from biopsy is important.

Although TRUS-GB remains the golden standard in PCa diagnosis, its large sampling error suggests low reliability. The GS is often underestimated by TRUS-GB, which contributes to upgraded GS after RP. King et al. [7] declared the upgraded GS rate after RP to be 35–43%; Cohen et al. [6] found the upgraded GS to be 30%; a study from Lahey clinical center (n=2890) showed the upgraded GS rate to be 36% (consistent with Cohen's study[6]); Milonas et al. [26] reported an upgraded GS rate of 38.2% (n=241); and Suer et al. [27] in a study of 632 patients who underwent RP, found an upgraded GS rate of 28.9%, with a GS concordance rate of 59.8%. Our study showed an upgraded GS rate of 22.7%, which was concordant with previous studies.

In multivariate logistic regression analysis, we found biopsy modality and smaller prostate volumes (< 30 ml) were independent predictors of upgraded GS after RP. We also found MRI-GB to provide higher concordance on histological GS between biopsy and RP specimens than did TRUS-GB. Previous studies reported GS concordance rates between in-bore MRI-GB and RP specimens as 57–90% [5, 12], which aligned with our results. The study of Le et al. [28] suggested that the GS concordance rate was 81%, and the upgraded GS rate was 17%, among 54 patients who underwent targeted biopsy using MRI ultrasound fusion. However, Arsov et al.[19] found the upgraded GS rates for MRI-GB and TRUS-GB were 40.4% and 50.0%, respectively.

We found that PV < 30 ml was an independent risk factor for upgraded GS after RP. Of the 64 patients whose PV was less than 30 ml, 62.5% (40/64) had upgraded GS, compared with 7.3% (12/165) of the patients with larger PV. Freedland et al. [29] reported that the smaller prostates are correlated with higher pathological grade and have biologically more aggressive behavior. Because of a greater likelihood that high grade disease exists, smaller prostates are more likely upgraded. Another explanation is that the PSA level is commonly influenced by gland volume and not by cancer. However, PSA level drives biopsy recommendations. As described by previous studies [30-32], the concomitant presence of a large volume, benign gland is a confounding factor in the relationship between prostate cancer and PSA. Turley et al. [33] found that men with PV ≤ 20 cm^3 were 5 times more likely to be upgraded than were men with PV > 60 cm^3. Moon et al. [34] found that PV ≤36.6 cm^3 was an independent risk factor for upgraded GS among patients from Asia. Chung et al. [35] reported that smaller PV was a predictor of upgraded GS after RP; men with PV ≤ 25 cm^3 were 2.7 times more likely to be upgraded than men with PV > 40 cm^3.

There are limitations in this study. Firstly, this retrospective study was a single center design with a small sample size. Secondly, trails are needed to test MRI as a screening or upfront test compared to standard 12-core TRUS. Thirdly, some researchers reveals that mpMRI holds the promise of eliminating unnecessary biopsies, mpMRI can then be used as a triage test in the population with negative test result[36-38]. However, this topic was not discussed in our study.

In a word, we found that MRI-GB decreased the rate of upgraded GS after RP, and biopsy modality and smaller PV were independent predictors of upgraded GS. Further studies are needed to explore the relationship between MRI-GB and GS to aid urologists in assessing patients and making therapeutic decisions.

Clinical Practice Points

Numerous studies indicate that targeted biopsies reveal significantly greater percentages of cancer involvement in biopsy cores. However, the relationship between MRI-GB and final RP specimen histopathology has not been widely studied. We found that MRI-GB may enhance the diagnostic

accuracy of prostate cancer detection in final histopathology with lower rate of upgraded GS than TRUS-GB, which may contribute to better therapeutic decisions. Biopsy modality and smaller PV were independent predictors of upgraded GS.

Acknowledgements

Funding

This study was supported by the Joint Foundation of Fujian Province for Science and Technology Innovative Research Project (Grant number: 2017Y9093), Natural Science Foundation of Fujian Province (Grant number: 2017J01197), the Youth Foundation of Health and Family Planning Commission of Fujian Province, China (Grant number: 2017-1-58), Natural Science Foundation of Fujian Province (Grant number: 2018J01177), and Startup Fund for scientific research, Fujian Medical University (Grant number: 2017XQ2041), the Creative Program of Health and Family Planning Commission of Fujian Province, China (Grant number: 2015-CX-24).

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Ethics approval and consent to participate

The project was approved by the Institutional Ethics Committee of First Affiliated Hospital of Fujian Medical University. Informed consent was obtained from all the patients or their relatives prior to analysis.

Authors' contributions

Conception/Design: Ning Xu, Yu-Peng Wu, Xiao-Dong Li; Provision of study material or patients: Min-Yi Lin, Qing-Shui Zheng; Collection and/or assembly of data: Shao-Hao Chen, Jun-Feng Li; Data analysis and interpretation: Yong Wei, Xue-Yi Xue; Manuscript writing: Ning Xu, Yu-Peng Wu, Xiao-Dong Li; Final approval of manuscript: Qing-Shui Zheng, Yong Wei, Xue-Yi Xue.

Competing Interests

The authors have declared that no competing interest exists.

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