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Health-related quality of life in Japanese patients with prostate cancer following proton beam therapy: an institutional cohort study

Kyoko Matsukawa[1,2], Takeshi Arimura[2], Makiko Orita[1], Hisayoshi Kondo[1], Ikuko Chuman[2], Takashi Ogino[2], Yasuyuki Taira[1], Takashi Kudo[3], and Noboru Takamura[1,*]

[1]Department of Global Health, Medicine and Welfare, Nagasaki University Graduate School of Biomedical Sciences, Atomic Bomb Disease Institute, Nagasaki, Japan, [2]Medipolis Proton Therapy and Research Center, Ibusuki, Japan, and [3]Department of Radioisotope Medicine, Nagasaki University Graduate School of Biomedical Sciences, Atomic Bomb Disease Institute, Nagasaki, Japan

*For reprints and all correspondence: Noboru Takamura, Department of Global Health, Medicine and Welfare, Nagasaki University Graduate School of Biomedical Sciences, Atomic Bomb Disease Institute, 1-12-4, Sakamoto, Nagasaki 852-8523, Japan. E-mail: takamura@nagasaki-u.ac.jp

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Abstract

Objective: Many treatment options have guaranteed long-term survival in patients with localized prostate cancer and health-related quality of life has become a greater concern for those patients. The purpose of this study was to reveal the health-related quality of life after proton beam therapy and to clarify the differences from other treatment modalities for prostate cancer.

Methods: Between January 2011 and April 2016, 583 patients were enrolled in the study and health-related quality of life outcomes using the Expanded Prostate Cancer Index Composite questionnaire were evaluated and compared with previous research targeted at Japanese patients.

Results: We found a significant decrease in the least square mean scores for urinary and bowel domains excluding the incontinence subscale after proton beam therapy ($P < 0.0001$) and recovery at a year following treatment. The scores for sexual function in patients without androgen deprivation therapy decreased each year after proton beam therapy ($P < 0.0001$). The scores for hormones in patients without androgen deprivation therapy remained high and those of patients with androgen deprivation therapy were lower before treatment but were comparable to those of non-androgen deprivation therapy patients at 2 years post-treatment. We found that the impact of radiotherapy including proton beam therapy on urinary condition and sexual function was lower than that of surgery.

Conclusions: For the first time in Japan, we investigated health-related quality of life using Expanded Prostate Cancer Index Composite questionnaires in patients with prostate cancer after proton beam therapy and compared it with other treatment modalities.

Key words: prostate cancer, proton beam therapy, health-related quality of life, Japanese patients

Introduction

In Japan, prostate cancer (PCa) is the fourth most frequently diagnosed malignancy and has been increasing in the past decades (1). However, the mortality rate ranks sixth in men and has generally been declining due to improved treatment modalities and the spread of early detection methods for PCa. The 5 year relative survival rate in patients with PCa was 66.8% from 1993 to 1996 and increased to 97.5% from 2006 to 2008; hence, PCa has been recognized as a disease having the most favorable prognosis of common cancers in Japan.

Although more than 70% of PCa patients were diagnosed at a localized stage in Japan and were guaranteed long-term survival by the many treatment options available (1,2), there is little compelling evidence to indicate any difference in efficacy between those treatments (3). Therefore, most patients narrow down their choices for treatment based on learning beforehand about possible adverse effects of each procedure (4).

A variety of treatments for localized PCa can each cause serious physical, emotional and sexual function damage to patients, which results in a substantial impairment of health-related quality of life (HRQOL) (5). Several studies have investigated the impacts on HRQOL of patients with PCa following treatment and have revealed a more significant decline in sexual function following surgery compared with external beam radiation therapy (EBRT) (6).

Although proton beam therapy (PBT) is one type of EBRT, proton beams have several features that distinguish them from X-rays, such as a sharp radiation-dose gradient called the Bragg peak, which can minimize damage to surrounding normal tissues and result in better outcomes of HRQOL in patients than that of X-ray (7–9).

Recent studies from the US and Germany showed favorable results on HRQOL of patients with localized PCa in PBT (10–18). However, HRQOL is largely subject to the cultural background and lifestyle of patients and these results may not be applicable to Japanese patients (19). Moreover, although there are many studies on HRQOL targeted at Japanese patients with PCa, to the best of our knowledge there have been no reports in Japan on HRQOL after PBT.

