A Preliminary Research of Cystoprostatectomy on Patients with Prostate Cancer Extending to Bladder

Xiaoliang Sun
Shandong Provincial Hospital Affiliated to Shandong First Medical University
Min Liu
Shandong Second Provincial General Hospital
Yong Zhao
Shandong Provincial Hospital Affiliated to Shandong First Medical University
Kang Leng
Shandong Provincial Hospital Affiliated to Shandong First Medical University
Haiyang Zhang (zhyhope77@163.com)
Shandong Provincial Hospital Affiliated to Shandong First Medical University https://orcid.org/0000-0003-3790-4874

Research Article

Keywords: cystoprostatectomy, prostate cancer, prostate cancer-specific survival, quality of life

Posted Date: April 11th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1531729/v1

Abstract

Background

This is an exploratory research of cystoprostatectomy (CP) in treating prostate cancer (PCa) extending to bladder, which aimed to evaluate the effects of CP on long-term survival outcomes and improving quality of life (QoL) on these patients.

Methods

A total of 27 PCa patients extending to bladder were subjected to CP and followed-up at regular intervals in our center. Prostate cancer-specific survival (PCSS) and prostate specific antigen (PSA) recurrence-free survival (PFS) were assessed by Kaplan-Meier analysis. Multivariate Cox regression was performed to evaluate clinical characteristics predicting survivals. QoL and pelvic symptoms were also evaluated.

Results

Median follow-up was 42.0 months. Five patients (18.5%) died as a direct result of tumor progression. Median PCSS was not reached over the period of follow-up. 5-year PCSS rate was 82.1%. PSA recurrence after surgery was observed in 11 patients (40.7%). Median PFS was 66.0 months. 5-year PFS rate was 58.5%. Multivariate analysis showed Gleason score (≥ 8) (hazard ratio (HR) 2.55, 95% confidence interval (CI) 1.28–4.04, $p = 0.033$), positive local lymph node status (HR 3.52, 95% CI 1.57–7.38, $p = 0.006$) and bladder muscle-invasion (HR 4.75, 95% CI 1.37–7.53, $p < 0.001$) were independent predictors of worse PCSS. The number of patients suffering pelvic symptoms was significantly decreased, and QoL scores were significantly down-regulated after surgeries.

Conclusion

CP offered effective and durable palliation in patients of locally advanced prostate cancer with invasion of bladder, providing better QoL and relieving local symptoms.

Background

When prostate cancer invades the bladder, it can be regarded as clinical T4 (cT4) stage and locally advanced prostate cancer (LAPCa) according to the latest classification system narrated in the European Association of Urology guidelines. To date, no studies have identified the most optimal treatment option in the absence of high level evidence [1]. Generally, radical prostatectomy (RP) in selected patients with no tumor fixation to the pelvic wall or no invasion of the urethral sphincter is considered as part of multimodality therapies, including androgen deprivation therapy (ADT), new hormonal treatments, radiotherapy, chemotherapy and various combinations of these treatment modalities [2]. However, for

those patients with tumor invading ureteric orifices and bladder outlet obstructions, such conservative treatments often result in a refractory state and patients may endure a lifelong dependence on ureteral stents, urethral catheters, or nephrostomy tubes [3, 4]. They have to endure multiple invasive procedures for routine tube exchange.

Scarce studies were reported on surgeries in treating LAPCa due to traditional thought that the patients with LAPCa, especially those extending to bladder would fare poorly. However, data from retrospective case series of LAPCa demonstrated over 60% cancer-specific survival (PCSS) at 15 years and over 75% overall survival (OS) at 10 years [5–7]. In addition, the substantially lower mortality in very high-risk LAPCa with exposure to RP suggested that radical treatment decreased mortality even for whom such treatment had been considered ineffective [8]. In an international multidisciplinary systematic review, when comparing RP with external beam radiotherapy, retrospective series reported benefit in OS and PCSS ranged from 10–28% and from 4–8%, respectively [1]. Therefore, RP was recommended as primary treatment in high-risk and LAPCa as part of multimodal treatment.

