^{125}I low-dose-rate prostate brachytherapy and radical prostatectomy in patients with prostate cancer

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Abstract. Radical prostatectomy (RP) and low-dose-rate prostate brachytherapy (LDR) are two widely used treatment options for patients with T1c-T3a prostate cancer. In the present study, the efficacy of the two treatments was compared. A total of 429 patients who underwent either LDR (n=218) or RP (n=211) between January 2010 and June 2015 were retrospectively reviewed. Biochemical relapse-free survival time (bRFS) and clinical relapse-free survival time (cRFS) were assessed. The log-rank test compared bRFS between the two modalities, and Cox regression identified factors associated with bRFS. The median follow-up time and patient age were 46.6 months and 71 years, respectively. The bRFS at 1, 2 and 5 years was 89.4, 87.2 and 79.9% for LDR, respectively, and 91.0, 82.8 and 72.2% for RP, respectively (P=0.077). The cRFS at 1, 2 and 5 years was 99.1, 97.7 and 94.9% for LDR, respectively, and 99.0, 96.2 and 94.5% for RP, respectively (P=0.630). It was indicated that LDR produced equivalent bRFS and cRFS rates compared with RP. The risk of biochemical failure (bF) was higher for the RP group compared with the LDR group in patients with a Gleason score ≤3+4 (P=0.022) or initial prostate specific antigen ≤10 ng/ml (P=0.002). Based on the univariate and multivariate logistic regression analysis of all 429 patients, T stage ≥T2b was an independent predictor for bF.

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Abbreviations: ADT, androgen deprivation therapy; bF, biochemical failure; bRFS, biochemical relapse-free survival time; cRFS clinical relapse-free survival time, EBRT, external beam radiation therapy; iPSA, initial prostate-specific antigen; LDR, low-dose-rate brachytherapy; Pca, prostate cancer; PCSM, prostate cancer-specific mortality time; RP, radical prostatectomy

Key words: prostatic neoplasms, brachytherapy, radical prostatectomy, treatment outcomes, comparative effectiveness

Introduction

Radical prostatectomy (RP) and low-dose-rate prostate brachytherapy (LDR) are two widely used treatment options for patients with T1c-T3a prostate cancer (Pca) (1). However, the optimal treatment remains a subject of debate. Contemporary guidelines recommend that treatment decisions should be made based on tumor features, baseline prostate specific antigen (PSA) levels, patient age, comorbidity, life expectancy, and quality of life (2-4).

A number of studies have investigated the oncological outcomes of different treatments, in order to identify the population who would most benefit from a specific treatment and to determine which treatment is superior in terms of improving the length or quality of the patient's life (5-7). However, the comparison of the oncological outcomes of PR and LDR treatments remains a challenge, due to differential definitions for recurrence and methodological biases arising from the differences in baseline characteristics, including age, comorbidity and cancer risk features, such as PSA, biopsy Gleason score (8) and clinical stage (5,9,10). Therefore, results from the aforementioned previous studies are inconclusive, yielding only weak evidence regarding which treatment is superior. A randomized controlled trial is the ideal approach for comparing competing treatment modalities (11,12). However, treatment options for Pca are diverse, and therapeutic decisions are largely based on patient preference and physician discretion (5). Compared with candidates for RP, patients who are offered LDR generally tend to be older and have higher comorbidity scores and more aggressive cancer-associated risk features, such as initial PSA, clinical stage and percentage of positive biopsies within our clinic. Therefore, a random trial is impractical (9,13). Attempts at randomized, prospective trials to compare PR and LDR treatments have failed, since patients ultimately prefer to make their own treatment decisions (14).

Therefore, to the best of our knowledge, evidence of informed clinical decisions regarding adequate treatment for patients with T1c-T3a PCa is lacking and the comparative effectiveness of RP and LDR for Pca in Chinese patients has yet to be reported. Therefore, the aim of the present study was to compare biochemical relapse-free survival time (bRFS) in patients with T1c-T3a Pca treated with either RP or LDR at Peking Union Medical College Hospital, Beijing, China.

