Original Article

Safety and feasibility of robot-assisted radical prostatectomy for clinically localized prostate cancer in elderly Japanese patients

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A B S T R A C T

Background: This study was conducted to assess the safety and feasibility of robot-assisted radical prostatectomy (RARP) for elderly Japanese (aged $\geq$ 70 years) patients with clinically localized prostate cancer (PCa).
Methods: From April 2012 to March 2016, a total of 302 consecutive patients with clinically localized PCa underwent RARP at our institute. In this series, 109 (36.1%) and 193 (63.9%) of the patients were divided into older (aged $\geq$ 70 years) and younger (aged <70 years) groups, respectively. The correlation between the categorized patient age and various clinicopathological factors, including preoperative characteristics, perioperative outcome, and urinary continence outcome after RARP, was retrospectively analyzed.
Results: Except for age and Gleason score at biopsy, there was no difference in the preoperative features between the two groups. A nonnerve-sparing RARP was performed more often in the younger group; however, other perioperative variables in the elderly group were comparable to those in the younger group. Similarly, the urinary continence rates at 1 month, 3 months, and 6 months after the surgery were equally favorable in the younger and older groups.
Conclusion: RARP may be a reasonable therapeutic option for elderly patients with PCa and provides comparable perioperative and functional outcomes to those in younger patients.

1. Introduction

Prostate cancer (PCa) is the most common malignancy among elderly men, accounting for 65% of new cases diagnosed in men aged $\geq$ 65 years and 25% in men aged $\geq$ 75 years.[1] In the context of demographic changes in the Japanese population, life expectancy has steadily increased; a 70-year-old man will still have a life expectancy of 14.1 years. With this increase, the percentage of the population aged 65 years or older is projected to increase from 25.0% in 2014 to an estimated 35.7% by 2050.[2] It is expected that in the near future, many elderly men with a long remaining life expectancy will present with localized PCa. Although the optimal treatment for elderly men diagnosed with PCa is controversial,[3] the effective management of this population is becoming increasingly important.

Radical prostatectomy (RP) has been regarded as one of the most effective treatment options for clinically localized PCa and is generally recommended for patients with a life expectancy of >10 years,[4] whereas Miller et al[5] concluded that men older than 70 years bore the greatest burden of this potential overtreatment because of perceptions of increased side effects and complications. However, the recent introduction of robotic technologies has been shown to provide surgeons with certain inherent advantages to perform RP with precise techniques, leading to fewer postoperative complications and better perioperative and functional outcomes than those of traditional RP.[6] Therefore, this paradigm shift in RP procedures might increase the suitability of elderly candidates for surgery. Despite the fact that the potential role for robot-assisted RP (RARP) in elderly patients needs to be further defined as the elderly population grows, there have been few reports of RARP in these patients,[7–10] and none in elderly Japanese men with PCa.

Considering these findings, we retrospectively assessed the influence of age on perioperative and functional outcomes after RARP in one institution.

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2. Materials and methods

From April 2012 to March 2016, 302 consecutive men underwent RARP for localized PCa at our institution. In this study, two surgeons performed 302 RARP (A, 207; B, 95) in a standard fashion, using the DaVinci system (Intuitive Surgical, Sunnyvale, CA, USA). The original surgical technique used for RARP was previously described by Patel et al.[11] Clinicopathological information on these patients was extracted from their medical records. Patients who had RARP were retrospectively divided into two groups based on their chronological age, with 109 men aged ≥ 70 years and 193 aged <70 years. Patients who had a follow-up of <6 months were excluded from this study. Collected data consisted of preoperative variables including age, body mass index, serum prostate-specific antigen (PSA) at diagnosis, clinical tumor stage, Gleason score at biopsy, and D'Amico risk group.[12] Comorbidities were also evaluated using the age-adjusted Charlson comorbidity index scoring system.[13] Perioperative factors analyzed in this study included the total and console operative time, estimated blood loss, status of preservation of the neurovascular bundles, prostate weight, and duration of catheterization and hospitalization. Complications were recorded using the Dindo modification of the Clavien Grading System.[14] In this study, the continence status was classified into requiring one precautionary pad or less per day and two or more pads per day, and the continence status was evaluated by interviews prior to and 1 month, 3 months, and 6 months after RARP. The design of the current study was approved by the Research Ethics Committee of our institution and, prior to participating in this study, informed consent was obtained from each patient.