We hypothesize that, for highly selected PCa patients with bladder invasion in the absence of fixing to the pelvic wall, or invading the urethral sphincter or rectum, or distant metastases, cystoprostatectomy (CP) may be a reasonable treatment option. At least, this will help them to get rid of local symptoms of bladder invasion and boring procedures of tube exchange during their whole lives. In 2005, study from Leibovici et al firstly reported the effectiveness of salvage CP for cT4 PCa patients with bladder invasion, providing palliation of lower urinary tract symptoms and 31 months of median PCSS [4]. Then in 2009, Kumazawa et al also reported that CP might be a feasible treatment option to achieve excellent local control for patients with previously untreated PCa involving bladder, even in the presence of pelvic lymph node metastasis [3]. However, neither reports evaluated effects of differing presentations of cT4 PCa on survival, nor did they assess CP in improving quality of life (QoL) to patients. In the present study, the issues narrated above were investigated.

Methods

Patients

The Ethics Committee of Shandong Provincial Hospital approved the study protocol. Informed consents were obtained from all participants before any traumatic procedure. Between January 2014 and June 2020, 28 PCa patients firstly diagnosed having bladder invasion without distant organ/lymph node metastasis, tumor fixation to the pelvic wall, or invasion of rectum/pelvic wall received CP in our center.

All patients were diagnosed by preoperative transrectal needle biopsies. Bone scan, chest x-ray and pelvic magnetic resonance imaging (MRI) were used for preoperative staging. Bladder invasion was determined by MRI, cystoscopy and pathological analysis. All patients received preoperative therapies for three to six months, including neoadjuvant hormone therapy, i.e. complete androgen blockade (CAB) by using luteinizing hormone releasing hormone analogue and antiandrogen agents, and neoadjuvant

chemotherapy, i.e. docetaxel. After surgeries, all patients were treated with ADT, and part of patients received chemotherapy or external beam radiation therapy.

Surgical interventions

All operations were performed by two skilled surgeons (Dr. Yong Zhao and Dr. Haiyang Zhang) of our center. Rectal neobladder (n = 10), ileal conduit (n = 11), and ureterocutaneostomies (n = 7) were performed.

Data collection

Basic pathophysiologic features of all patients, including age, prostate specific antigen (PSA), Gleason score, results of bone scan, chest x-ray and pelvic MRI, pelvic symptoms (hematuria, obstructive voiding symptoms, pelvic pain, hydronephrosis and indwelling tubes), and QoL were recorded. After surgeries, the following parameters were recorded: Gleason score, PSA, lymph node status, seminal vesicle status, surgical margins, invasion depth of bladder wall, pelvic symptoms, complications and QoL. All patients were followed up at three monthly intervals in the first two years, then at six monthly intervals, and assessed for PSA and pelvic symptoms. PCSS and PSA recurrence-free survival (PFS) were analyzed. PSA recurrence was defined by two consecutive PSA > 0.2 ng/mL and rising [9].

Statistical analysis

Data were analyzed with SPSS 17.0 (IBM Software, USA). Continuous variables were expressed as mean ± standard error of mean and analyzed by the Student's t test. Patients were censored if they had not experienced the endpoint of interest by the last follow-up. Survival curves were estimated with the Kaplan-Meier method with log-rank test. Univariate analysis and multivariate Cox regression model were used to assess the influences of clinicopathological features of PCa and therapeutic strategies on PCSS and PFS. Chi-square test was applied to compare the occurrences of pelvic symptoms between preoperation and postoperation. Statistical significance was set at $p < 0.05$.

