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ORIGINAL ARTICLE

Significance of erection hardness score as a diagnostic tool to assess erectile function recovery in Japanese men after robot-assisted radical prostatectomy

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Abstract The objective of this study was to characterize time-dependent recovery of erectile function in Japanese patients following robot-assisted radical prostatectomy (RARP) using the erection hardness score (EHS). This study prospectively included 170 Japanese patients with localized prostate cancer (PC) undergoing RARP without neoadjuvant hormonal therapy. The erectile function of each patient was assessed based on the International Index of Erectile Function-5 (IIEF-5) and EHS at the baseline and on every visit to an outpatient clinic after RARP. In this series, potency was defined as the ability to have an erection sufficient for intercourse, corresponding to EHS ≥ 3, while patients with EHS ≥ 2 were regarded as those with erectile function. Of these 170 patients, 20 and 75 underwent bilateral and unilateral nerve-sparing procedures, respectively; however, non-nerve-sparing procedures were performed in the remaining 75. A proportional increase in the IIEF-5 score according to EHS was noted at 24 months after RARP. At 6, 12 and 24 months after RARP, the recovery rates of erectile function were 11.9, 21.7 and 35.8 %, respectively, while those of potency were 3.8, 9.8 and 13.7 %, respectively. Of several factors examined, the age, preoperative IIEF-5 score and nerve-sparing procedure were identified as independent predictors of erectile function recovery. These findings suggest that favorable erectile function recovery could not be achieved in Japanese PC patients even after the introduction of RARP; therefore, it might be preferable for such a cohort to use EHS rather than IIEF-5 as an assessment tool for the postoperative recovery of erectile function.

Keywords Prostate cancer · Robot-assisted radical prostatectomy · Erectile function · Erection hardness score

Introduction

In recent years, the proportion of patients treated with radical prostatectomy (RP) as initial management for prostate cancer (PC) has been rising, since the number of patients diagnosed with PC at an early stage has markedly increased [1]. It has been well recognized that RP can achieve excellent cancer control, with 10-year cancer-specific survival rates >90 % [2]. However, despite recent advances in knowledge of the pelvic anatomy and surgical techniques [3], RP is still frequently accompanied by several types of postoperative adverse event, particularly that associated with erectile function [3, 4], which has been shown to negatively affect the postoperative quality of life of patients undergoing RP [5].

Over the last decade, the introduction of robot-assisted RP (RARP) has resulted in a paradigm shift in the field of surgical management for patients with localized PC; that is, RARP has become a dominant procedure over other surgical approaches, since robotic technologies enable surgeons to perform precise and accurate movements that help preserve key anatomic structures associated with the achievement of favorable functional outcomes [6]. In fact, previously conducted systematic reviews of the literature showed the comparatively superior functional outcomes following RARP compared with those after other approaches [3, 4]. To date, however, there has been limited information reported on the recovery of erectile function in

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Japanese men undergoing RARP, who have been shown to exhibit sexual activity different from Western populations [7].

In this study, we prospectively included a total of 170 consecutive Japanese patients with localized PC who underwent RARP without neoadjuvant hormonal therapy, and investigated time-dependent changes in erectile function recovery after RARP using the erection hardness score (EHS), a single item scale questionnaire that assesses erectile function based on penile rigidity [8, 9].

Methods

This study prospectively included a total of 170 consecutive Japanese patients with clinically localized PC who underwent RARP without neoadjuvant hormonal therapy between July 2011 and December 2012. The Research Ethics Committee of our institution approved the design of this study.

At our institution, RARP was performed employing a four-arm da Vinci® robotic system (Intuitive Surgical Inc., Sunnyvale, CA, USA) via a transperitoneal approach, as previously described [10]. Briefly, an anterior approach was adopted by initially isolating and ligating the dorsal venous complex, followed by bladder neck dissection. After mobilization of the seminal vesicles, the prostatic vascular pedicles were then ligated, and the prostate was removed. Preservation of the neurovascular bundle on the negative side on needle biopsy was generally conducted by interfascial dissection into the avascular plane between the prostatic capsule and Denonvilliers' fascia. Posterior reconstruction of the rhabdomyosphincter, but not anterior suspension, was routinely performed, and vesicourethral anastomosis was carried out as reported by Van Velthoven et al. [11].