Variables that may predict differences in biochemical control, including treatment modality as a variable, were identified using the most recent consensus definitions of biochemical failure (bF) (15,16).

Materials and methods

Study population and data collection. A total of 429 consecutive patients (mean age 69.41 years; range, 46-83 years) with T1c-T3a Pca treated with curative intent were retrospectively reviewed, and all the patients were treated at Peking Union Medical College Hospital (Beijing, China) between January 2010 and June 2015. The Tumor-Node-Metastasis classification system (3) for the study population, was performed according to the standards provided by the National Comprehensive Cancer Network (NCCN) updated in 2016 (3). T1c is defined as: A tumor identified via needle biopsy found in one or both sides, but not palpable; T2 is defined as: Tumor is palpable and confined within the prostate; and T3a is defined as: extraprostatic extension tumor (unilateral or bilateral). High risk is defined as PSA ≥20.0 ng/ml, or a Gleason score of 8-10, or tumor stage T2c. Intermediate risk is defined as: PSA 10-20 ng/ml, or a Gleason score of 3+4=7, or tumor stage T2b-T2c. Low risk is defined as: PSA <10 ng/ml and a Gleason score of ≤6 and tumor stage T1-T2a (3). The inclusion criteria were the following: A clinical T-stage between T1c and T3a, ≥2 years follow-up post-treatment, and no distant metastasis. Patients who received adjuvant radiation therapy/chemotherapy and/or patients with distant metastasis were excluded from the present study. A total of 211 (49.2%) patients underwent RP and 218 (50.8%) patients received LDR. The choice of treatment, LDR versus RP, was determined by the patient and/or the doctor .Written informed consent was obtained from all individual participants included in the present study. Patients were informed of the benefits and consequences of each therapeutic option.

The following variables were evaluated for all participating patients: Medical history,physical examination, digital rectal examination, serum PSA prior to treatment, including initial PSA (iPSA) and pathologic grading. The pathologic grading conformed to the 2006 update of the Gleason grading system (8). Gleason grading reported here is from biopsy tissue. Clinical staging was based on digital rectal examination and specific examinations, including chest radiography, bone scintigraphy, computerized tomography (CT)-scan and/or magnetic resonance imaging of the pelvis.

Treatments. RP was recommended for patients who either desired surgical treatment or were determined as optimal surgical candidates, due to favorable clinical characteristics, such as better cardiopulmonary function and no previous history of abdominal surgery. Surgery was performed by a pure laparoscopic prostatectomy, with the extent of pelvic lymph node dissection being based upon the risk category of the patient. The procedure was performed according to the technique described by Walsh (17). The vesico-urethral anastomosis was made with a running suture with the suture line Y604 (Ethieon, USA).

Treatment with LDR was planned, so that the prostate and proximal seminal vesicles received 145 Gy with a 5-mm margin laterally, anteriorly, and inferiorly (18). No margin was planned superiorly, including the bladder and posteriorly, including the rectum. ^{125}I seeds were accurately introduced into preplanned positions by a brachytherapy stepping unit MICK200 (Computerized Medical Systems, Inc., St. Louis, MO, USA) using a standard 0.5 cm brachytherapy template placed over the perineum. One week following implantation, dosimetric analysis was performed by CT scan, and the D90, which was defined as the minimum dose covering 90% of the prostate, was obtained for each patient and ranged from 140 Gy to 155 Gy, with an average of 144 Gy.

Follow-up and study endpoints. Patients were monitored by serum PSA and digital rectal examination monthly during the first 3 months following treatment and every 3 months thereafter. If PSA level were stable, routine follow-up was scheduled every 6 months for 2 years following treatment. In cases with a rise in PSA level or patient presenting with bone pain, a CT scan of the chest/abdomen/pelvis along with bone scintigraphy should be performed, as recommended by the EAU and NCCN guidelines (3,19).