Results

Pathophysiologic characteristics of patients

One patient died of severe bleeding during operation, which was excluded from final analysis involving 27 cases left. Mean age of patients was 63.2 years. Mean serum PSA level was 40.2 ng/ml. Detailed pathophysiologic characteristics of patients are shown in Table 1. Follow-up time was 52.2 ± 18.3 months (median = 42.0).

Table 1
Clinical characteristics of patients

No. Patients	**27**
Age (years)	63.2 ± 7.6
Preoperative PSA	7 (25.9)
No. ≤20 ng/ml (%)	20 (74.1)
No. >20 ng/ml (%)	
Pelvic symptoms	
No. Hematuria (%)	24 (88.9)
No. Obstructive voiding symptoms (%)	22 (81.5)
No. Pelvic pain (%)	19 (70.4)
No. Hydronephrosis (%)	23 (85.2)
No. Indwelling tubes (%)	25 (92.6)
Therapeutic methods	
No. Neo CAB + Post ADT (%)	5 (18.5)
No. Neo CAB + Post ADT + Post Che (%)	10 (37.0)
No. Neo CAB + Post ADT + Post Rad (%)	9 (33.3)
No. Neo Che + Post ADT + Post Che (%)	3 (11.2)
Gleason score[a]	
No. ≤6 (%)	2 (7.4)
No. 7 (%)	10 (37.0)
No. ≥8 (%)	15 (55.6)
Local lymph node status[a]	
No. pN0 (%)	9 (33.3)
No. pN1 (%)	18 (66.7)
Seminal vesicle status[a]	
No. Negative (%)	10 (37.0)
No. Positive (%)	17 (63.0)
Surgical margins[a]	

No. Patients	27
No. Negative (%)	16 (59.3)
No. Positive (%)	11 (40.7)
Invasion depth of bladder wall[a]	
No. Non muscle-invasion (%)	11 (40.7)
No. Muscle-invasion (%)	16 (59.3)

[a] These issues were determined by postoperative pathological analyses. ADT, androgen deprivation therapy; Che, chemotherapy; PSA, prostate specific antigen; CAB, maximal androgen blockade; Neo, neoadjuvant; Post, postoperative; Rad, radiation therapy.

Survival analysis

Five patients (18.5%) died as a direct result of tumor progression. Median PCSS was not reached over the period of follow-up. PCSS at 5-year was 82.1% (Fig. 1a). PSA recurrence after surgery was observed in 11 patients (40.7%). Median PFS was 66.0 months. 5-year PFS rate was 58.5% (Fig. 1b).

To determine the potential clinical features affecting prognosis, analyses of PCSS and PFS were stratified by preoperative PSA level, by therapeutic method, by Gleason score, by local lymph node status, by seminal vesicle status, by surgical margin status and by invasion depth of bladder wall, based upon postoperative pathological results.

Univariate analysis in Table 2 showed those patients with pN0 ($p = 0.036$) and non bladder wall muscle-invasion ($p = 0.021$) had significantly higher PCSS compared with patients with pN1 and muscle-invasion, respectively. PCSS was comparable in those patients stratified by preoperative PSA level ($p = 0.504$), by therapeutic method ($p = 0.391$), by Gleason score ($p = 0.066$), by seminal vesicle status ($p = 0.406$) and by surgical margin status ($p = 0.338$). Those patients with PSA $\leq$ 20 ng/ml ($p = 0.031$), smaller Gleason score ($p = 0.015$), negative surgical margins ($p = 0.014$) and non muscle-invasion ($p = 0.038$) presented significantly prolonged PFS compared with respective subgroups. While patients stratified by therapeutic method ($p = 0.352$), by local lymph node status ($p = 0.219$) and by seminal vesicle status ($p = 0.266$) had comparable PFS, respectively.