The purpose of this study was to investigate patient-reported HRQOL outcomes using the Expanded Prostate Cancer Index Composite (EPIC) questionnaire in a single institutional cohort of patients with localized PCa who received definitive PBT (19–21), and to explore the differences in HRQOL from other treatment modalities for PCa in Japan.

Patients and methods

Patients and study design

Patients who met the following criteria were eligible for the study: (i) pathologically confirmed with prostate biopsy; (ii) no metastasis with computed tomography (CT), bone scintigraphy and magnetic resonance imaging (MRI) and/or positron-emission tomography (PET) within 3 months before treatment; (iii) no prior malignancy within 5 years; (iv) no history of surgery or radiotherapy in pelvis; (v) life expectancy of greater than 5 years with Eastern Cooperative Oncology Group (ECOG) performance status of ≤ 1.

The primary endpoint of the study was HRQOL outcomes of PBT for patients with PCa. The secondary endpoint was the impact of androgen deprivation therapy (ADT) on HRQOL in PCa patients. We considered patients who underwent ADT before treatment as patients with ADT regardless of whether they were involved with ADT following PBT or not.

Between January 2011 and April 2016, 602 consecutive patients with PCa were admitted to our center. Of these, 10 patients who had undergone surgery, 5 who were not Japanese, 2 with bone metastasis, 1 with a history of irradiation and 1 who declined to enter the study were excluded, while the remaining 583 were enrolled on the study.

HRQOL profiles were obtained prospectively with the Japanese EPIC questionnaire before the initiation of treatment (pre-PBT), the last irradiation day of PBT (post-PBT) and every 12 months annually following treatments. The questionnaire was mailed to the patients and returned to us at specified timings. We did not press the patients for reply if there was no response from them.

This study was approved by the institutional review boards (MEDI 10-9 and 16042889), and written informed consent was obtained from all patients prior to enrollment. All procedures were performed in accordance with the ethical standards outlined in the Helsinki Declaration of 1975, as revised in 2000.

Proton beam therapy

The gross tumor volume was not indicated for all patients, but the clinical target volume (CTV) was defined as the prostate gland for low- and intermediate-risk patients, and the seminal vesicle was added to the CTV for high-risk patients. The planning target volume was set as the CTV plus 7 mm lateral margins and 10 mm margins in all other directions.

Although we initially performed PBT using 74 Gray Equivalent (GyE) with 37 fractions (fr) for low- and intermediate-risk patients and 78 GyE/39 fr for high-risk patients, a protocol of 70 GyE/28 fr was initiated for all patients in 2013. Patients were all treated with 210 MeV proton horizontal beams, which were produced by a beam-wobbling system for a flatter irradiated field, with a ridge filter (Mitsubishi Electric Corporation, Tokyo, Japan).

All patients were administered magnesium oxide for preventing constipation and with dimethicone for reducing intestinal gas during PBT. Moreover, they were required to defecate 30–60 min before irradiation. The details of simulation, planning and treatment procedures have been previously described (21).

Follow-up and evaluation of recurrence

All patients were evaluated for prostate-specific antigen (PSA) values, adverse events and disease-related symptoms every 3–6 months by self-referring urologists. Biochemical failure was determined based on the Phoenix definition, and clinical recurrence was decided via imaging modalities such as bone scintigraphy, CT, PET and MRI (22). Meanwhile, ADT was left to the self-referring physicians' discretion for all risk group classifications.

Statistical analysis

The scores measured via EPIC were calculated according to the instrument instructions (19,20). The scores ranged from 0 to 100, with high scores representing more favorable HRQOL. Statistical analyses were performed with SAS Release 8.2 (SAS Inst., Cary, NC, USA) for these calculated scores. We estimated the least squares means (LSM) and standard errors (SE) for each assessment timing and used them to compare the scores statistically in the same domains and subscales with the randomized block method. A P value of <0.05 was considered statistically significant.

Table 1. Patient characteristics

Factors	Items	Value (unit)
No. of patients		583
Age	Median	66 years
	Range	39–88 years
Risk classification (NCCN)	Low	72 (12%)
	Intermediate	268 (46%)
	High	243 (42%)
Protocol (GyE/fraction)	74/37	157 (27%)
	78/39	119 (20%)
	70/28	307 (53%)
ADT	Yes	191 (33%)
	No	392 (67%)
No. of corresponding patients	Pre-treatment	583 (100%)
	Post-treatment	569 (98%)
	1 year	474 (81%)
	2 years	367 (63%)
	3 years	247 (42%)
	4 years	140 (24%)
Recurrence	Biochemical	12 (2.1%)
	Bone	8 (1.4%)
	Lymph node	2 (0.3%)
	Liver	1 (0.2%)
	Prostate	1 (0.2%)
	Others	1 (0.2%)

No., number; NCCN, National Comprehensive Cancer Network; GyE, Gray Equivalent; ADT, androgen deprivation therapy.