The erectile function of the included patients was assessed using the International Index of Erectile Function-5 (IIEF-5) [12] and EHS [8, 9] at the baseline and on every visit to an outpatient clinic following RARP. In this series, potency was defined as the ability to have an erection sufficient for intercourse, corresponding to EHS ≥ 3, while patients with EHS ≥ 2 were regarded as those with erectile function.

All statistical analyses were performed using Statview 5.0 software (Abacus Concepts, Inc., Berkeley, CA, USA), and p values less than 0.05 were considered significant. The recovery rates of erectile function and potency were calculated employing the Kaplan–Meier method, and differences were determined by the log-rank test. The effects of certain factors on erectile function recovery were assessed using the Cox proportional hazards regression model. Differences in the IIEF-5 scores according to the EHS scores were compared using an unpaired t test.

Results

The clinicopathological characteristics of the 170 Japanese patients with clinically localized PC included in this study are summarized in Table 1. At the baseline, the mean IIEF-5 score and EHS in these 170 patients were 9.2 and 2.2, respectively. In this series, RARP could be completed in all 170 cases without conversion to other surgical approaches. Of these 170, 20 (11.8 %) and 75 (44.1 %) underwent bilateral and unilateral nerve-sparing surgeries, respectively; however, the remaining 75 (44.1 %) received non-nerve-sparing surgery.

In this series, time-dependent improvement was not noted in postoperative IIEF-5 scores in the 170 patients, showing 4.0, 4.1 and 4.0 at 6, 12 and 24 months after RARP, respectively. We then compared the IIEF-5 scores based on the EHS at 2 years after RARP, and found a significantly proportional increase in the IIEF-5 score according to EHS; that is, IIEF scores were 1.8, 5.6 and 13.8 in patients with EHS of 0–1, 2 and 3–4, respectively (Fig. 1). Figure 2a, b shows the time-dependent changes in the recovery rates of erectile function and potency in the 170 patients. The recovery rates of erectile function at 6, 12 and 24 months after RARP were 11.9, 21.7 and 35.8 %, respectively, while those of potency at 6, 12 and 24 months after RARP were 3.8, 9.8 and 13.7 %, respectively.

Table 1 Patients' characteristics

Mean age (years) (range)	65.3 (51–79)
Mean serum PSA (ng/mL) (range)	8.8 (2.9–26.7)
Mean BMI (kg/m²) (range)	23.8 (17.5–33.7)
Mean Charlson comorbidity index (range)	1.2 (0–5)
Preoperative IIEF-5 score	9.2 (1–25)
Nerve-sparing procedure (%)	
Non-nerve-sparing surgery	75 (44.1)
Unilateral nerve-sparing surgery	75 (44.1)
Bilateral nerve-sparing surgery	20 (11.8)
Pathological stage (%)	
pT2	127 (74.7)
pT3a	36 (21.2)
pT3b	7 (4.1)
Gleason score (%)	
6	6 (3.5)
7	140 (82.4)
8–10	24 (14.1)

PSA prostate-specific antigen, *BMI* body mass index, *IIEF-5* International Index of Erectile Function-5
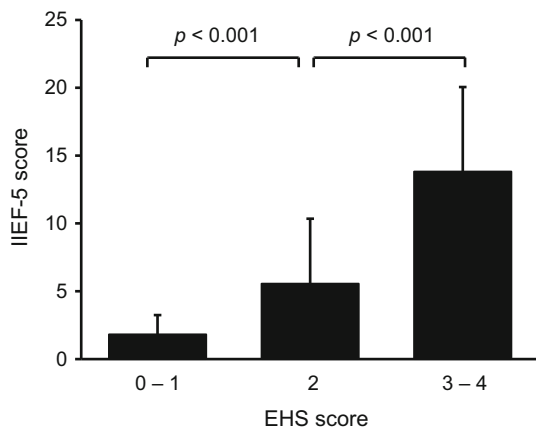
Fig. 1 Association between the erection hardness score (EHS) and International Index of Erectile Function-5 (IIEF-5) score in 170 Japanese patients with clinically localized prostate cancer who underwent robot-assisted radical prostatectomy at 24 months after surgery