All statistical analyses were performed using Statview 5.0 software (Abacus Concepts, Berkeley, CA, USA), and P values < 0.05 were considered significant. Differences in several parameters between the two groups according to chronological age were compared using an unpaired t test or the chi-square test.

3. Results

Table 1 lists the preoperative baseline clinicopathological characteristics. Of the 302 men analyzed, 36.1% and 63.9% were aged ≥ 70 years and <70 years, respectively. Except for age and

Table 1
Comparison of preoperative characteristics between the two groups

	A: ≥70 yr (n = 109)	B: <70 yr (n = 193)	P
Age (yr)	72.7 (70–78)	63.7 (46–69)	<0.005
BMI (kg/m²)	23.2 (16.7–29.8)	24.0 (17.4–34.4)	0.10
PSA(ng/mL)	10.1 (4.1–45.7)	10.4 (1.2–70.4)	0.71
Prostate volume (mL)	28.7 (11–88)	28.2 (10–100)	0.72
Clinical stage			0.066
cT1c	21 (19.3)	63 (32.6)	
cT2a	68 (62.4)	95 (49.2)	
cT2b	8 (7.4)	13 (6.7)	
cT2c	8 (7.4)	9 (4.7)	
cT3a	4 (3.7)	13 (6.7)	
Gleason score at biopsy			0.013
6	11 (10.1)	39 (20.2)	
7	63 (57.8)	101 (52.4)	
8	13 (11.9)	33 (17.1)	
9	22 (20.2)	20 (10.4)	
D'Amico risk classification			0.082
Low	10 (9.2)	34 (17.6)	
Intermediate	64 (58.7)	93 (48.2)	
High	35 (32.1)	66 (34.2)	
Mean Charlson comorbidity	2 (0–3)	2 (0–3)	0.64

Data are presented as mean (range) or n (%).
BMI, body mass index; PSA, prostate-specific antigen.

Gleason score at biopsy (compared with younger men, older men had a significantly higher Gleason score at biopsy; $P = 0.013$), there was no difference in the clinical features including body mass index, PSA, clinical tumor stage, D'Amico risk group, and Charlson comorbidity index between the two groups.

Although a nonnerve-sparing RARP was performed more often in the younger group (19.3% in older group vs. 32.6% in younger group; $P = 0.040$), the total and console operative time, estimated blood loss during surgery, and prostate weight did not significantly differ between the two groups. The postoperative factors including duration of catheterization and hospitalization and complications were also similar between the groups, as shown in Table 2.

In this study, all patients were continent prior to the surgery. Table 3 shows the short-term continence status of the two groups. Continence rates, as defined by no leak or the use of a security pad, were equivalent between the two age groups at 1 month, 3 months, and 6 months after RARP.

4. Discussion

Because of the increasing life expectancy and the widespread use of PSA tests, a growing number of elderly men are being diagnosed with PCa. With the aging of the population, the issue of managing PCa in the elderly is of increasing importance. In the case of clinically localized PCa, the patient's age as well as tumor characteristics are considered to be a key determinant in terms of treatment decisions. However, the management of localized PCa in older populations is often challenging, because disease progression can occur slowly, and most elderly patients with localized PCa will not die from their PCa.[1] In fact, Albertsen et al[15] revealed that in patients aged 70 to 74 years with clinically localized PCa diagnosed and managed by either surveillance or androgen withdrawal alone, only 29% died from PCa over a 20-year follow-up period. Meanwhile, Alibhai et al reported that in elderly patients with few comorbidities and moderately or poorly differentiated localized PCa, RP results in significantly improved life expectancy and quality-adjusted life years.[16] In addition, treatment for localized PCa involves watchful waiting, active surveillance, surgery, external beam radiation therapy, brachytherapy, cryosurgery, hormonal therapy, or their combinations. Collectively, although it is difficult to establish standard strategies for elderly patients with PCa owing to a lack of comparative randomized controlled trials, decisions in this population should be made after careful consideration of the tumor aggressiveness, life expectancy based on comorbidities, and potential adverse effects of treatment.