Results

Patient characteristics

The patient characteristics are summarized in Table 1. The patients' median age was 66 (range, 39–88 years). The low-, intermediate- and high-risk groups comprised 72 (12%), 268 (46%) and 243 (42%) patients, respectively. The 70 GyE/28 fr, 74 GyE/37 fr and 78 GyE/39 fr protocols were performed in 307 (53%), 157 (27%) and 119 (20%) patients, respectively. One hundred and ninety-one patients (33%) were administered with ADT before initiation of irradiation. The number of corresponding patients at each assessment timing were 583 (100%) at pre-PBT, 569 (98%) at post-PBT, 474 (81%) at a year, 367 (63%) at 2 years, 247 (42%) at 3 years and 140 (24%) at 4 years after treatment, respectively. Biochemical recurrence, bone-, lymph node- and liver-metastasis and local recurrence were seen in 12 (2.1%), 8 (1.4%), 2 (0.3%), 1 (0.2%) and 1 (0.2%) patients, respectively, during follow-up in the study. There were significant differences between the base-line HRQOL scores obtained from patients with and without ADT on all sexual and hormonal domains ($P < 0.01$).

Urinary domain

Scores of urinary summary and subscales (function, bother, irritative/obstructive and incontinence) are shown in Table 2. There was a significant difference in all scores on urinary parameters between post-PBT and other assessment timings except for incontinence subscale ($P < 0.0001$). These results demonstrated that there was a substantial decrease in urinary function, bother and irritative/obstructive parameters immediately after PBT and recovery at a year after treatment excluding urinary incontinence.

Table 2. Scores on urinary domain

Assessment time	Summary				Subscale															
					Function				Bother				Irritative/obstructive				Incontinence			
	n (%)	LSM	SE	*P* value	*n* (%)	LSM	SE	*P* value	*n* (%)	LSM	SE	*P* value	*n* (%)	LSM	SE	*P* value	*n* (%)	LSM	SE	*P* value
Pre-PBT	470 (81)	91.5	0.4	–	488 (84)	95.6	0.4	–	471 (81)	88.6	0.5	–	467 (80)	90.6	0.5	–	445 (76)	95.2	0.5	–
Post-PBT	474 (83)	82.9	0.4	<0.0001	490 (86)	90.6	0.4	<0.0001	472 (83)	77.4	0.5	<0.0001	472 (83)	79.5	0.5	<0.0001	460 (81)	93.5	0.5	0.5709
1 year	321 (68)	91.5	0.5	1.0000	326 (69)	95.4	0.5	0.9997	309 (65)	88.7	0.6	1.0000	320 (68)	90.9	0.6	0.9992	317 (67)	94.6	0.6	0.9999
2 years	208 (57)	91.1	0.6	0.9961	210 (57)	95.7	0.7	1.0000	209 (57)	87.7	0.8	0.9304	207 (56)	90.9	0.8	0.9998	204 (56)	94.2	0.7	0.8677
3 years	116 (47)	91.6	0.8	1.0000	116 (47)	94.8	0.9	0.9687	116 (47)	89.2	1.0	0.9949	116 (47)	91.6	1.0	0.9573	113 (46)	93.7	1.0	0.9630
4 years	79 (56)	91.4	1.0	1.0000	79 (56)	96.2	1.1	0.9943	79 (56)	87.9	1.2	0.9947	79 (56)	91.6	1.2	0.9789	78 (56)	93.1	1.2	0.9987

LSM, least squares mean; SE Standard error.

