Prostate Int 3 (2015) 127–131

Contents lists available at ScienceDirect

Prostate International

journal homepage: http://p-international.org.

Original Article

Nonvisible tumors on multiparametric magnetic resonance imaging does not predict low-risk prostate cancer

Seung Hwan Lee [1], Kyo Chul Koo [2], Dong Hoon Lee [3], Byung Ha Chung [2,*]

[1] Department of Urology, Severance Hospital, Yonsei University College of Medicine, Seoul, South Korea
[2] Department of Urology, Gangnam Severance Hospital, Yonsei University Health System, Seoul, South Korea
[3] Department of Urology, Busan National University College of Medicine, Busan, South Korea

ARTICLE INFO

Article history:
Received 10 August 2015
Received in revised form
20 September 2015
Accepted 24 September 2015
Available online 8 October 2015

Keywords:
Active surveillance
Low risk
Magnetic resonance imaging
Prostate cancer

ABSTRACT

Purpose: To determine whether multiparametric MRI could help predict the diagnosis of low-risk prostate cancer (PCA).
Methods: We retrospectively analyzed consecutive 623 patients with PCA who underwent multiparametric MRI before radical prostatectomy(RP). High-resolution T1- and T2-weighted, diffusion-weighted, and dynamic precontrast and postcontrast image sequences were obtained for each patient. Of the 623 patients, 177(28.4%) exhibited non visible tumors on MRI of clinical stage T1c. The imaging results were compared with the pathological findings with respect to both stage and Gleason scores (GS).
Results: Of the 177 prostatectomy patients with non visible tumors on MRI, pathological findings resulted in the upgrading of 49(27.7%) patients to a sum of GS 7 or more. 101(57.1%) patients exhibited tumor volumes greater than 0.5cc. The biochemical recurrence rate was significantly higher in the pathological upgraded group compared with the nonupgraded group after a mean follow-up time of 29 months. In the multiple logistic analysis, non visible tumor on MRI was not a significant predictor of low-risk PCA.
Conclusions: Even though cancer foci were not visualized by postbiopsy MRI, the pathological tumor volumes and extent of GS upgrading were relatively high. Therefore, nonvisible tumors by multiparametric MRI do not appear to be predictive of low-risk PCA.

1. Introduction

The detection of low-risk prostate cancer (PCA) has increased as cancer screening programs and detection mechanisms have improved.[1] Since the number of patients diagnosed with low-risk PCA has increased in recent times, the ability to precisely localize tumor foci within the prostate has become an important goal. Accurately identifying the positions of PCA tumors would increase staging accuracy, improve patient selection for active surveillance (AS), and facilitate treatment planning.[2]

A growing body of evidence indicates that AS is the most suitable approach for a select group of men with low-risk PCA.[3] However, pretreatment diagnosis of low-risk PCA is often difficult since PCA is a multifocal, heterogeneous disease.[4] Moreover, the current criteria used to define low-risk PCA cannot reliably determine whether AS is the best treatment option for each patient. Some studies have reported that even low-risk PCA may demonstrate disease upgrading or upstaging.[5,6] Even known indicators of the severity of PCA, such as prostate-specific antigen (PSA) kinetics or initial biopsy results at the time of PCA diagnosis, do not reliably predict adverse pathology when men are monitored by AS.[7] Therefore, imaging techniques have played an increasingly important role in the management of localized PCA. However, no imaging modality presently available is able to measure the actual cancer volume.[8] Moreover, no current criteria for AS reliably includes clinical staging based on the imaging modality. Therefore, the aim of the present study was to determine whether multiparametric magnetic resonance imaging (MRI) could help predict the diagnosis of low-risk PCA. Focusing on nonvisible tumors on multiparametric MRI of clinical stage T1c, we assessed the clinicopathological relationships between the biopsy and pathological results.

* Corresponding author. Department of Urology, Yonsei University College of Medicine, Gangnam Severance Hospital, 712 Eonjuro, Gangnam-gu, Seoul, South Korea.
E-mail address: chung646@yuhs.ac (BH Chung).

http://dx.doi.org/10.1016/j.prnil.2015.09.005

2. Materials and methods

We retrospectively analyzed 623 consecutive patients with PCA who underwent multiparametric MRI before radical prostatectomy (RP) at our institution. Patients who had undergone prostate biopsy at another institution, hormone therapy, or radiation therapy before the RP were excluded from the study.

All patients underwent a transrectal, ultrasound-guided 12-core needle biopsy. In all patients, the serum PSA level was obtained before digital rectal examination and transrectal ultrasonography. Clinical staging was performed according to the TNM staging system, and the ellipsoid formula was used to derive the prostate volume via transrectal ultrasonography.

For all clinical staging protocols, all patients underwent imaging using a 3.0T MRI system (Intera Achieva 3.0T, Phillips Medical System, Best, The Netherlands) equipped with a phased array coil (6-channel) before RP. All patients also underwent diffusion weighted-MRI, in addition to the routine prostate MRI protocol used at our institution. Two b values (0 and 1,000) were used, and diffusion restriction was quantified using ADC mapping. T2-weighted images were acquired in three orthogonal planes (axial, sagittal, and coronal). Dynamic contrast-enhanced MRI was also performed. All images were retrospectively reviewed by two experienced uroradiologists who were blinded to biopsy results and who conducted a consensus review of the MRI of all patients.