Primary endpoints to determine efficacy were bRFS, clinical relapse-free survival time (cRFS), and Pca-specific mortality time (PCSM). bF was defined as a PSA value of ≥0.2 ng/ml for patients who underwent RP (15) and an increase of 2 ng/ml or >nadir PSA value (16) for patients receiving LDR. If a patient received salvage radiotherapy or endocrine therapy, the patient was considered as having experienced a bF. cRFS was defined as metastases identified by medical imaging, with or without localizing symptoms, or as biopsy-proven local recurrence. PCSM was defined as mortality due to Pca, as noted on the death certificate alongside the biochemical and clinical information, or the presence of uncontrolled metastatic disease at the time the patient succumbed.

Statistical analysis. Factors considered to influence the endpoint were recorded for baseline analysis. The age and iPSA of the patients are presented in Table I as the mean (standard deviation), with number of patients in each group (n) stated at the top of the table. Student's t-test was used to evaluate differences in the mean of continuous variables. A χ^2 test was performed to compare ratios and Mann-Whitney U test to compare medians. Differences between two survival curves were evaluated by log-rank tests. Cox proportional-hazard models were constructed to identify factors associated with bRFS. Baseline data analysis was performed by programs the present study created in R programming language (v.3.3.1; R Foundation for Statistical Computing, Vienna, Austria). Survival analysis was performed with the help of survival package (v.2.38, Therneau T) (20). P<0.05 was considered to indicate a statistically significant difference.

Results

A total of 429 patients were included in the present study, with 218 (50.8%) patients receiving LDR and 211 (49.2%) patients that had undergone RP. The median follow-up time for PR and LDR groups was 46.6 months. The median age of the patients was 71 years overall, with 74 and 66 years for LDR and RP,

Table I. Pretreatment characteristics for LDR and PR groups.

Parameters	LDR (n=218)	RP (n=211)	All (n=429)	P-value
Clinical symptoms				0.253
Dysuria	112	121	233	
Health examination	106	90	196	
Age, years				<0.001[a]
Mean (standard deviation)	73.41 (5.21)	65.28 (6.49)	69.41 (7.14)	
Median	74	66	71	
Range	51-83	46-78	46-83	
Biopsy Gleason score				0.104
6	147	128	275	
7 (3+4)	34	46	80	
7 (4+3)	24	18	42	
8	3	10	13	
9	10	9	19	
Prostate volume, ml				0.092
≤30	120	98	218	
>30	98	113	211	
Clinical T stage				0.113
T1c	54	43	97	
T2a	67	56	123	
T2b	21	38	59	
T2c	71	67	138	
T3	5	7	12	
iPSA, ng/ml				0.067
≤4	9	3	12	
4.1-10	61	89	150	
>10	148	119	267	
Mean (standard deviation)	13.25 (6.63)	12.13 (6.00)	12.70 (6.34)	
NCCN risk category				0.813
low	49	53	102	
intermediate	83	78	161	
high	86	80	166	
Duration ADT, months				<0.001
0	24	159	183	
1-6	87	27	114	
>6	107	25	132	
Follow-up time, months				<0.001[a]
Median	50.1	42.9	46.6	
Range	29-86.9	1-90	1-90	
Biochemical recurrence				0.217
No	177	160	337	
Yes	41	51	92	
Clinical failure				0.939
No	208	200	408	
Yes	10	11	21	
Patient status				>0.999
Alive	214	208	422	
Prostate cancer associated -mortality	4	1	5	
Other cause-associated mortality	0	2	2	

[a]Significant at P<0.05. LDR, low-dose-rate brachytherapy; iPSA, initial prostate-specific antigen; RP, radical prostatectomy; ADT, androgen deprivation therapy; SD, standard deviation; NCCN, National Comprehensive Cancer Network; Pca, prostate cancer.