Table 3. Scores on bowel, sexual and hormonal domains

Domain	Assessment time	Summary				Subscale Function				Bother			
		n (%)	LSM	SE	*P* value	*n* (%)	LSM	SE	*P* value	*n* (%)	LSM	SE	*P* value
Bowel	Pre-PBT	471 (81)	93.9	0.3	–	485 (83)	92.5	0.3	–	478 (81)	95.3	0.4	–
	Post-PBT	472 (82)	90.8	0.3	<0.0001	483 (84)	89.0	0.3	<0.0001	476 (83)	92.5	0.4	<0.0001
	1 year	315 (66)	93.1	0.4	0.6147	322 (67)	91.6	0.4	0.6090	320 (67)	94.6	0.5	0.8440
	2 years	206 (56)	93.0	0.5	0.5850	209 (56)	92.0	0.6	0.9749	208 (56)	94.0	0.6	0.4067
	3 years	112 (45)	93.1	0.7	0.8758	114 (46)	92.0	0.8	0.9916	114 (46)	94.3	0.8	0.8391
	4 years	77 (55)	93.5	0.8	0.9956	78 (55)	91.7	0.9	0.9666	77 (55)	95.2	0.9	1.0000
Sexual													
With ADT	Pre-PBT	143 (74)	32.7	0.7	–	145 (75)	8.7	0.9	–	134 (70)	88.0	1.5	–
	Post-PBT	144 (77)	32.7	0.7	1.0000	143 (76)	6.1	0.9	0.2504	140 (74)	93.4	1.5	0.9915
	1 year	99 (64)	31.0	0.8	0.5890	101 (66)	10.0	1.1	0.9470	95 (62)	78.5	1.9	0.0031
	2 years	57 (48)	31.5	1.1	0.9186	58 (54)	8.7	1.5	1.0000	58 (54)	82.0	2.5	0.3089
	3 years	32 (40)	29.0	1.4	0.1428	31 (38)	9.1	2.0	1.0000	31 (38)	74.4	3.3	0.0022
	4 years	19 (46)	32.2	1.9	0.9998	19 (46)	12.3	2.5	0.7421	18 (43)	76.7	4.3	0.1389
Without ADT	Pre-PBT	318 (80)	48.0	0.6	–	319 (81)	33.5	0.7	–	317 (80)	81.2	1.1	–
	Post-PBT	322 (84)	43.2	0.6	<0.0001	322 (84)	25.0	0.7	<0.0001	314 (82)	84.1	1.1	0.4073
	1 year	199 (61)	42.3	0.8	<0.0001	198 (61)	26.7	0.9	<0.0001	198 (61)	77.2	1.5	0.2751
	2 years	137 (54)	38.7	1.0	<0.0001	137 (54)	23.1	1.1	<0.0001	137 (54)	73.8	1.8	0.0060
	3 years	80 (47)	38.3	1.3	<0.0001	76 (44)	22.1	1.5	<0.0001	79 (46)	75.9	2.4	0.3119
	4 years	54 (55)	35.6	1.6	<0.0001	54 (55)	19.3	1.7	<0.0001	54 (55)	72.3	2.8	0.0379
Hormonal													
With ADT	Pre-PBT	147 (76)	86.6	0.8	–	149 (78)	83.5	1.0	–	145 (75)	89.0	0.7	–
	Post-PBT	142 (75)	88.3	0.8	0.5327	149 (79)	84.1	1.0	0.9974	142 (75)	91.6	0.8	0.0968
	1 year	103 (67)	91.8	1.0	0.0006	106 (69)	89.2	1.2	0.0071	103 (67)	93.9	0.9	0.0011
	2 years	59 (50)	93.6	1.3	<0.0001	61 (51)	91.3	1.6	0.0007	59 (50)	95.1	1.2	0.0003
	3 years	32 (40)	95.8	1.7	<0.0001	31 (38)	93.5	2.2	0.0006	32 (40)	97.6	1.6	<0.0001
	4 years	19 (46)	93.3	2.2	0.0430	19 (46)	91.0	2.9	0.1327	19 (46)	94.9	2.1	0.0931
Without ADT	Pre-PBT	310 (79)	93.8	0.4	–	319 (81)	91.8	0.5	–	314 (80)	95.4	0.4	–
	Post-PBT	313 (81)	94.4	0.4	0.8480	323 (84)	92.3	0.5	0.9650	318 (83)	96.1	0.4	0.7397
	1 year	201 (62)	94.4	0.5	0.9327	208 (65)	93.0	0.6	0.6113	204 (63)	95.7	0.5	0.9954
	2 years	141 (56)	94.5	0.6	0.9024	144 (57)	93.6	0.7	0.3198	142 (84)	95.4	0.6	1.0000
	3 years	77 (45)	93.1	0.8	0.9623	79 (46)	91.3	1.0	0.9975	78 (46)	95.0	0.8	0.9978
	4 years	57 (58)	95.1	0.9	0.7494	57 (58)	93.2	1.2	0.8714	57 (58)	96.7	0.9	0.7376