We subsequently evaluated the impact of several parameters on the prediction of erectile function recovery. As presented in Table 2, univariate analysis using the Cox proportional hazards regression model identified the age, Charlson comorbidity index, preoperative IIEF-5 score and nerve-sparing procedure as significant predictors of erectile function recovery. Of these four significant factors, the age, preoperative IIEF-5 score and nerve-sparing procedure were shown to be independently associated with erectile function recovery on multivariate analysis. To more precisely predict the recovery status of erectile function in this cohort of patients, we classified them into three groups according to the positive number of 3 independent risk factors erectile function recovery identified by multivariate analysis; that is, erectile function recovered in 14 of 16 patients who were negative for all risk factors (87.5 %), 47 of 111 positive for 1 or 2 risk factors (42.3 %), and 4 of 43
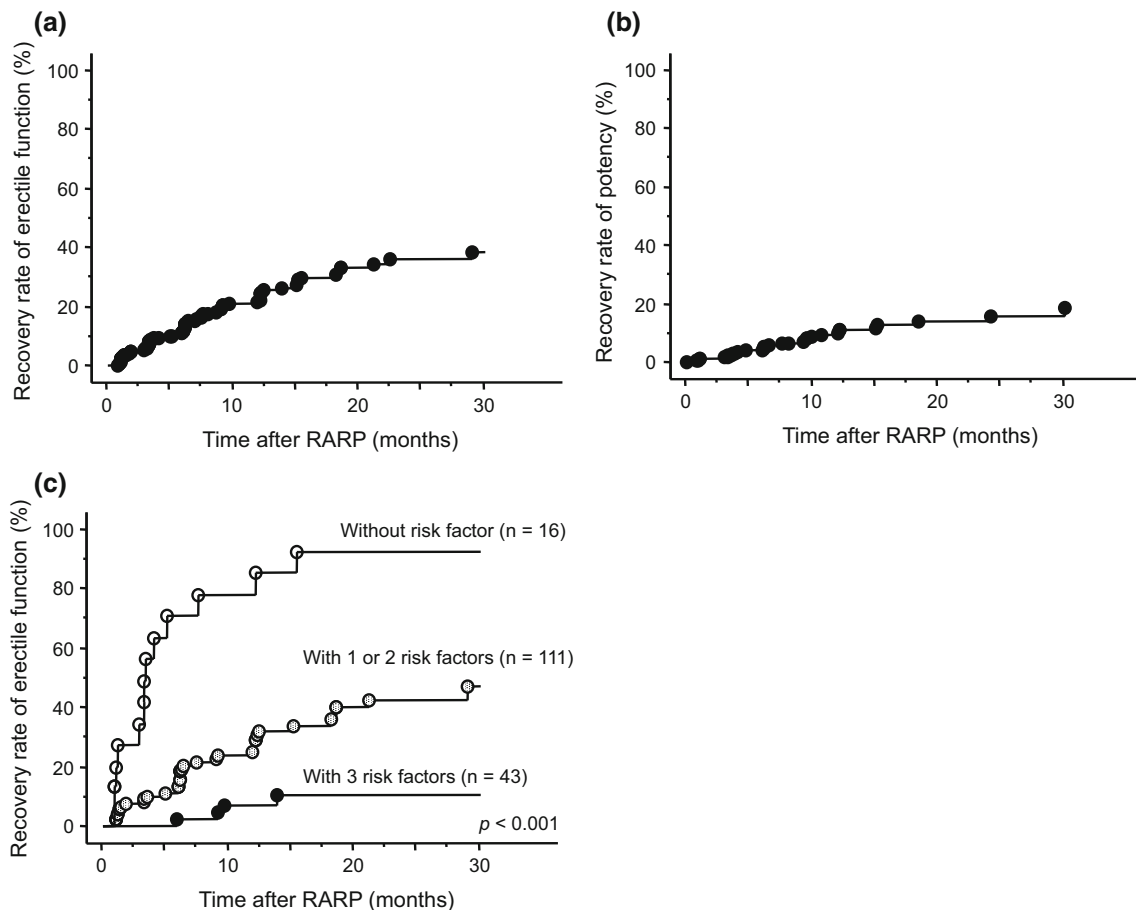