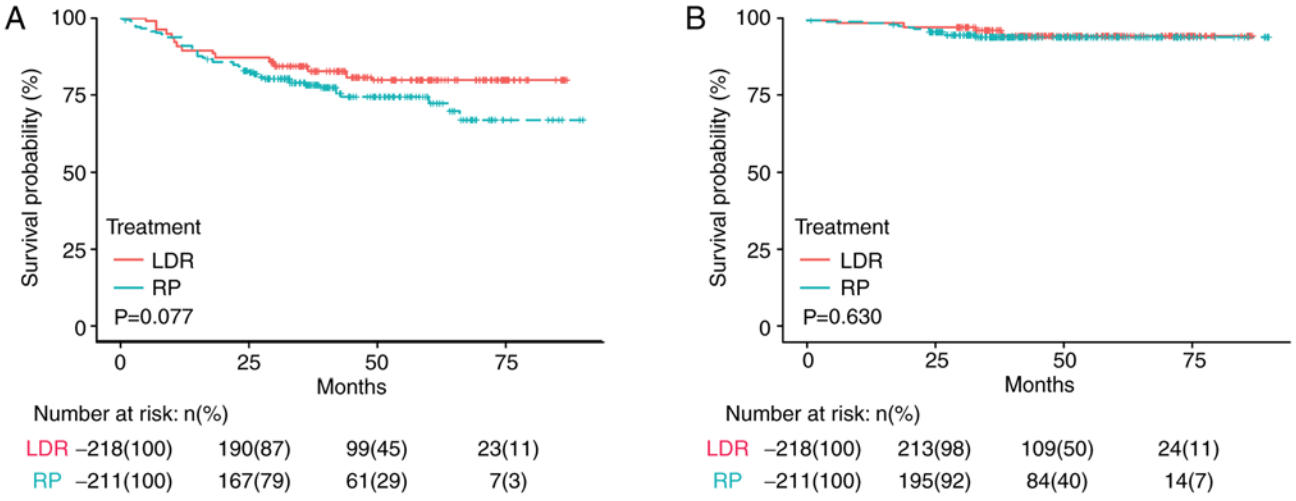

Figure 1. Efficacy plots. (A) Kaplan-Meier estimates of biochemical relapse-free survival time for LDR and RP. (B) Kaplan-Meier estimates of clinical relapse-free survival time for LDR and RP. LDR, low-dose-rate; RP, radical prostatectomy.