Table 4. Comparison with previous reports on HRQOL in the various treatment options for prostate cancer

Reports	Year	Treatment	Patients (number)	Age		F/U time (months)	Dose (Gy)	Fraction	HRQOL	Urinary		Bowel		Sexual		Hormone	
				median	range				Summary	Subscale	Summary	Subscale	Summary	Subscale	Summary	Subscale	
Hashine et al. (27)	2009	RRP	96	66	51–79	1–12	–	–	EPIC, SF-8		○		○		○		
		LDR-BT	88	69	52–84		145	1									
Yamamoto et al. (28)	2014	IMRT	91	70	56–79	3–24	70–78	35–39	EPIC, SF-8, IPSS		○		○		○		○
Hashine et al. (29)	2014	ORP	107	67	51–79	1–12	–	–	EPIC, SF-8, IPSS		○		○		○		
		LRP	105	66	51–78												
Muramaki et al. (30)	2014	LRP	57	67[a]	61–72[b]	16–42[b]	–	–	EPIC, SF-8	○	○	○	○	○	○	○	○
		MIE-RP	58	67[a]	62–72[b]	16–38[b]											
Hashimoto et al. (31)	2015	HDR-BT	118	67[a]	50–79	1–24	18	2	EPIC	○	○						
		EBRT					45	15									
Miyake et al. (32)	2016	RARP	298	66[a]	49–79	1–24	–	–	EPIC, SF-8	○	○	○	○	○	○	○	○
Okihara et al. (33)	2017	LDR-BT	482	67	50–89	3–36	167[c]	1[c]	EPIC					○	○		
Koike et al. (34)	2017	RARP	105	66	49–79	3–12	–	–	EPIC, SF-8	○	○	○	○	○	○	○	○
		LRP	229	68	52–78												
Hashine et al. (35)	2018	LRP	105	66	51–78	1–36			EPIC, SF-8, IPSS		○		○		○		
		RRP	107	67	51–79												
Hashimoto et al. (36)	2018	IMRT	195	74	67–76	1–24	66	22	EPIC	○		○		○		○	
Ueno et al. (37)	2018	RP[d]	850	71	67–76	3–12		–	EPIC, SF-8	○		○		○		○	
		ADT	370	73	67–76												
Nakai et al. (38)	2018	IMRT	121	73	55–82	1–24	74–76	37–38	EPIC, SF-8, IPSS, OABSS	○		○		○		○	
Maruyama et al. (39)	2019	RARP	201	68	63–72	1–12	–	–	EPIC	○	○	○		○		○	
Our study	2019	Proton	583	66	39–88	2–60	70–78	28–39	EPIC	○	○	○	○	○	○	○	○

F/U, follow-up; HRQOL, health-related quality of life; RRP, retropubic radical prostatectomy; LDR-BT, low dose-rate brachytherapy; EPIC, Expanded Prostate Cancer Index Composite; SF-8, medical outcome study 8 items short form health survey; IMRT, intensity-modulated radiation therapy; IPSS, international prostate symptom score; LRP, laparoscopic radical prostatectomy; MIE-RP, minimum incision endoscopic radical prostatectomy; ORP, open radical prostatectomy; HDR-BT, high dose-rate brachytherapy; EBRT, external beam radiation therapy; RARP, robot-assisted radical prostatectomy; RP, radical prostatectomy; ADT, androgen deprivation therapy; OABSS, overactive bladder symptom score.

[a]Mean values.

[b]Time between the maximum and minimum standard deviation values.

[c]Mean value of D90 for prostate in I-125 monotherapy.

[d]Includes retropubic/perineal/laparoscopic/robotic assisted RP.