Fig. 2 a Time-dependent changes in recovery rates of erectile function in 170 Japanese patients with clinically localized prostate cancer who underwent robot-assisted radical prostatectomy (RARP). **b** Time-dependent changes in recovery rates of potency in 170 Japanese patients with clinically localized prostate cancer who underwent RARP. **c** Time-dependent changes in erectile function recovery in 170 Japanese patients with clinically localized prostate cancer who underwent RARP according to the number of independent risk factors for erectile function recovery, including elderly age, low preoperative International Index of Erectile Function-5 score and non-nerve-sparing procedure

Table 2 Uni- and multivariate analyses of several factors predicting postoperative recovery of erectile function

	Univariate		Multivariate	
	HR	*P* value	HR	*P* value
Age (years) (65 ≤ versus <65)	4.56	<0.001	5.10	<0.001
Serum PSA (ng/mL) (10 ≤ versus <10)	1.09	0.85	–	–
BMI (kg/m^2) (25 ≤ versus <25)	1.34	0.31	–	–
Charlson comorbidity index (3 ≤ versus <3)	2.04	0.025	1.25	0.64
Preoperative IIEF-5 score (20 < versus ≤20)	3.65	<0.001	1.98	0.026
Nerve-sparing procedure (yes versus no)	7.81	<0.001	8.31	<0.001
Pathological stage (pT2 versus pT3)	1.26	0.44	–	–
Gleason score (6 or 7 versus 8–10)	1.20	0.47	–	–

HR hazard ratio, *PSA* prostate-specific antigen, *BMI* body mass index, *IIEF-5* International Index of Erectile Function-5

positive for 3 risk factors (9.3 %). As shown in Fig. 2c, there were significant differences in erectile function recovery among these three groups.

Discussion

RARP has become a widely accepted surgical approach for men with clinically localized PC. In the United States, it is currently estimated that 80 % of RP procedures are performed with the da Vinci® robot system, and this trend has been markedly increasing in other countries as well [6]. Despite the lack of data with a high evidence level, recently accumulated findings suggest that RARP is equivalent to other surgical procedures in cancer control, but it might be more advantageous for the promotion of postoperative functional outcomes [3, 4, 6]. However, the majority of data concerning the outcomes of RARP have been generated from high-volume centers in Western countries; thus, it remains unclear whether the postoperative findings on RARP in Japanese patients are similar to those in previously published studies. Taken together, we prospectively investigated the clinical outcomes focusing on erectile function recovery based on the data from a total of 170 consecutive Japanese patients with localized PC who were treated with RARP without neoadjuvant hormonal therapy.

To date, it has been well-documented that there may be a considerable racial difference in sexual profiles between Japanese and Western men, characterized by a markedly lower sexual activity in Japanese men than that in Western men [7]. In fact, in addition to baseline differences in the erectile function between these two cohorts, erectile dysfunction and decreased libido were also shown to be noted in a greater proportion of Japanese men than in Western men [13]. In this series as well, the mean baseline IIEF-5 score, one of the most widely used tools to identify and

grade the severity of erectile dysfunction [12], was only 9.2. Furthermore, the IIEF-5 score in these patients was reduced to 4.0 at 6 months after surgery, and was not significantly changed thereafter within 2 years after RARP. Considering these findings, it may not be suitable to use the IIEF-5 score for a cohort with inactive sexual profiles, like Japanese men, in order to assess precise changes in erectile function after RP. In this study, therefore, we also examined the postoperative changes in EHS, a single-item scale that has demonstrated favorable psychometric properties for assessing erectile function through the evaluation of erectile rigidity [8, 9]. Although EHS has been shown to be positively correlated with self-confidence, self-esteem and satisfaction with sexual intercourse [8, 14], it was formally validated in patients treated with phosphodiesterase-5 (PDE-5) inhibitors [9], but its applicability to other treatments, including RP, has not yet been clarified. In this series, however, we found a significantly proportional increase in the IIEF-5 score according to EHS at 2 years after RARP; accordingly, we used EHS as an alternative to the IIEF-5 score to evaluate erectile function recovery in the 170 Japanese patients included in this study.

