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Original article

Clinical effect of a positive surgical margin without extraprostatic extension after robot-assisted radical prostatectomy

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Abstract

Objectives: The aim of this study was to investigate the effect of positive surgical margin (PSM) without extraprostatic extension after robot-assisted radical prostatectomy (RARP).

Materials and methods: We retrospectively reviewed 837 patients who underwent RARP for clinically localized prostate cancer without neoadjuvant endocrine therapy. The pT2+ category lesions were defined according to World Health Organization classification. The actuarial probabilities of biochemical recurrence-free survival (BCR-FS) were determined using Kaplan-Meier analysis. Univariate and multivariate Cox proportional hazards regression analyses were also used to identify independent predictors for BCR.

Results: Of the 837 patients, 102 (12.2%) experienced BCR during the follow-up period. The BCR-FS rate was significantly higher in patients with pT2+ category tumors than in those with pT3a category tumors, and significantly lower in patients with pT2+ category tumors than that in those with pT2 category tumors without PSM. The BCR-FS rate of patients with pT2+ category tumors was significantly higher than that with pT3a category tumors with PSM but not significantly different from that with pT3a category tumors without PSM. In a multivariate analysis, the pathological T category considering pT2+ category was one of independent predictive factors for BCR.

Conclusions: This study support the hypothesis that the pT2+ category disease is associated with a significantly increased risk of BCR in patients with organ-confined prostate cancer after RARP. As PSM can be avoided in some cases, urologists should continually seek to improve their operative skills and to reduce the rate of PSM, especially in patients with organ-confined prostate cancer.

Keywords: Positive surgical margin; Robot-assisted radical prostatectomy; Biochemical recurrence; Pathological T2+ category

1. Introduction

Radical prostatectomy (RP) is an effective treatment that has been shown through randomized prospective trials to have a cancer-specific survival benefit for localized prostate cancer compared with watchful waiting [1–3]. As the goal of all surgical oncology procedures is the complete removal of cancer, the presence of positive surgical margins (PSM) after RP is considered an adverse outcome associated with failure of the surgery to achieve cure of the prostate cancer [1,4,5]. The occurrence of PSM without extraprostatic extension (EPE) at the site of the PSM is not infrequent, with this being reported in 9%–62% of cases with PSM [6]. In the World Health Organization (WHO) classification, Eble et al. [6] reported that the category designation to denote PSM in the absence of EPE anywhere in the gland is category pT2+, because extraprostatic tumor at the site of the PSM cannot be excluded. To date, the clinical effect of the PSM in cases of pT2+ category prostate cancer has not been adequately evaluated.

Robot-assisted RP (RARP) in place of open or laparoscopic RP is currently a very popular treatment choice for clinically localized prostate cancer. Because RARP has the advantage of enhanced vision, use of this operative technique might lead to a decreased PSM rate compared with open or laparoscopic RPs [7,8]. To our knowledge, there have been few reports regarding the clinical significance of the pT2+ category following RARP. As we transition from an era of open or laparoscopic RP to an era of RARP, it will be important to investigate the effect of pT2+ category disease on patient outcome. Therefore, the present study

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was undertaken to investigate the effect of PSM without EPE after RARP.

2. Patients and methods

From August 2006 to December 2013, 1,096 patients with localized prostate cancer underwent RARP at our institution. Of the 1,096 patients, 240 patients who were treated with neoadjuvant endocrine therapy and 19 patients who lacked postoperative data were excluded from the study. We retrospectively reviewed data from the remaining 837 patients. Most procedures were performed using the 6-port technique. Most of the nerve-sparing procedures were performed using the interfascial technique previously reported by Coughin et al. [9]. The prostatectomy specimens were fixed in 10% formalin and completely inked first to enable accurate assessment of the surgical margin status. The apex and base of each surgical specimen were then amputated in the sagittal plane, and the remainder of the prostate was sectioned transversely at 3- to 5-mm intervals [10]. We evaluated those specimens according to the WHO classification [6] and the General Rules for Clinical and Pathological Studies on Prostate Cancer in Japan, fourth edition [10]. A PSM was defined as tumor extension into the inked surface of the resected specimen. If malignant cells were present at the inked margin and the histologic boundary was not present, it was impossible to evaluate EPE precisely (Fig. 1); these lesions were defined as pT2+ category lesions according to the WHO classification.

Biochemical recurrence (BCR) was defined as 2 consecutive values of serum prostate-specific antigen (PSA) $\geq$ 0.2 ng/ml [11]. Statistical analysis of BCR-free survival (BCR-FS) was performed using the Kaplan-Meier method. BCR-FS was compared between groups using the log-rank test. In addition, univariate and multivariate Cox proportional hazards regression analyses were also used to evaluate prognostic significance for BCR-FS. A $P < 0.05$ was considered statistically significant. All statistical analyses were performed using Stata software (ver. 11.0; StataCorp, College Station, TX) and R version 3.2.0 for Windows.

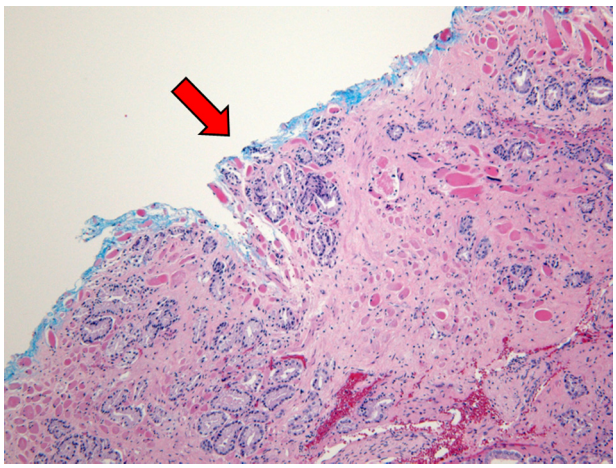

Fig. 1. This is an example of the positive surgical margin owing to capsular incision. The arrows show pT2+ category disease, with malignant cells present at the surgical margin with no histologic boundary. The contralateral part of the section shows the normal contour. (Color version of figure is available online.)

3. Results

Patient demographics are shown in Table 1. A total of 243 (29.0%) patients had PSM, and the PSM rates for pT4, pT3b, pT3a, and pT2 categories were 100%, 60.0%, 50.4%, and 23.2%, respectively. The mean and median follow-up periods after surgery were 24.4 and 20.5 months. Overall, 102 patients experienced BCR during the follow-up period, including 40 out of 594 patients without PSM and 62 out of 243 patients with PSM. The 1-, 3-, and 5-year BCR-FS rates for the entire cohort were 91.4%, 83.0%, and 78.3%, respectively. No patient died of prostate cancer during the follow-up period, and 3 patients died of other causes.

Table 1
Patients' characteristics

Age, y, median (range)	65 (39–78)
Follow-up period, median (range)	20.5 (1.3–91.3)
Clinical T category	
cT1c	634
cT2a	111
cT2b	46
cT2c	39
cT3	7
PSA, median (range)	6.90 (3–47.4)
Biopsy Gleason sum	
$\leq$6	215
3 + 4	328
4 + 3	153
$\geq$8	141
Pathological T category	
pT2	520
pT2+	157
pT3a	117
pT3b	40
pT4	3
Pathological Gleason sum	
$\leq$6	65
3+4	377
4+3	230
$\geq$8	165
Nerve sparing	
Bilateral	47
Unilateral	299
Non–nerve sparing	491
Surgical margin	
Positive	243
Negative	594