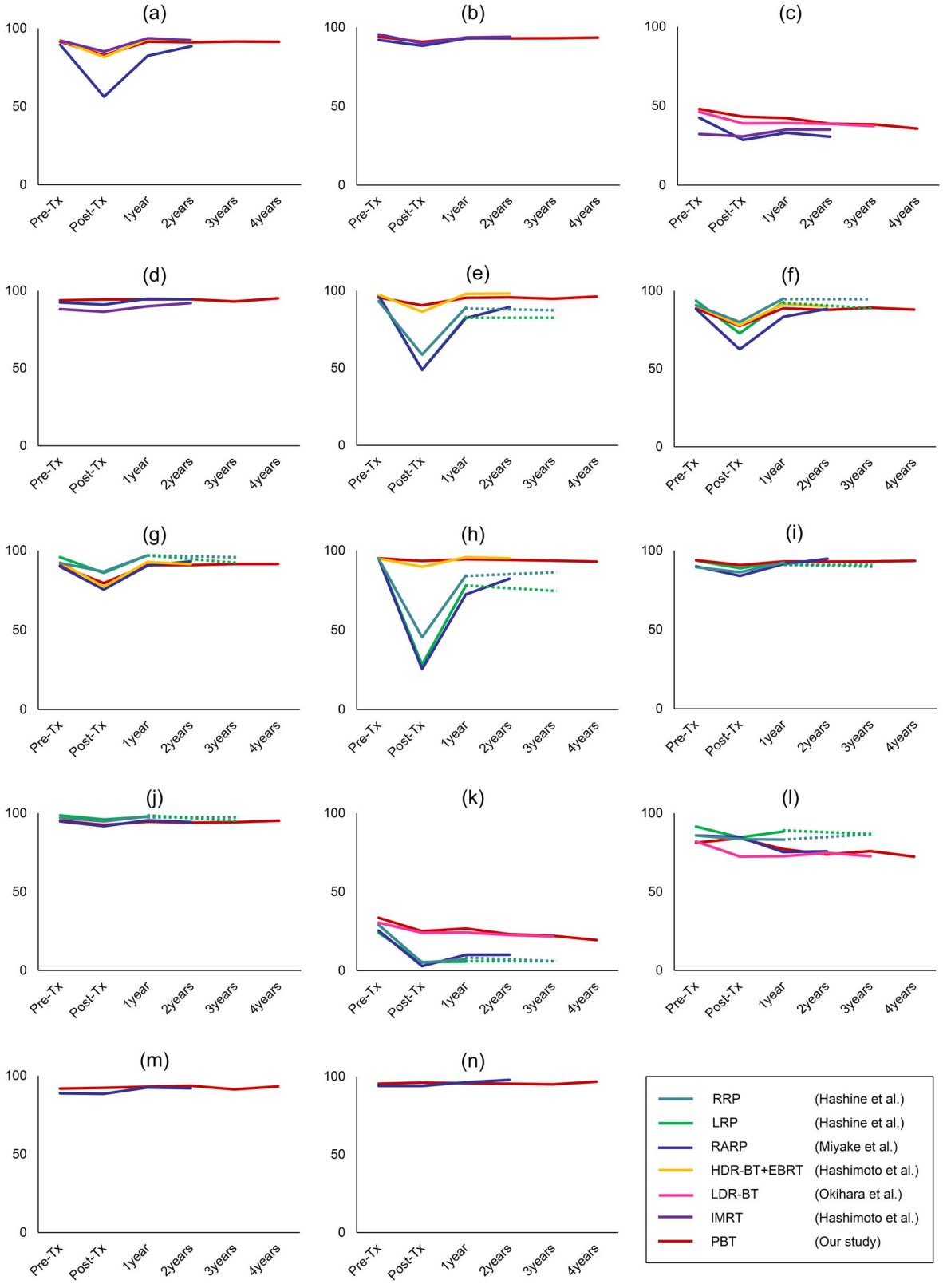

Figure 1. The transitions of HRQOL following treatments (Tx): radical retropubic prostatectomy (RRP), laparoscopic radical prostatectomy (LRP), robot-assisted laparoscopic radical prostatectomy (RARP), high dose-rate brachytherapy (HDR-BT) combined with external beam radiation therapy (EBRT), high dose-rate brachytherapy (LDR-BT), intensity-modulated radiation therapy (IMRT) and proton beam therapy (PBT) in the summary of urinary (a), bowel (b), sexual (c) and hormonal (d) domains and function (e), bother (f), irritative/obstructive (g) and incontinence (h) in the urinary subscales, and bowel function (i) and bother (j), sexual function (k) and bother (l), and hormonal function (m) and bother (n), respectively. The dotted lines represent the existence of missing data.

Bowel domain

Scores of bowel summary and subscales (function and bother) are shown in Table 3. There was a significant difference in all scores of bowel domain between post-PBT and other assessment timings ($P < 0.0001$). These results revealed that there was a substantial decrease in bowel function and bother immediately after PBT and recovery at a year after treatment.

Sexual domain

The scores on sexual summary and subscales (function and bother) are shown in Table 3. Although there was no significant difference in sexual summary and function subscale in patients with ADT between pre- and post-PBT, we found a significant difference between pre-PBT and 1 year ($P = 0.0031$), and also 3 years after PBT ($P = 0.0022$), in sexual bother subscale, respectively.