Table 2
Univariate survival analysis in patients

	PCSS		PFS	
	Median PCSS in months (95% CI)	*P* value	Median PFS in months (95% CI)	*P* value
Preoperative PSA (ng/ml)		0.504		0.031
≤20	67.2 (55.5–72.1)		67.8 (60.7–73.2)	
>20	64.4 (58.6–71.0)		59.9 (55.3–69.6)	
Gleason score[a]		0.066		0.015
≤6	Not reached		Not reached	
7	67.8 (62.6–68.4)		63.7 (59.3–66.6)	
≥8	64.1 (57.1–65.6)		50.0 (39.4–57.8)	
Therapeutic methods		0.391		0.352
Neo CAB + Post ADT	Not reached		62.5 (57.2–70.1)	
Neo CAB + Post ADT + Post Che	71.3 (68.8–73.2)		64.3 (53.0-67.4)	
Neo CAB + Post ADT + Post Rad	66.9 (64.3–70.1)		61.7 (58.2–65.7)	
Neo Che + Post ADT + Post Che	67.9 (63.5–69.5)		65.0 (63.8–72.5)	
Local lymph node status[a]		0.036		0.219
pN0	72.2 (68.8–74.5)		68.4 (62.2–69.9)	
pN1	64.3 (61.1–67.0)		69.4 (65.7–72.6)	
Seminal vesicle status[a]		0.406		0.266
Negative	71.3 (67.7–72.7)		70.3 (66.2–72.3)	
Positive	68.6 (65.6–71.0)		69.8 (64.0-71.7)	
Surgical margins[a]		0.338		0.014
Negative	70.6 (66.7–71.9)		70.2 (65.4–72.8)	
Positive	68.8 (67.2–69.6)		59.7 (57.8–66.3)	

	PCSS		PFS	
Invasion depth of bladder wall[a]		0.021		0.038
Non muscle-invasion	68.8 (65.9–73.0)		Not reached	
Muscle-invasion	61.5 (54.2–68.1)		60.4 (55.6–67.1)	

[a] These issues were determined by postoperative pathological analyses. ADT, androgen deprivation therapy; Che, chemotherapy; CI, confidence interval; HR, hazard ratio; CAB, maximal androgen blockade; Neo, neoadjuvant; PCSS, prostate cancer-specific survival; PFS, PSA recurrence-free survival; Post, postoperative; PSA, prostate specific antigen; Rad, radiation therapy.

In multivariate Cox proportional hazards regression analysis, Gleason score (≥ 8) ($p = 0.033$), local lymph node status (pN1) ($p = 0.006$) and invasion depth of bladder wall (muscle-invasion) ($p < 0.001$) were significant predictors of worse PCSS. While Gleason score (= 7, $p = 0.029$; ≥8, $p = 0.026$), therapeutic methods (neoadjuvant chemotherapy + postoperative CAB + postoperative chemotherapy) ($p = 0.041$), local lymph node status (pN1) ($p = 0.011$) and invasion depth of bladder wall (muscle-invasion) ($p = 0.020$) were significant predictors of worse PFS. The multivariate analysis is detailed in Table 3.

Table 3
Multivariate survival analysis in patients

	PCSS		PFS	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Preoperative PSA (ng/ml)				
≤20	Reference		Reference	
>20	1.85 (0.76–3.88)	0.163	2.08 (0.88–3.05)	0.219
Gleason score[a]				
≤6	Reference		Reference	
7	1.15 (0.74–2.16)	0.061	2.28 (1.19–3.96)	0.029
≥8	2.55 (1.28–4.04)	0.033	1.96 (1.33–3.89)	0.026
Therapeutic methods				
Neo CAB + Post ADT	Reference		Reference	
Neo CAB + Post ADT + Post Che	1.57 (0.63–2.63)	0.673	0.96 (0.90–1.38)	0.363
Neo CAB + Post ADT + Post Rad	2.89 (0.55–5.01)	0.419	1.42 (0.79–1.78)	0.186
Neo Che + Post ADT + Post Che	1.80 (0.79–2.61)	0.309	1.17 (1.02–2.71)	0.041
Local lymph node status[a]				
pN0	Reference		Reference	
pN1	3.52 (1.57–7.38)	0.006	2.60 (1.47–3.38)	0.011
Seminal vesicle status[a]				
Negative	Reference		Reference	
Positive	2.16 (0.76–5.04)	0.266	0.89 (0.61–1.58)	0.068
Surgical margins[a]				
Negative	Reference		Reference	
Positive	1.26 (0.58–2.51)	0.075	2.24 (0.58–3.06)	0.421
Invasion depth of bladder wall[a]				
Non muscle-invasion	Reference		Reference	
Muscle-invasion	4.75 (1.37–7.53)	< 0.001	1.46 (1.06–3.02)	0.020

