Laparoscopy/Robotics

Efficacy of Using Three-Tesla Magnetic Resonance Imaging Diagnosis of Capsule Invasion for Decision-Making About Neurovascular Bundle Preservation in Robotic-Assisted Radical Prostatectomy

Kazushi Tanaka, Katsumi Shigemura, Mototsugu Muramaki, Satoru Takahashi, Hideaki Miyake, Masato Fujisawa

Division of Urology, Department of Surgery Related, Kobe University Graduate School of Medicine, Kobe, Japan

INTRODUCTION

Prostate cancer (PC) increasingly presents as early-stage disease clinically owing to increased screening, including prostate-specific antigen (PSA) screening. The standard of care for organ-confined cancers has been retropubic radical prostatectomy, which carries a substantial risk of morbidity, including incontinence and impotence [1]. Robot-assisted radical prostatectomy (RARP) provides improved visualization of the surgical field and improved instrument control compared with open and laparoscopic prostatectomy [2]. However, surgeons performing RARP lack the tactile feedback upon which they have traditionally relied to determine the extent of resection [3].

In this situation, preoperative detection of extracapsular extension (ECE) may be necessary to guide the surgi-
onal strategy in radical prostatectomy, to achieve PC-negative margins, and to spare the neurovascular bundles (NVBs) as much as possible to preserve erectile function and good postoperative continence [4-6].

In most cases, current PC staging is based on clinical assessment, notably, digital rectal examination (DRE), to sense a nodule or an extraprostatic rigid mass during prostate palpation. This clinical approach seems outdated, however, because DRE has low specificity [7]. Prostatic magnetic resonance imaging (MRI) appears to be a promising method for detecting PC and even for evaluating ECE during the pretreatment workup [8-10]. However, data about the specific role of prostatic MRI in PC staging are still lacking [11]. Moreover, racial differences have been reported in PC tumor aggressiveness and invasion characteristics [12]. Specific racial guidelines for decision making about nerve sparing may need to be established.

In this study, we evaluated the utility of 3-T MRI for assessing ECE and indicating the appropriateness of NVB sparing during RARP in a Japanese patient population.

MATERIALS AND METHODS

1. Patients
In this single-institution study, 67 patients with clinical T2 or T3 disease diagnosed by MRI and who did not undergo neoadjuvant hormonal therapy were included between October 2010 and September 2012. All patients had biopsy-proven PC. Preoperative 3-T MRI was performed to determine the feasibility and extent of a nerve-sparing RP. The following data were collected: age at diagnosis, preoperative PSA level, clinical staging, pathological staging, operative PSA level, clinical staging, pathological staging, and Gleason score from biopsy and surgical specimens. The Kobe University Institutional Review Board approved this protocol. Written informed consent was obtained from all participants before inclusion in the study.

2. Three-tesla MRI
MRI was performed by using a 3-T MR scanner (Intera Achieva, Philips Healthcare, Amsterdam, The Netherlands) with a phased-array pelvic coil for signal reception. No endorectal coil was used in this study. All patients underwent sagittal, coronal, and axial oblique turbo spin-echo T2-weighted imaging, and all MRI findings were evaluated by a single radiologist (S.T.). Additionally, patients underwent echo-planar diffusion-weighted imaging (DWI) with calculation of apparent diffusion coefficients and dynamic contrast-enhanced imaging. The criteria for a positive cancer finding were as follows: 1) low-intensity imaging in both T2-weighted imaging and apparent diffusion coefficient or 2) enhancing in the early phase but washed out in dynamic imaging. An antiperistaltic agent, 0.5 mg glucagon, was administered intravenously just before the MRI examinations, and an additional 0.5 mg was administered immediately preceding the acquisition of dynamic contrast-enhanced MR. A minimum of 8 weeks was required between the date of the MRI and the previous biopsy to reduce the influence of postbiopsy change in diagnostic accuracy on the basis of Hricak’s study [5], in which the median interval between MRI and biopsy was 8 weeks. Prostate biopsy was performed transrectally with 12 cores (6 sextant, 2 from the far peripheral zone [PZ], and 4 cores from the transitional zone [TZ]).

Common criteria was used to determine ECE and local staging grade. Low-intensity lesions on T2-weighted MR images within the PZ of the prostate were considered suspicious for tumor [13]. In the TZ, areas with homogeneous low signal intensity, ill-defined margins, or lack of capsule were interpreted as tumor foci. Asymmetric bulging, an irregular margin, or direct extension of the lesion in the periprostatic fat or NVB was graded as capsular penetration (stage T3a). Signs of seminal vesicle invasion included low intensity in one or both seminal vesicles (stage T3b). The radiological findings were compared with the final operative histological reports.

3. RARP procedure
RARP with lymph node resection was performed with a da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA, USA) using the standard procedure [14]. Briefly, 4 robotic arms and 2 additional trocars as assistants were used in a 30-degree Trendelenburg position by a transperitoneal approach. Nerve-sparing procedures used an athermal, antegrade interfascial method with minimization of traction. The decision for nerve-sparing was based on MRI findings and preoperative International Index of Erectile Function Questionnaire-25 scores.

4. Histological evaluation
The prostate was serially sectioned from base to apex into different levels (depending on the size of the prostate) for histological analysis and labeled as right or left and anterior or posterior apex, midgland, and base. Seminal vesicles were also analyzed separately. All reports were reviewed to determine the presence of ECE and seminal vesicle invasion and to compare staging at the pathologic examination and MRI in each prostate lobe (2 lobes in one patient).