There was a significant difference in sexual summary and function subscale in patients without ADT between pre-PBT and other assessment timings ($P < 0.0001$), and also between pre-PBT and 2 years ($P = 0.0060$) and 4 years ($P = 0.0379$) after PBT in sexual bother subscale, respectively.

The scores on sexual function subscale in patients with ADT subsequently remained at low levels for 4 years, whereas those of patients without ADT were clearly higher than those with ADT but decreased year after year. However, the scores on sexual bother subscale in patients both with and without ADT were relatively high and almost similar.

Hormonal domain

The scores of hormonal summary and subscales (function and bother) are shown in Table 3. There was a significant difference in patients with ADT between pre-PBT and 1 year ($P = 0.0006$)/2 years ($P < 0.0001$)/3 years ($P < 0.0001$)/4 years ($P = 0.0430$) after PBT in summary, and 1 year ($P = 0.0071$)/2 years ($P = 0.0007$)/3 years ($P = 0.0006$) after PBT in function subscale, and 1 year ($P = 0.0011$)/2 years ($P = 0.0003$)/3 years ($P < 0.0001$) after PBT in bother subscale, respectively.

There was no significant difference in any scores on this domain in patients without ADT between pre-PBT and other assessment timings.

The scores on hormonal domain in patients without ADT subsequently remained at a high level; however, those of patients with ADT gradually increased after treatment and were comparable to those of non-ADT patients after about 2 years in every item of this domain.

Discussion

Although PBT has been recognized as one of the definitive treatment modalities for localized PCa in Japan since the national health insurance began coverage of PBT for PCa in April 2018 and we can refer to treatment outcomes on efficacy and adverse events of PBT (21,23,24), there were no reports available on HRQOL in Japanese patients with PCa who underwent PBT. The HRQOL is subject to the cultural background and lifestyle of patients in the region and country and the information on HRQOL after PBT derived from Western countries may not be applicable to Japanese patients (19). Therefore, we thought that it was necessary to investigate HRQOL outcomes in Japanese patients with PCa who received PBT in Japan.

In our study, we examined patients up to a maximum follow-up period of 4 years; however, the number of corresponding patients at 4 years after PBT was 140, which was only 24% of all targeted patients. Moreover, the corresponding rates from those patients at that timing ranged from 46 to 58% as described in Tables 2 and 3. Therefore, we must highlight the decreased scientific significance of the data for HRQOL at 4 years post-PBT in the study.

The period of ADT can influence the HRQOL of patients with PCa since some adverse events are associated with decreased testosterone due to ADT and may resolve due to the recovery of testosterone after discontinuation of ADT (25). However, accurate data from all patients in the study regarding the period of ADT were unavailable; hence we were able to analyze the data based only on the presence or absence of ADT before PBT. Nevertheless, there was a significant difference observed between the base-line HRQOL scores obtained from patients with and without ADT in the study. Therefore, we considered it relevant to present the difference between patients with and without ADT in the PBT despite the insufficiency in the data.

Although the mean and standard deviation of scores were utilized to compare HRQOL outcomes in the several previous studies (10,11), we instead presented the values of LSM and SE obtained statistically with the randomized block method for the purpose of statistical accuracy. This was because uninterrupted follow-up for the entire 4 years of the study, with entirely completed questionnaires, was not attainable for most patients. We did not insist on patients completing the set of questionnaires in the study because of the possibility that the patient would feel uncomfortable and thus provide inaccurate answers (26). Nevertheless, we believe that the other available data obtained from their responses should not be ignored nor discarded. Both methods led to identical results with regard to their statistical significances except for some minor variations of P values in the study.

Table 4 shows the previous results on HRQOL for localized PCa in Japan for various definitive treatment modalities covered by the Japanese national health insurance system. The median age of patients in the study was 66 years, and its range was 39–88 years, the largest range compared with previous studies in Japan. Compared with other studies, the number of patients in the study was the second largest and the follow-up time was the longest. Although we measured HRQOL in PCa patients with only EPIC, all domains and subscales in the evaluation method were investigated in the study.

Figure 1 shows the transitions of HRQOL in different treatments for localized PCa in Japan. These diagrams were produced based on published literature as a reference and not based on original data. Age-matching or propensity-matching were not performed on the cohorts in our study; therefore, we cannot directly compare and analyze the results of each treatment modality statistically and academically. The scores before treatment in our study were almost the same as those in other studies, which supports the premise that those patients had a similar cultural and social background.