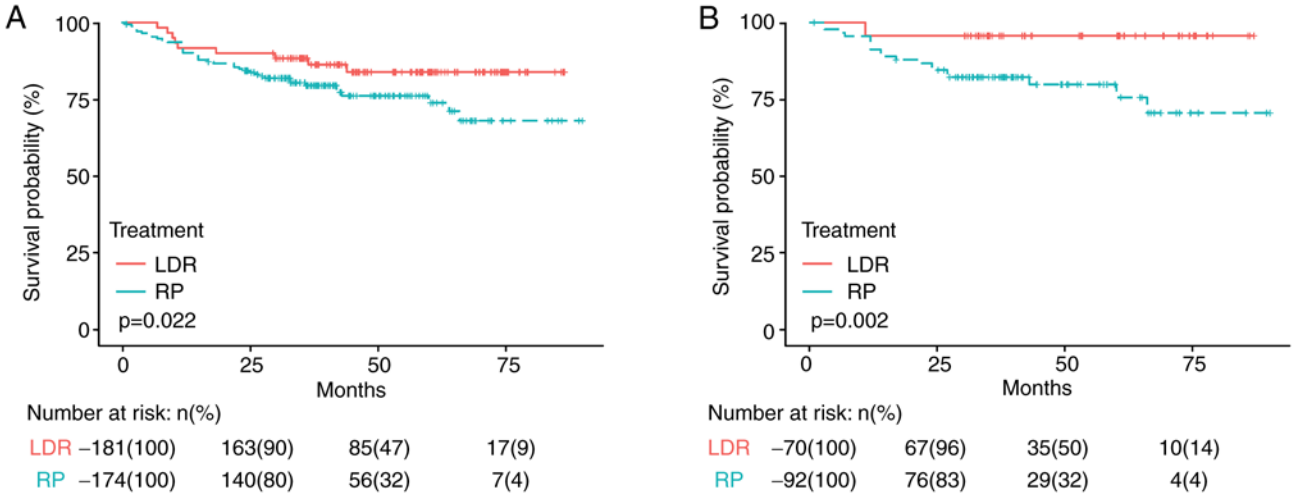

Figure 2. Efficacy plots. (A) Kaplan-Meier estimates of bRFS for LDR and RP when the biopsy Gleason score was less than or equal to 3+4. (B) Kaplan-Meier estimates of bRFS for LDR and RP when initial PSA was less than or equal to 10 ng/ml. bRFS, biochemical relapse-free survival time; LDR, low-dose-rate; RP, radical prostatectomy.

respectively. At the last follow-up visit, 98.4% of the patients had remained disease-free. All patients in the RP group had received a pure laparoscopic prostatectomy. For patients receiving LDR, the activity of ^{125}I seeds ranged between 0.35 and 0.50 mci, and the total activity ranged between 15 to 44.5 mci, with an average of 25.1 mci. The mean D90 for the LDR group was 144 Gy (1 standard deviation = 20.58 Gy). Neoadjuvant or adjuvant androgen deprivation therapy (ADT) was administered to 89% of the patients in the LDR group and to 24.6% of the patients in the RP group. Table I presents a full comparison of pretreatment characteristics between the LDR and PR groups. Patients treated with LDR were older, experienced a longer follow-up time and had a higher preponderance of combined ADT treatment. The survival rates were expressed as point estimates with 95% confidence intervals (CI). The bRFS at 1, 2 and 5 years was 89.4 (95% CI, 85.5-93.6), 87.2 (95% CI, 82.8-91.7) and 79.9 (95% CI, 74.4-85.7) for LDR, and 91.0 (95% CI, 87.2-94.9), 82.8 (95% CI, 77.3-87.7) and 72.2 (95% CI, 65.0-80.3) for RP, respectively. The log-rank test indicated that bRFS for patients who had received a RP were lower compared with patients who had received LDR treatment. However, this difference was not statistically significant (P=0.077; Fig. 1A). cRFS at 1, 2 and 5 years was 99.1 (95% CI, 97.8-100), 97.7 (95% CI, 95.7-99.7) and 94.9 (95% CI, 91.9-98.1) for LDR, and 99.0 (95% CI, 97.7-100), 96.2 (95% CI, 93.6-98.8) and 94.5 (95% CI, 91.4-97.7) for RP, respectively. The log-rank test was not significant for cRFS between RP and LDR groups (P=0.630; Fig. 1B).

bRFS curves between LDR and RP. Log-rank test was used to compare the bRFS curves between LDR and RP in terms of different variables according to pretreatment characteristics. Risk of bF was significantly higher with RP compared with LDR in the patients with a biopsy Gleason score ≤3+4 (P=0.022; Fig. 2A) or iPSA ≤10 ng/ml (P=0.002; Fig. 2B). However, the survival time of patients who received LDR was not significantly different from patients who received

Table II. Comparison of the bRFS curves between LDR and RP groups, according to different variables using a log-rank test.

Variables	P-value
Age, years	
>65	0.133
≤65	0.511
Biopsy Gleason score	
≤3+4	0.022[a]
≥4+3	0.642
Prostate volume, ml	
>30	0.251
≤30	0.143
iPSA, ng/ml	
>10	0.481
≤10	0.002[a]
Clinical T Stage	
T1c,T2a	0.341
T2b	0.712
T2c,T3	0.132
NCCN risk category	
High-risk	0.221
Low- and intermediate-risk	0.079

[a]Significant at P<0.05. bRFS, biochemical relapse-free survival; LDR, low-dose-rate brachytherapy; RP, radical prostatectomy; iPSA, initial prostate-specific antigen; NCCN, National Comprehensive Cancer Network.

RP for any of the following: Age, biopsy Gleason score ≥4+3, prostate volume, iPSA >10 ng/ml, clinical T stage and NCCN risk category (3). Comparisons of bRFS curves between LDR and RP groups in terms of different variables are presented in Table II.