5. Statistical analyses
Diagnostic accuracy was measured as sensitivity, specificity, positive predictive value, and negative predictive value. Univariate analysis was calculated for ECE and achievement of nerve-sparing. A p-value of 0.05 or less was considered as statistically significant. A Mann-Whitney U test and a chi-square test were used to determine significant differences. Statistical analysis was conducted with XLSTAT (Addinsoft, New York, NY, USA).

RESULTS

1. Extracapsular invasion
The characteristics of all patients are shown in Table 1. All patients underwent 3-T MRI before RALP (Table 1). The
preoperative 3-T MRI results showed that when the samples were divided by prostate side or lobe (right side or left side), 106 of 134 sides were ECE negative and 28 of 134 were ECE positive (Table 2). The representative MRI findings of the positive ECE and negative ECE sides are shown in Fig. 1. Pathologic examination of the surgical specimens in all 67 patients revealed that 50 patients (74.6%) had disease confined to the prostate (pT2) and 17 patients (25.4%) had locally advanced disease (pT3). The pathological stages were pT2a (n=11), pT2b (n=6), pT2c (n=33), pT3a (n=15), and pT3b (n=2) (Table 1).

**TABLE 1. Patients’ characteristics**

| Characteristic          | Value     |
|-------------------------|-----------|
| No. of patients         | 67        |
| Age (y), median (range) | 67 (51-74) |
| PSA (ng/mL), median (range) | 6.99 (2.87-27.6) |
| Clinical stage          |           |
| T2a                     | 28        |
| T2b                     | 3         |
| T2c                     | 20        |
| T3a                     | 16        |
| Pathological stage      |           |
| T2a                     | 11        |
| T2b                     | 6         |
| T2c                     | 33        |
| T3a                     | 15        |
| T3b                     | 2         |
| Gleason score of biopsy |           |
| 6                       | 13        |
| 7                       | 30        |
| 8                       | 24        |
| Gleason score of prostatectomy |       |
| 6                       | 2         |
| 7                       | 54        |
| 8                       | 11        |

PSA, prostate-specific antigen.

**TABLE 2. Comparison between MRI and pathological findings**

| Parameter                        | Pathological stage |
|----------------------------------|--------------------|
|                                  | T3     | T2     |
| Magnetic resonance imaging stage | Positive ECE | 12     | 16     |
|                                  | Negative ECE   | 8      | 98     |
| Sensitivity                      | 60.0%             |
| Specificity                      | 86.0%             |
| Positive predictive value        | 42.9%             |
| Negative predictive value        | 92.5%             |

ECE, extracapsular extension.

2. **Comparison between MRI and pathological data**

In the MRI and pathological findings, the overall sensitivity, specificity, and positive predictive value for predicting ECE according to the findings by every prostate side and the negative predictive value were 60.0% (12 of 20 sides), 86.0% (98 of 114 sides), 42.9% (12 of 28 sides), and 92.5% (98 of 106 sides), respectively (Table 2).

3. **Correlation of MRI with nerve-sparing and pathological data**

On the basis of the 3-T MRI findings, nerve-sparing surgery was performed on 42 of 134 sides (31.3%). Nerve-sparing surgery was achieved in 38.7% of sides with no ECE reported by 3-T MRI. All 41 sides with negative ECE on MRI underwent nerve-sparing surgery with no positive surgical margins (100%). Table 3 shows the nerve-sparing procedure, pathological stage, and positive surgical margin rate in the MRI groups with and without ECE. All values were significantly different (Table 3).

**FIG. 1.** Representative cases with positive (prostate cancer-positive part is shown by an arrow) (A) and negative (B) extracapsular extension magnetic resonance imaging findings are shown.
surgeons to individually sculpt the extent of surgical resection, resulting in a lower positive surgical margin rate than did patients who were not suspicious for ECE. Additionally, there were no positive surgical margins with nerve-sparing procedures in the group shown to be ECE negative on MRI.

This study have some limitations. First, the number of cases may not have been enough for definitive conclusions. Second, we did not use an endorectal coil. Even though an endorectal coil could have provided better spatial resolution, this approach has several limitations, including increased cost and examination time, a nonuniform signal-to-noise ratio up to twofold, increased cost and examination time, a nonuniform signal-to-noise ratio up to twofold, increase in motion artifacts owing to rectal peristalsis. Third, this was a single-arm study and did not include a comparative group, for instance, a 1.5-T MRI group. These limitations will be overcome in our future studies.

**CONCLUSIONS**

We found that 3-T MRI showed comparatively acceptable quality images for decision-making about nerve-sparing surgery. Dynamic contrasted-enhanced (DCE) MRI is another complementary functional MR technique that assesses the relative tissue perfusion within the prostate. Detection and characterization are improved by the addition of DCE-MRI to T2-weighted images. For overall PC detection, multiparametric MRI showed better quality than any individual MRI sequence. In this study, we used T2-weighted imaging, DWI, and DCE-MRI for PC staging, which may have contributed to our results showing a statistically significant trend for the surgeon to perform fewer NVB-sparing procedures if the MRI reported ECE than if no ECE was reported. The same trend was also mentioned by Roethke et al as significant (p < 0.01) in their study. An important question is the influence of preoperative MRI on the positive surgical margin rate. In our study, patients with ECE on MRI had a higher positive surgical margin rate than did patients who were not suspicious for ECE. Additionally, there were no positive surgical margins with nerve-sparing procedures in the group shown to be ECE negative on MRI.
results for staging PC and accurately detecting ECE to guide decision-making for nerve-sparing surgery in RARP. Our data offer evidence that 3-T MRI might improve decision-making about nerve-sparing surgery, although a prospective study with a comparison group and larger number of cases is still needed.

CONFLICTS OF INTEREST
The authors have nothing to disclose.

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