We selected some principal literature on HRQOL in treatments for patients with PCa in Japan and compared a plurality of graphs in an overlapped manner, which included the following: radical retropubic prostatectomy (RRP) by Hashine et al. (35), laparoscopic radical prostatectomy (LRP) by Hashine et al. (35), robotic-assisted radical prostatectomy (RARP) by Miyake et al. (32), high dose-rate brachytherapy (HDR-BT) plus external beam radiation therapy (EBRT) by Hashimoto et al. (31), low dose-rate brachytherapy (LDR-BT) by Okihara et al. (33) and intensity-modulated radiation therapy (IMRT) by Hashimoto et al. (36), and PBT in the study.

The transitions of scores on urinary summary and subscales in RRP, LRP, RARP, HDR-BT plus EBRT, IMRT and PBT are shown in Fig. 1(a, e, f, g and h). Our results were almost the same as those of HDR-BT plus EBRT in the urinary domain. The magnitude of decline in scores of urinary function and incontinence subscales after surgery was even larger than those after radiotherapy including HDR-BT plus EBRT, IMRT and PBT, whereas we did not find any substantial differences in transitions of scores on urinary bother and irritative/obstructive subscales among those treatments.

The transitions of scores on bowel domain in RRP, LRP, RARP, IMRT and PBT are shown in Fig. 1(b, i and j). Although there was a significant difference in all scores of bowel domain between post-PBT and other assessment timings in the study ($P < 0.0001$), we found that a decline in scores on bowel domain immediately after PBT was too small to register a change on a scale of 0–100 in EPIC and we did not find an obvious trend or difference in those treatment procedures. We consider that these results are mainly attributable to the digestive tract not having been irradiated except for a part of the rectum in both IMRT and PBT (21,36).

The transitions of scores on sexual domain in RRP, LRP, RARP, LDR-BT, IMRT and PBT are shown in Fig. 1(c, k and l), in which we displayed graphs for only patients without ADT in order to compare the results in each treatment modality. The scores of sexual summary in LDR-BT and PBT decreased in a gradual and similar manner during the observation period, although the decline in scores after RARP was slightly larger than those of the previous two treatment modalities. The low score before treatment in patients who received IMRT by Hashimoto et al. was considered to be influenced by ADT administered before the definitive treatment (36). In sexual function subscale, the graphs clearly delineated two groups: one was a radiotherapy group that included LDR-BT and PBT, another was a surgery group that contained LRP, RRP and RARP. The scores on sexual function subscale in the radiotherapy group decreased gradually every year, which indicated a possibility that effects of aging were larger than the impact of radiotherapy in sexual function (31). Whereas in the surgery group, the scores dropped markedly after treatments and hovered at low levels in the observation period. Nevertheless, the scores of the surgery group on the sexual bother subscale maintained high levels and were equal to or more than those of the radiation group. These results support a hypothesis that loss of sexual function due to surgery might emancipate patients from sexual bother in contrast to the maintenance of sexual activity with radiotherapy in Japan.

The transitions of scores on hormonal domain in RARP, IMRT and PBT are shown in Fig. 1(d, m and n). There was little difference in the scores of hormonal summary, function and bother subscales between RARP and PBT in the observation period. On the other hand, the scores on hormonal summary in IMRT were slightly lower than those of the previous two modalities although the difference diminished by 2 years after treatment. This result was considered to be caused by ADT performed before the definitive treatment (36,40).

In conclusion, we investigated patient-reported HRQOL outcomes with EPIC for patients with PCa who underwent definitive PBT and explored the differences in HRQOL between PBT and other treatment modalities in Japan. Although there was little difference in HRQOL between PBT and the other radiation therapies, there were large differences between PBT and various surgical procedures. We believe that our results would be of assistance to Japanese patients with PCa selecting an appropriate treatment procedure, and could also be useful to medical staff advising patients on HRQOL after treatments.

Author contributions

K.M. analyzed the data and drafted the manuscript. T.A. and M.O. directed the study and edited the manuscript. H.K. offered guidance for statistics. I.C. was involved in planning, leading the study and collecting data from patients. T.O., Y.T., T.K. and N.T. managed and supervised the study. All authors reviewed the manuscript and approved the final version.

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Conflict of interest

No authors have any conflicts of interest to disclose.

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