Cox proportional-hazard models were constructed to identify factors associated with bRFS, and results are presented in Table III. With univariate analysis of the entire cohort, clinical stage ≥T2b (P<0.001), iPSA >10 ng/ml (P=0.004), biopsy Gleason score >3+4 (P=0.002) and high risk according to the NCCN risk category (P<0.001) were associated with significantly worse bRFS. On multivariate analysis of the entire cohort, only clinical stage ≥T2b (P<0.001) was associated with significantly worse bRFS. Treatment modality was not predictable by multivariate analysis [hazard ratio (HR), 1.30; 95% CI, 0.80-2.12; P=0.295). However, LDR was favored over RP by univariate analysis, but was not statistically significant (HR, 1.44; 95% CI, 0.96-2.18; P=0.080).

Discussion

RP, radiotherapy/brachytherapy, cryoablation and high-intensity focused ultrasound are the common treatment methods for T1c-T3a Pca (3). The American Brachytherapy Society consensus guidelines suggest that brachytherapy is a safe and efficacious procedure, acknowledged as a standard therapy for men with localized Pca (21). The present study statistically analyzed the data of 429 patients with T1c-T3a Pca treated at Peking Union Medical College Hospital. The results indicated that the bRFS rates at 5 years were 79.9 and 72.2% for LDR and RP, respectively. The log-rank test indicated the bRFS for RP was lower compared with LDR; however, these differences were not statistically significant. The univariate and multivariate analysis of the entire cohort, indicated no significant difference in bRFS between RP and LDR. This result was consistent with recent publications in the literature, which indicated that the bRFS rates at 5, 10 and 15 years after surgery, external radiotherapy and brachytherapy were similar in patients with low-risk Pca (22,23); however, not all current publications are randomized prospective studies, including the present study, thereby limiting the available comparisons. In terms of tumor-associated outcomes, Ciezki *et al* (24) reported high-risk Pca treated with external beam radiation therapy (EBRT), LDR or RP yields efficacy equivalent to cRFS, as well as a PCSM advantage of LDR and RP over EBRT. In the present study, there was also no statistically significant difference in the 5-year cRFS between the two therapeutic groups. Only three patients in the RP group died, one due to Pca and the other two due to unknown causes. A total of four patients succumbed to Pca in the LDR group. Therefore, it was difficult to compare cancer-specific mortality and other causes of mortality in these two groups, which would require additional analysis with a larger group of patients over a longer follow-up period.

Neither treatment modality has been proven superior to the other with respect to RP and LDR; therefore, the optimal treatment for different risk categories in Pca remains a matter of debate (25-28). Although the study's median follow-up time of 46.6 months was sufficient to capture a considerable number of systemic failure events, it may have remained too brief to achieve mortality results. Therefore, bRFS was selected as the main evaluation criterion of curative effect. Colberg *et al* (28), reported that LDR produced an equivalent 5-year bRFS compared with RP in patients with early Pca. Taussky *et al* (29), also reported that RP and LDR treatment did not result in significantly different outcomes at 4 years post-treatment, in patients with low- and low-intermediate-risk Pca. However, Ferreira *et al* (30) reported that the 5-year bRFS of patients with early Pca, who had undergone brachytherapy was significantly higher compared with those who had undergone surgery. Furthermore, Ciezki *et al* (24) reported that high-risk Pca treated with EBRT, LDR or RP yields efficacy with an improved bRFS for LDR and EBRT compared with RP (24).

Although there are a number of published studies evaluating a large number of low-risk Pca cases who underwent LDR, they are notably heterogeneous, since the LDR technique employed across various centers is different, and the methodology used when comparing the results between RP and LDR also differs (23,31). One such example is whether, prior to comparing results, postoperative patients receiving salvage therapy should be excluded. It seems that the inclusion of surgical patients who received radiation and/or postoperative hormone therapy can skew the results in favor of surgery, as observations from the present study. When comparing results across different

Table III. Univariate and multivariable analyses for bRFS.