	PCSS		PFS	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value

[a] These issues were determined by postoperative pathological analyses. ADT, androgen deprivation therapy; Che, chemotherapy; CI, confidence interval; HR, hazard ratio; CAB, maximal androgen blockade; Neo, neoadjuvant; PCSS, prostate cancer-specific survival; PFS, PSA recurrence-free survival; Post, postoperative; PSA, prostate specific antigen; Rad, radiation therapy.

Effects of CP on pelvic symptoms and QoL

The numbers of patients with enduring major pelvic symptoms, including hematuria, obstructive voiding symptoms, pelvic pain, hydronephrosis and the number of patients of indwelling of tubes were significantly less after surgeries (Table 4).

Table 4
Effects of CP on occurrences of pelvic symptoms

	Preoperation	Postoperation	*P* value
No. Hematuria (%)	24 (88.9)	4 (14.8)	< 0.001
No. Obstructive voiding symptoms (%)	22 (81.5)	2 (7.4)	< 0.001
No. Pelvic pain (%)	19 (70.4)	7 (25.9)	< 0.001
No. Hydronephrosis (%)	23 (85.2)	11 (40.7)	0.018
No. Patients of indwelling tubes (%)	25 (92.6)	8 (29.6)	< 0.001

CP, cystoprostatectomy.

For QoL evaluation, CP significantly down-regulated scores, from 5.5 ± 0.4 at baseline to 2.1 ± 0.3 ($p < 0.001$), 1.8 ± 0.6 ($p < 0.001$), 1.9 ± 0.3 ($p < 0.001$), 1.9 ± 0.5 ($p < 0.001$), 2.0 ± 0.6 ($p < 0.001$), and 1.8 ± 0.3 ($p < 0.001$) at 6, 12, 24, 36, 48, 60 months after surgeries.

Complications

Postoperative complications mainly included rectal injury (n = 2, 7.4%), wound infection (n = 3, 11.1%), urinary tract infection (n = 3, 11.1%), prolonged intestinal paralysis (n = 5, 18.5%), acute pyelonephritis (n = 1, 3.7%), anastomotic stricture (n = 2, 7.4%) and enterocutaneous fistula (n = 2, 7.4%). All complications were disappeared after symptomatic and supportive treatments. No severe complications occurred after interventions.

Discussion

When performing CP for PCa involving bladder, some medical centers might claim the surgical significance or the possibility of overtreatment. However, the refractory and disappointing state after traditional therapies often reduces the patients' QoL seriously by recurrent lower urinary tract symptoms