Table 2
Comparison of intra- and postoperative outcomes of the two groups

	A: ≥70 yr (n = 109)	B: <70 yr (n = 193)	P
Total operative time (min)	239 (153–479)	248 (156–549)	0.21
Console operative time (min)	184 (104–434)	192 (83–436)	0.10
Estimated blood loss (mL)	10.1 (4.1–45.7)	10.4 (1.2–70.4)	0.71
NVB preservation			< 0.001
Negative	72 (19.3)	78 (32.6)	
Universal	34 (62.4)	94 (49.2)	
Bilateral	3 (7.4)	21 (6.7)	
Prostate weight (g)	42.3 (14–85)	40.5 (16–93)	0.22
Duration of catheterization (d)	6.2 (5–54)	5.7 (4–60)	0.50
Duration of hospitalization (d)	8.2 (6–31)	7.8 (5–30)	0.22
Postoperative complications			0.97
None	91 (83.5)	159 (82.4)	
Clavien–Dindo Grade 1, 2	9 (8.3)	17 (8.8)	
Clavien–Dindo Grade 3a	9 (8.3)	17 (8.8)	

Data are presented as mean (range) or n (%).
NVB, neurovascular bundles.

Table 3
Short-term continence status in two groups

Continence status	A: $\geq$70 yr (n = 109)	B: <70 yr (n = 193)	P
1 mo after RARP (pads/d)			0.97
0 or 1 pad for safety	42 (38.5)	74 (38.3)	
$\geq$2	67 (61.5)	119 (61.7)	
3 mo after RARP (pads/d)			0.56
0 or 1 pad for safety	71 (65.1)	132 (68.4)	
$\geq$2	38 (34.9)	61 (31.6)	
6 mo after RARP (pads/d)			0.53
0 or 1 pad for safety	96 (88.1)	165 (85.5)	
$\geq$2	13 (11.9)	28 (31.6)	

Data are presented as n (%).
RARP, robot-assisted radical prostatectomy.

Conventionally, patients >70 years have not been offered RP because of poor functional results and minimal survival benefits owing to a life expectancy of <10 years. Alternatively, other managements such as radiotherapy, hormonal therapy, watchful waiting, and active surveillance have been recommended. Radiotherapy has been considered to be less invasive than surgery and used in these elderly patients; however, it has significant side effects such as gastrointestinal and/or genitourinary toxicity. Hormonal therapy also has no evident survival benefits in this population but does have side effects such as decreased muscle mass, osteoporosis, loss of libido, and increased risks of diabetes and cardiovascular disease. Watchful waiting and active surveillance might aggravate the psychological stress associated with cancer diagnosis. Despite the optimal treatment for men $\geq$ 70 years diagnosed with PCa still being controversial, the demographic finding that most PCa deaths are observed in elderly men may suggest that some cases of PCa are not treated adequately in this population.[3,7,8]

RARP has recently become a predominant procedure for the treatment of localized PCa, as the application of robotic technologies has been shown to provide surgeons with certain inherent advantages to perform RP with precise techniques that result in fewer overall complications, quicker convalescence, and lower rates of estimated blood loss and transfusion.[17] Compared with traditional RP, these advances in RARP may bring benefits to elderly patients with PCa who have not been regarded as candidates for curative surgery such as open RP. For example, Greco et al[7] reported that the perioperative and functional outcomes following RARP in elderly men are largely comparable to those in younger men, and suggested that an advanced chronological age is not a contraindication for RARP in patients with clinically localized PCa. To date, some studies with respect to the usefulness of RARP for elderly men with PCa have been reported.[7–10] In recent years, Kumar et al[9] carried out a propensity score matched study to evaluate the perioperative, functional, and intermediate term oncological outcomes of RARP in patients older than 70 years with the largest cohort and longest observation periods for RARP so far. Out of 3,241 PCa patients undergoing RARP, this study involved 400 younger (<70 years) and 400 older ($\geq$70 years) patients with a good functional status (Charlson comorbidity index <3) after using a Rosenbaum optimal matching algorithm. They found that peri- and postoperative complications were similar between the two groups. Moreover, they reported that during a follow-up of almost up to 36 months, the average time to continence and mean time to biochemical recurrence were also comparable between the two groups—that is, the average time to continence was 3.1 months in the younger group and 3.2 months in the older group (P = 0.76), and the mean time to biochemical recurrence was 16.0 months in the younger group and 22.6 months in the older group (P = 0.07). These findings suggest that RARP is a reasonable treatment option