	Univariate analysis		Multivariate analysis	
Factor	P-value	HR (95% CI)	P-value	HR (95% CI)
Treatment				
RP vs. LDR	0.080	1.44 (0.96-2.18)	0.295	1.30 (0.80-2.12)
Age, years				
≤65 vs. ≥65	0.068	1.50 (0.97-2.30)	0.497	1.19 (0.72-1.98)
Clinical T Stage				
≥T2b vs. ≤T2[a]	<0.001[a]	2.94 (1.88-4.61)	<0.001[a]	2.31 (1.42-3.76)
iPSA, ng/ml				
>10 vs. ≤10	0.004[a]	2.03 (1.26-3.28)	0.077	1.57 (0.95-2.60)
Biopsy Gleason score				
>3+4 vs. ≤3+4	0.002[a]	2.06 (1.30-3.23)	0.126	1.45 (0.90-2.35)
Prostate volume, ml				
≤30 vs. >30	0.619	1.11 (0.74-1.67)	0.763	1.07 (0.70-1.62)
NCCN risk category				
High-risk vs. intermediate/low-risk	<0.001[a]	3.63 (2.36-5.59)	-	-

[a]Significant at P<0.05. bRFS, biochemical relapse-free survival; RP, radical prostatectomy; LDR, low-dose-rate brachytherapy; HR, hazard ratio; CI, confidence interval; iPSA, initial prostate-specific antigen; NCCN, National Comprehensive Cancer Network.

treatment modalities in the absence of randomization, one must acknowledge the number of factors that can influence reported outcomes. These factors include, but are not limited to: Patient selection, definition of failure, treatment specifics, including type of surgery and dose of radiotherapy, and philosophy of treatment, including stepwise utilization of modalities (surgery versus upfront combination in radiotherapeutic approaches) (1).

In the present study, the log-rank test was employed to compare the bRFS curves between LDR and RP under different conditions/variables, according to pretreatment characteristics, including patient age, biopsy Gleason score, prostate volume, iPSA, clinical T stage and NCCN risk category. It was observed that bRFS was significantly higher with LDR compared with RP in patients with a biopsy Gleason score ≤3+4 or iPSA ≤10 ng/ml. In patients with low- and intermediate-risk Pca, bRFS for patients receiving LDR was higher compared with patients, who had undergone RP; however, the result was not statistically significant, consistent with a recent study (29). Ferreira *et al* (30), reported 129 patients, who had undergone either brachytherapy (64 patients) or surgery (65 patients), and when stratified according to treatment, the survival time of patients who had undergone brachytherapy (79.70%) was higher compared with those who had undergone surgery (44.30%). Risk of bF was higher for surgery compared with brachytherapy (30). Taking into consideration the results of the present study, brachytherapy may be a better option compared with RP in patients with a biopsy Gleason score ≤3+4 or iPSA ≤10 ng/ml. In terms of the pretreatment characteristics, patients treated with LDR were older, experienced longer follow-up time, and had a higher preponderance of combined ADT treatment. Differences in the definition of bF in each modality may have caused some bias when interpreting the results. Therefore, a prospective study comparing eligible patients is required, in order to draw a more accurate conclusion.

There are a number of factors affecting the prognosis of Pca, including general situation, tumor stage, tumor grade, iPSA, age and bone scintigraphy (32-34). Ciezki *et al* (24) reported that clinical stage T3, biopsy Gleason score 8-10, higher pretreatment PSA, shorter ADT duration and more frequent PSA testing following therapy were all associated with a significantly worse bRFS. Taussky *et al* (29), reported that younger age, higher percentage of positive biopsies and PSA at diagnosis were predictive of bF. In the present study, seven variables that may affect prognosis of Pca, including patient age, clinical stage, biopsy Gleason score, iPSA, prostate volume, NCCN risk category and treatment modality, were analyzed. In the univariate analysis of the entire cohort, a lower bRFS was identified in patients with clinical stage ≥T2b, iPSA >10 ng/ml, a biopsy Gleason score >3+4 and a high risk according to the NCCN risk category. The treatment modality, age and prostate volume had no significant effect on bRFS. Previous studies have reported that clinical stage was the most dangerous factor influencing Pca prognosis (35,36). In the multivariate analysis of the entire cohort, only clinical stage ≥T2b was associated with significantly worse bRFS, therefore, it was an important independent prognostic factor. The bRFS of patients with early Pca was significantly higher compared with patients with advanced stage Pca, suggesting that early detection and early diagnosis are key to improving the outcomes for Pca.