and enduring a lifelong dependence on tubes and catheters. Improving local control and providing a better QoL to the patients are imperative clinical goals independent of the survival outcome. Up to date, CP as a treatment strategy of cT4 PCa invading into bladder, is still controversial without fully evaluation. Only limited literatures have been published [3, 4], partly because of a decreased incidence of T4 disease, but mainly due to stubborn thoughts of poor prognosis of these patients. However, data from LAPCa cohort studies showed 15-year PCSS of 60% and 10-year OS of 75% [5–7]. The oncological effectiveness of RP as part of a multi-modal treatment strategy for LAPCa remains unknown. A prospective phase III randomised controlled trial comparing RP against primary external beam radiotherapy and ADT among patients with LAPCa is currently recruiting (https://clinicaltrials.gov/ct2/show/NCT02102477). Several retrospective studies showed selected T4 patients received RP acquired better OS and PCSS than those undergoing no surgery or radiation therapy [10, 11]. In 2015, CP was performed to treat castration-resistant prostate cancer (CRPC) with infiltration of dorsal bladder by Axel Heidenreich and his colleagues [12]. Mean OS in their patient cohort was 20.4 (1–28) months and mean symptom-free survival was 15.3 (1–25) months, covering 75% of the total survival time. The authors concluded that palliative radical CP was a challenging but feasible local treatment option in well-selected bladder invasive CRPC patients, if performed by experienced hands. In our follow-up with a median period of 42.0 months, 5-year PCSS rate of patients received CP reached 82.1%, comparable with 87.1% of previous study [3]. Omar Fahmy et al. reported that 5-year PCSS rates of patients with LAPCa who were treated with RP, radiation therapy and hormone therapy were 94.2%, 95.7%, and 78.5%, respectively [13]. Probably, more advanced and higher risk of tumors in the participated patients in the present study resulted into the discrepancies. The significantly lower QoL scores after surgeries suggested that CP had a role in improving quality of life in patients with PCa extending to bladder. Moreover, our results supported a role of CP in relieving pelvic symptoms, especially in ceasing dependence on tubes, which is consistent with previous reports [3, 4].

CP itself is still a technically challenging procedure. In a previous study of salvage CP for radiation failure in PCa, one early death (12.5%) occurred from a pulmonary embolism within 60 days of surgery, accompanied by 4 (50%) of rectal injury [14]. In the present study, one immediate death occurred during surgical procedure due to severe bleeding of internal iliac artery, and only 7.4% of patients suffered postoperative rectal injury because patients with tumor invasion of rectum were excluded from the series.

Our study showed that the entered patients had frequent lymph node metastasis (66.7%). Although pN1 was a predictor of worse prognosis as shown in the present study, the median PCSS even with lymph node metastasis was 64.3 months. One of limitations in our study was lacking controlling trial of patients subjected to non-CP interventions, making it impossible to compare the effects of CP on PCa patients with conservative therapies. Jutta Engel et al [15] reported that RP was a strong independent predictor of survival in patients with node-positive PCa, improving OS by 24% versus those patients with aborted RP. There have been several retrospective observational studies showing dramatic improvements in PCSS in favour of RP versus non-RP in patients who were found to be lymph node metastasis [16]. From the results of these studies and our study, CP is also suggested to be applicable in T4 PCa patients with node-positive disease. Moreover, Fizazi K et al reported upfront usage of docetaxel only improved clinical relapse-free survival for T4 patients, with no long-term survival benefit [17]. This conclusion was further

confirmed in the present study. Multivariate analysis demonstrated that PCSS was not improved by adding neoadjuvant chemotherapy versus neoadjuvant CAB. In addition, choices of combines of postoperative adjuvant therapies did not affect PCSS.

Patients entered in this study had 55.6% of high grade tumors (Gleason score ≥ 8), which are commonly considered as potent significant risk factors of poor outcomes. Nevertheless, some retrospective case series reported good outcomes after RP for patients with high grade PCa in combination with radiation plus hormonal therapy [18, 19]. In the present study, the median PCSS with Gleason score ≥ 8 was 64.1 months. However, for the patients who received CP, Gleason score ≥ 8 was a predictor of worse PCSS and PFS.

Muscle-invasive bladder cancer is a frequently occurring disease with a high mortality rate despite optimal treatment due to common involvement of nodes and high grade urothelial carcinomas [20, 21]. For the first time in the world, we assessed CP on the prognosis of PCa regarding to invasion depth of bladder wall. For the patients received CP, median PCSS of those with bladder muscle-invasion was 61.5 months, shorter than those with non muscle-invasion (68.8 months). Multivariate analysis suggested bladder muscle-invasion was an independent predictor of poor outcomes for patients who received CP.