for appropriately selected elderly patients with clinically localized PCa. However, current reports of RARP in this cohort are still limited, and there are none on elderly Japanese patients with PCa. Therefore, in this study, we retrospectively assessed the influence of age on perioperative outcome and functional continence status after RARP in our institute.

In this series, 109 (36.1%) and 193 (63.9%) of 302 patients were categorized into older (aged $\geq$ 70 years) and younger (aged <70 years) groups, respectively. Between the two groups, there were no significant differences in preoperative baseline characteristics except for age (P < 0.005) and Gleason score at biopsy (P = 0.013). Although the difference was not observed in the D'Amico risk group, our results might be comparable with those of previous studies—that is, older men tend to be diagnosed with more aggressive PCa, which may lead to an increased cancer-specific mortality.[15,18] For example, Fitzpatrick[1] reported that disease-specific mortality in elderly patients depended on the aggressiveness of PCa, which was particularly strongly related to Gleason score. In addition, Mullins et al[19] reported that almost 30% of the patients whose pathological Gleason sum was 7 or greater had evidence of extraprostatic disease, and of these men, 70% who were 70 years or older were alive 10 years after RP. These findings provide a good rationale for offering RP to elderly PCa patients. Perioperative outcomes were also estimated, and we confirmed that except for the proportion of patients undergoing nerve-sparing RARP, other perioperative variables and continence outcomes in elderly patients are similar to those of their younger counterparts. Although Alibhai et al[20] showed that categorized age predisposes to higher 30-day morbidity after open RP, most studies with regard to the correlation between age and surgical complications in RARP revealed that chronological age alone does not have a strong impact on perioperative complications in patients undergoing RARP.[7–10] However, it remains controversial whether RARP could provide advantages of better functional outcomes regarding recovery of urinary continence and potency compared with traditional RP. For example, Tewari et al[21] reported that no superior functional (potency and continence) efficacy is observed after RARP on comparing open and laparoscopic RP, whereas Kumar et al[9] reported that at a mean follow-up of up to 3 years, the continence rate was comparable between younger and older patients, but potency outcomes were poorer in the elderly group. Similarly, Labanaris et al[22] suggested that even RARP in patients aged older than 75 years is a feasible treatment with excellent continence outcomes as well as acceptable potency outcomes. Although our study failed to show an association between age and potency after surgery, our data showing a favorable continence status of elderly patients undergoing RARP support the feasibility of this surgical procedure for these patients.

There are several limitations of the present study. First, this was a retrospective study and included relatively few men aged $\geq$ 70 years. Further analysis of a larger elderly cohort is needed to confirm the safety and feasibility of RARP for these patients. Second, a selection bias might exist—that is, only elderly patients who were physiologically able to tolerate an invasive surgical procedure and perform normal activities of daily living, were offered RARP. Therefore, the elderly patients in this series did not reflect the average patient of the same age. Finally, despite being an important issue, this study focused only on the safety and feasibility of RARP for elderly patients because of the limited observation period; hence, it would be more suitable to assess the oncologic outcomes after extending the observation period.

In conclusion, this is the first study to review the safety and feasibility of RARP for clinically localized PCa in elderly Japanese patients. RARP may be a reasonable therapeutic option for patients older than 70 years, and provides comparable perioperative and

functional outcomes to those of younger patients; therefore, surgery may not be a contraindication for these elderly patients on the basis of their chronological age alone.

Conflicts of interest

All authors declare no conflicts of interest.

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