To evaluate the advantages of different treatment modalities for Pca despite survival rates, it is also necessary to evaluate other factors, including safety, complications and

treatment costs. The present study did not directly address complication rates; however, previous reports could be referred to (24,37,38). Although there have been notably a limited number of direct comparisons of RP with brachytherapy, multiple quality-of-life studies would suggest that even in the absence of adjuvant radiotherapy or ADT, the side effects of surgery are considerable (24,39,40). Buron *et al* (40), reported that impotence and urinary incontinence were more pronounced following RP, whereas urinary frequency, urgency and urination pain were more frequent following LDR. Mean societal costs did not differ between LDR and RP regardless of the period. The same conclusion has been reported in other previous studies (41,42). Giberti *et al* (43), reported 18% incontinence in patients who underwent surgery in a study of 174 patients completing a 5-year assessment. In addition, incontinence was sufficiently severe in these patients that 5% of them required corrective surgery compared with none of the patients receiving brachytherapy (43). Strictures were more common following surgery, observed in 6.5% of the cases compared with 2% following brachytherapy. Symptoms of irritation remained common at 1 year in the brachytherapy group (20%) compared with 5% in patients who underwent surgery, and by 5 years, there was no difference in potency of 65 and 68%, in the brachytherapy and surgery group, respectively. The latest study reported that the 10-year cumulative incidence of grade 3 genitourinary toxicity was 7.2 for LDR and 16.4% for RP, while the 10-year cumulative incidence of grade 3 gastrointestinal toxicity was 1.1 and 1.0% for LDR and RP, respectively (24).

The present study presents with a number of limitations. The baseline characteristics of the two groups did not completely match, which was inevitable due to random grouping in a retrospective study. In addition, the aim of the present study was to provide a guide to aid clinical decision-making at diagnosis. Therefore, duration of ADT following initial treatment, which may contribute to survival, was not adjusted. However, in previous studies using models adjusted for risk, ADT was not reported to be an independent predictor (13,44). The definition of PSA recurrence was different for the RP versus the LDR group. All patients with T1c-T3a Pca were included in the present study, comprising high-, intermediate- and low-risk Pca, resulting in a very heterogeneous sampling of patients. Furthermore, the follow-up period was relatively short compared with previous similar studies (1,10,22,24,29,45). In the present study, a limited number of patients died; therefore, whether higher bRFS rates observed in patients could translate into superior oncological endpoints requires further investigation. A longer observational period is required for a meaningful comparison of overall survival time. The present study also did not investigate differences in adverse events and quality of life, which are crucial clinical endpoints; however, this was not the focus of the present study.

Therefore, taking into consideration the results in this study and the aforementioned literature, it can be concluded that LDR, with or without androgen deprivation, is the optimal treatment option for patients with T1c-T3a Pca, producing equivalent bRFS and cRFS rates compared with RP. Clinical T stage ≥T2b was an independent predictor for worse bRFS. A longer follow-up may be necessary to detect a difference in biochemical outcome between these two treatments.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

ZZ, WY and HL conceived the study and its design. ZZ, YZ and FZ acquired the data. ZZ and ZJ analyzed and interpreted the data and drafted the manuscript. WY, FZ, ZJ and HL performed critical revision of the manuscript. WY supervised the study. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

All procedures performed in the present study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1975 Declaration of Helsinki and its later amendments or comparable ethical standards. The present study was approved by the Institutional Review Board of Peking Union Medical College Hospital (Beijing, China; protocol no. S-K710). Written informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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