Several limitations should be stated before conclusion. The main limitation is the small number of entered patients because of the low incidence of T4 PCa nowadays. Nevertheless, the involved patients in the present study were still more than the previous report, 17 in Kumazawa's study [3]. Moreover, as narrated above, our study was lacking controlling trial of patients received tradition therapies due to the limited participants. Hence, comparisons of CP and conservative therapies on PCa patients were not performed. We are currently performing a multi-center randomized study with large scale cases and long-term follow-up to acquire more evidencing results.

Conclusion

Our results supported the concept that CP offered effective and durable palliation in patients of LAPCa with invasion of bladder, providing better QoL and relieving local symptoms. With the summary of the total cases, Gleason score ≥ 8, local lymph node status of N1, and muscle-invasion of bladder wall were independent predictors of worse prognosis in these patients subjected to CP.

Declarations

Acknowledgements

Not applicable.

Authors’ contributions

Conception of work: HZ. Design of work: YZ, ML. Data acquisition/analysis: XS, ML. Interpretation of data: HZ, XS, ML. Manuscript drafting/revising: KL, XS. All authors have read and approved this manuscript.

Funding

This work was supported by grant from the National Natural Science Foundation of China (82070782).

Availability of data and materials

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The Ethics Committee of Shandong Provincial Hospital approved the study protocol (NO.2020-919). All procedures performed in studies involving human participants were in accordance with the ethical standards of the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The Ethics Committee of Shandong Provincial Hospital waived the requirement for informed consent because of the retrospective design of this study.

Consent for publication

Not applicable.

Competing interests

The authors declare no conflict of interest.

Author details

[1]Department of Urology, Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan, Shandong, 250021, China. [2]Department of Oncologic Chemotherapy, Shandong Second Provincial General Hospital, Jinan, Shandong, 250022, China. [3]Knuppe Molecular Urology Laboratory, Department of Urology, School of Medicine, University of California, San Francisco, CA 94143, USA.

References

1. Moris L, Cumberbatch MG, Van den Broeck T, Gandaglia G, Fossati N, Kelly B, et al. Benefits and Risks of Primary Treatments for High-risk Localized and Locally Advanced Prostate Cancer: An International Multidisciplinary Systematic Review. Eur Urol. 2020;77(5):614–27.
2. Mottet N, Bellmunt J, Bolla M, Briers E, Cumberbatch MG, De Santis M, et al. EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. Eur Urol In press; 2016.