According to the definition based on EHS described above, at 6, 12 and 24 months after RARP, the recovery rates of erectile function in the 170 Japanese patients were 11.9, 21.7 and 35.8 %, respectively, and those of potency were 3.8, 9.8 and 13.7 %, respectively. There have been several studies conducting systematic reviews and meta-analyses of erectile function following RARP [4, 15]. For example, Ficarra et al. reported that the 12- and 24-month potency rates ranged from 54 to 90 % and from 63 to 94 %, respectively [4], while Kilminster et al. revealed that the cumulative range of potency rates at 48 months was 60–100 % for RARP [15]. Considering the criteria of these studies, including only potent patients prior to RARP who had subsequently undergone nerve-sparing surgery, the

changes in potency rates in our study seem to still be unfavorable. It would be difficult to clearly explain the inferior postoperative recovery of potency in Japanese men; however, the different status of treatment for postoperative erectile dysfunction in addition to differences in the sexual profile between Japanese and Western men may have partially affected these outcomes. In fact, Namiki et al. reported that Japanese patients were shown to be much less likely to use PDE-5 inhibitors than United States patients after RP, despite reporting lower sexual function scores [16].

It is of interest to identify parameters predicting the postoperative status associated with the sexual function in this Japanese cohort. Due to the very small number of patients with potency in this series, we evaluated the impacts of several parameters on erectile function recovery using the Cox proportional hazards regression model, and found that the age, preoperative IIEF-5 score and nerve-sparing procedure were independently associated with its recovery. These outcomes are consistent with those of previous studies identifying parameters for predicting the recovery of potency [4, 5, 17]. For example, Ficarra et al. reported that the age, baseline potency status, comorbidities index and extension of the nerve-sparing procedure represented the most relevant predictors of potency recovery after RARP [4]. These findings also suggest that erectile function assessed by EHS could be an alternative to the survey of postoperative potency in patients undergoing RARP, particularly in those with inactive sexual profiles.

Another point of interest is to develop a system to more precisely predict the erectile function following RARP by combining potential predictors in order to allow better individualization of the management of patients undergoing RARP. Based on the outcomes achieved by multivariate analysis, the 170 patients were classified into the following three groups according to the positive number of independent risk factors associated with erectile function recovery: negative for any risk factors, positive for 1 or 2 risk factors and positive for 3 risk factors, and significant differences in erectile function recovery among these three groups were noted. Considering these findings, a simultaneous consideration of the three major factors identified in this series (age, baseline IIEF-5 score and nerve-sparing procedure) may contribute to the development of a novel system of prediction that can be more closely related to erectile function recovery after RARP.

Here, we would like to emphasize several limitations of this study. Despite being performed in a prospective setting including consecutive patients receiving RARP for localized PC, the sample size may be insufficient to draw a definitive conclusion concerning the impact of RARP on the postoperative sexual function. Thus, it would be difficult to perform the additional assessment including only potent patients prior to RARP, which may provide a variable criterion for future studies. Secondly, this study included heterogeneous patients characterized by several different parameters, such as the age, baseline erectile function and selected nerve-sparing procedures. However, only a few patients received penile rehabilitation following RARP, which may have a limited impact on the erectile function in the cohort of this study. Thirdly, this study included patients operated on by multiple surgeons, some of whom were still within the learning curve for RARP. Fourthly, there were several important information missing in this study, such as marital status and partner interest in sexual function. Finally, it is necessary to determine the optimal cut-off points of both the IIEF-5 score and EHS when these scores are to be applied to survey erectile function in a cohort with inactive sexual profiles.

Conclusion

We conducted a prospective observational study to assess changes in erectile function in a total of 170 Japanese patients with clinically localized PC who underwent RARP. Although these patients were characterized by an inactive sexual profile with a baseline IIEF-5 score and EHS of 9.2 and 2.2, respectively, a proportional increase in the IIEF-5 score according to EHS was noted at 24 months after RARP. When we defined the recovery of erectile function and that of potency as patients with EHS ≥ 2 and ≥ 3, respectively, the recovery rates of erectile function and potency at 24 months after RARP were 35.8 and 13.7 %, respectively. Of several parameters examined, the age, preoperative IIEF-5 score and nerve-sparing procedure were identified as independent predictors of erectile function recovery. Collectively, these findings suggest that favorable erectile function recovery could not be achieved in Japanese men with localized PC even after the introduction of RARP, particularly those positive for either risk factor independently associated with postoperative erectile function; accordingly, it might be preferable for such a cohort to use EHS as an alternative to IIEF-5 for the precise assessment of postoperative changes in erectile function.

Informed consent Informed consent was obtained from all individual participants included in the study.

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