Of the 623 patients included in the analysis, 177 (28.4%) had a nonvisible tumor on MRI of clinical stage T1c. The imaging results were then compared with the pathological findings with respect to stage and Gleason score (GS). All biopsy and RP specimens were reviewed by a single genitourinary pathologist, and all biopsy cores were individually labeled. For each biopsy protocol, the number of cores containing tumor tissue, the total length of tissue sampled, the total length of the cancer detected, and the GS were determined. Transverse whole-mount step section specimens were obtained at 3–4mm intervals on a parallel plane, and the genitourinary pathologist followed a standardized processing and reporting protocol.[9] Tumor volume (cc) was evaluated by visual estimation. Tumor area was measured in the x and y diameters, and the tumor area was then multiplied by the tumor depth, as determined by the presence of the tumor in subsequent sections and the thicknesses of those sections. The total sum of all tumor foci corresponded to the estimated tumor volume. To achieve objective interpretation, another reviewer integrated the radiology and pathology results.

Clinicopathologic outcomes were compared using the Chi-square test and independent *t* test for categorical and continuous variables, respectively. Low-risk PCA was defined as an organ-confined, postoperative GS 6 tumor with a volume less than 0.5 cm^3. For AS, the criteria outlined in the Prostate Cancer Research International: Active Surveillance protocol were used. The inclusion criteria for Prostate Cancer Research International: Active Surveillance include: a biopsy GS ≤ 6, a PSA level ≤ 10 ng/mL, a PSA density ≤ 0.2 ng/mL/cm^3, and no more than two positive cores. However, only patients with tumors of clinical stage T1c were included for AS in this study. Multivariate logistic regression analysis was then performed to identify predictors of low-risk PCA. All statistical tests were two-tailed and were performed using SPSS version 20.0 software (SPSS Inc., Chicago, IL, USA). A P value < 0.05 was considered statistically significant.

3. Results

The patient ages in this study ranged from 48 years to 74 years (mean ± standard deviation, 63.3 ± 6.2 years), and the serum PSA levels at diagnosis ranged from 3.2 ng/mL to 21.7 ng/mL (mean ± standard deviation, 6.0 ± 1.9 ng/mL). The median biopsy GS was 6 (range, 3–9). The mean interval between the *transrectal ultrasound*-guided biopsy and the postbiopsy MRI was 22.0 ± 1.3 days (range, 2–32 days). In all patients, RP was performed within 52 days (range, 6–52 days; median 21 days) after MR imaging.

The pathological findings of the 177 patients with nonvisible tumors on MRI (clinical stage T1c) before RP are shown in Table 1. These pathological findings resulted in the upgrading of 49 (27.9%) patients to a sum of GS 7 or more. One hundred and one (57.1%) patients exhibited a tumor volume greater than 0.5 cc. The numbers of patients with tumors of pathological stage T2 and T3 or above were 126 (71.0%) and 51 (29.0%), respectively.

The clinicopathological findings in the pathological upgraded group ($N = 49$) and the pathological nonupgraded group ($N = 128$) are compared in Table 2. Both the average level of PSA and the average PSA density were significantly different between the two groups ($P < 0.01$). Interestingly, the average number of cores involved and the maximum core diameters were significantly higher in the pathological upgraded group compared with the pathological nonupgraded group, even though the average GS at biopsy were not significantly different between the two groups ($P = 0.02$ and $P < 0.01$, respectively). Furthermore, the biochemical recurrence rate (BCR) was significantly higher after the follow-up period (mean, 29 months) in the pathological upgraded group compared with the nonupgraded group ($P < 0.01$; Table 2).

Of the 39 patients with tumors of clinical stage T1c who met the criteria for AS, seven patients (17.9%) showed pathological GS upgrading, and three patients (7.7%) were classified as pathological stage T3 or above. However, of the 138 patients with tumors of clinical stage T1c who did not meet the criteria for AS, 42 patients (30.4%) showed pathological GS upgrading, and 48 patients (34.8%) were classified as pathological stage T3 or above. Candidates who did not meet the criteria for AS and who exhibited nonvisible tumors on MRI had significantly higher incidences of pathological upgrading and upstaging compared with candidates who meet the criteria for AS with nonvisible tumors on MRI ($P < 0.01$ and $P = 0.02$, respectively). Of the entire study cohort, nonvisible tumors on MRI were detected in 177 patients (28.4%), whereas 446 patients (71.6%) had visible tumors (Fig. 1). No significant differences in the extent of pathological GS upgrading, staging classifications, or BCR rates were observed between the two groups.

Using multivariate logistic regression analysis to predict the development of low-risk PCA, both PSA level and PSA density were significantly associated with an increased likelihood for developing low-risk PCA. However, tumor visibility on the preoperative MRI scan did not exhibit this association (Table 3).

Table 1
Pathological findings from analyses of radical prostatectomy specimens from patients preoperatively classified as clinical stage T1c.

Findings	No. of patients (%)
Total no. of patients	177
Pathological Gleason score	
Upgraded	49 (27.9)
Downgraded	26 (14.7)
Identical	102 (57.6)
Stage	
T2a	53 (29.9)
T2b	51 (28.7)
T2c	22 (12.4)
≥T3	51 (29.0)
Positive surgical margin	62 (35.5)
Tumor volume (cc)	
0–0.5	76 (42.9)
>0.5	101 (57.1)