3. Kumazawa T, Tsuchiya N, Saito M, Inoue T, Narita S, Horikawa Y, et al. Cystoprostatectomy as a treatment of prostate cancer involving the bladder neck. Urol Int. 2009;83(2):141–5.
4. Leibovici D, Kamat AM, Pettaway CA, Pagliaro L, Rosser CJ, Logothetis C, et al. Cystoprostatectomy for effective palliation of symptomatic bladder invasion by prostate cancer. J Urol. 2005;174(6):2186–90.
5. Hsiao W, Moses KA, Goodman M, Jani AB, Rossi PJ, Master VA. Stage IV prostate cancer: survival differences in clinical T4, nodal and metastatic disease. J Urol. 2010;184(2):512–8.
6. Muralidhar V, Mahal BA, Nguyen PL. Conditional cancer-specific mortality in T4, N1, or M1 prostate cancer: implications for long-term prognosis. Radiat Oncol. 2015;10:155.
7. Chang K, Qin XJ, Zhang HL, Dai B, Zhu Y, Shi GH, et al. Comparison of two adjuvant hormone therapy regimens in patients with high-risk localized prostate cancer after radical prostatectomy: primary results of study CU1005. Asian J Androl. 2016;18(3):452–5.
8. Stattin P, Sandin F, Thomsen FB, Garmo H, Robinson D, Lissbrant IF, et al. Association of Radical Local Treatment with Mortality in Men with Very High-risk Prostate Cancer: A Semiecologic, Nationwide, Population-based Study. Eur Urol. 2017;72(1):125–34.
9. Moul JW. Prostate specific antigen only progression of prostate cancer. J Urol. 2000;163(6):1632–42.
10. Culp SH, Schellhammer PF, Williams MB. Might men diagnosed with metastatic prostate cancer benefit from definitive treatment of the primary tumor? A SEER-based study. Eur Urol. 2014;65(6):1058–66.
11. Moltzahn F, Karnes J, Gontero P, Kneitz B, Tombal B, Bader P, et al. Predicting prostate cancer-specific outcome after radical prostatectomy among men with very high-risk cT3b/4 PCa: a multi-institutional outcome study of 266 patients. Prostate Cancer Prostatic Dis. 2015;18(1):31–7.
12. Heidenreich A, Porres D, Pfister D. The Role of Palliative Surgery in Castration-Resistant Prostate Cancer. Oncol Res Treat. 2015;38(12):670–7.
13. Fahmy O, Khairul-Asri MG, Hadi S, Gakis G, Stenzl A. The Role of Radical Prostatectomy and Radiotherapy in Treatment of Locally Advanced Prostate Cancer: A Systematic Review and Meta-Analysis. Urol Int in press; 2017.
14. Pontes JE, Montie J, Klein E, Huben R. Salvage surgery for radiation failure in prostate cancer. Cancer. 1993;71(3 Suppl):976–80.
15. Engel J, Bastian PJ, Baur H, Beer V, Chaussy C, Gschwend JE, et al. Survival benefit of radical prostatectomy in lymph node-positive patients with prostate cancer. Eur Urol. 2010;57(5):754–61.
16. Steuber T, Budaus L, Walz J, Zorn KC, Schlomm T, Chun F, et al. Radical prostatectomy improves progression-free and cancer-specific survival in men with lymph node positive prostate cancer in the prostate-specific antigen era: a confirmatory study. BJU Int. 2011;107(11):1755–61.
17. Fizazi K, Faivre L, Lesaunier F, Delva R, Gravis G, Rolland F, et al. Androgen deprivation therapy plus docetaxel and estramustine versus androgen deprivation therapy alone for high-risk localised

prostate cancer (GETUG 12): a phase 3 randomised controlled trial. Lancet Oncol. 2015;16(7):787–94.

18. Bastian PJ, Gonzalgo ML, Aronson WJ, Terris MK, Kane CJ, Amling CL, et al. Clinical and pathologic outcome after radical prostatectomy for prostate cancer patients with a preoperative Gleason sum of 8 to 10. Cancer. 2006;107(6):1265–72.
19. Yossepowitch O, Eggener SE, Serio AM, Carver BS, Bianco FJ Jr, Scardino PT, et al. Secondary therapy, metastatic progression, and cancer-specific mortality in men with clinically high-risk prostate cancer treated with radical prostatectomy. Eur Urol. 2008;53(5):950–9.
20. Davies JD, Simons CM, Ruhotina N, Barocas DA, Clark PE, Morgan TM. Anatomic basis for lymph node counts as measure of lymph node dissection extent: a cadaveric study. Urology. 2013;81(2):358–63.
21. Alfred Witjes J, Lebret T, Comperat EM, Cowan NC, De Santis M, Bruins HM, et al. Updated 2016 EAU Guidelines on Muscle-invasive and Metastatic Bladder Cancer. Eur Urol. 2017;71(3):462–75.

Figures

Figure 1

Survival analyses assessed by Kaplan-Meier analysis. (**a**) Median PCSS was not reached over the period of follow-up. PCSS at 5-year was 82.1%. (**b**) Median PFS was 66.0 months. 5-year PFS rate was 58.5%.