# Overall Survival and Functional Results of Prostate-Sparing Cystectomy

## A Matched Case-Control Study

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**Purpose:** To compare two matched groups of men with bladder transitional cell carcinoma (TCC) who underwent prostate-sparing cystectomy (PSC) or conventional radical cystoprostatectomy (CRC).

**Materials and Methods:** Twenty-three men who have undergone PSC with the diagnosis of bladder TCC (Ta–T2) from 2003 to 2008 in Tehran, Iran were included in the study as the experimental group. The control group composed of 27 men with comparable tumor characteristics and age range, who had non-nerve-sparing radical cystoprostatectomy and orthotopic ileal W pouch reconstruction in the same center. All the procedures were performed by the same surgical group under the supervision of different attending staff.

**Results:** Mean follow-up period was 39 months in PSC and 35 months in CRC group. The 5-year overall survival was 47% and 30% in PSC and CRC groups, respectively. Median survival was 48 months in PSC and 36 months in CRC group, using Kaplan-Meier survival analysis ($P > .05$). Impotence was observed in 16.6% in PSC and in 83.3% in CRC group ($P = .002$). Mean International Index of Erectile Function-5 score of the PSC group was 19.8 compared with 5.7 in the CRC group ($P = .003$). Only one patient in each group was completely incontinent. Urethral anastomosis stricture occurred in 2 patients in CRC group.

**Conclusion:** Patients who underwent PSC did not show decreased overall survival compared to CRC, which provided better functional results.

**Keywords:** urinary bladder neoplasms, transitional cell carcinoma, cystectomy, male, prognosis, adverse effects

## INTRODUCTION

Formerly, radical cystoprostatectomy and urethrectomy were proposed for all men with bladder transitional cell carcinoma (TCC) indicated for cystectomy.[1,2] But to achieve better functional results with acceptable tumor control, conventional radical cystoprostatectomy (CRC) and orthotopic reconstruction are usually performed for invasive bladder cancer. However, this radical surgery potentially carries important inherent functional consequences that affect quality of life, especially in younger patients.

The concern about loss of sexual function is one of the main causes of delay in definitive surgery in men diagnosed with muscle-invasive bladder tumor; the delay imposes an increased mortality rate.[3] This encourages some surgeons perform prostate-sparing cystectomy (PSC), which has better sexual function results.[4-6] In 1990s, Schilling and Friesen described transprostatic cystectomy to preserve the neurovascular bundles and external sphincter and improve the potency results.[4] Although there is serious concern about the recurrence of TCC in the prostate,[6-8] some factors have been proposed which can help determine patients at high risk for the prostate involvement with TCC.[9] On the other hand, the incidence of incidental prostate adenocarcinoma has been shown to be low in a group of selected Iranian men who underwent CRC for the bladder TCC.[10] This study aimed to compare two matched groups of Iranian men with bladder TCC who underwent CRC or PSC, in terms of functional and tumor control results with especial focus on survival.

## MATERIALS AND METHODS

Indication for radical cystectomy was a history of muscle-invasive, recurrent, or unresectable bladder TCC. All the patients had pre-operative cystoscopy and bimanual examination. Patients with TCC involvement of the prostatic urethra or bladder neck on the pre-operative cystoscopy or any evidence of the carcinoma in situ (CIS) were excluded from the study.

Serum level of prostate-specific antigen (PSA) and digital rectal examination were normal in all the patients. Regarding the low incidence of incidental prostate adenocarcinoma in Iran,[10] pre-operative prostate biopsy was not performed in this study. On pre-operative imaging studies, including abdominopelvic spiral computed tomography (CT) scan with intravenous and oral contrast, all the patients had organ-confined bladder tumor (unresectable or recurrent Ta/T1, or T2). Data of pre-operative renal function and kidney ultrasonic examination were also collected.

Cystectomy was done through a lower midline incision or laparoscopically. Prostate adenoma was enucleated in continuity with the bladder specimen while urethral catheter was in place to prevent urine spillage. Intra-operative frozen section of distal surgical margin was negative in all the patients. In the intra-operative observations, no lymphadenopathy was detected. An orthotopic ileal W neobladder was reconstructed for all the patients. Pathological results of surgical specimens were collected.

Patients were followed up with abdominopelvic CT scan, chest radiography, liver function tests, and serum level of PSA. If there was a higher serum level of alkaline phosphatase or calcium, radionuclide whole body bone scan was performed. None of the patients underwent pre-operative radiotherapy or neoadjuvant chemotherapy, but adjuvant chemotherapy was given to patients with pathological stage of T3 or T4 in the final pathology report.

All the patients were questioned about their continence and sexual function status by a physician at least six months after the operation. Potency status was evaluated before and after the surgical procedure using a simple presented scale and also International Index of Erectile Function-5 (IIEF-5) questionnaire. Patients who used any pad during the day were marked as incontinent.

**Statistical Analysis**

All the data were analyzed by SPSS software (the Statistical Package for the Social Sciences, Version 16.0, SPSS Inc, Chicago, Illinois, USA). Data were presented as mean ± standard deviation (SD) or percentage. The significance of differences between two groups was analyzed using Chi-Square test for categorical variables and independent sample *t* test for numerical variables. Differences were considered significant if *P* value was less than .05. Kaplan-Meier estimate of survival was used for survival analysis.

## RESULTS

A total of 50 patients, 23 in PSC group and 27 in CRC group,

**Table 1.** Pre-operative characteristics of patients in two groups.[*§]

| Variable | Radical cystoprostatectomy | Prostate-sparing cystectomy | *P* |
|---|---|---|---|
| **Age, y** | 61 ± 12.0 | 59 ± 14.0 | .59 |
| **Serum creatinine, mg/dL** | 1.2 ± 0.4 | 1 ± 0.3 | .25 |
| **Hydronephrosis, n (%)** | | | |
| No | 11 (47.8) | 11 (64.7) | |
| Yes | 12 (52.5) | 6 (35.3) | .28 |
| **TURP stage, n (%)** | | | |
| Recurrent Ta | 1 (4.5) | 0 (0.0) | |
| Recurrent T1 | 4 (18.2) | 2 (10.5) | |
| T2 | 16 (72.5) | 13 (68.4) | |
| Unresectable[£] | 1 (4.5) | 4 (21.1) | .31 |
| **TURP grade, n (%)** | | | |
| I | 4 (20) | 1 (7.7) | |
| II | 5 (25) | 3 (23.1) | |
| III | 11 (55) | 9 (69.2) | .58 |

[*]Data are presented as mean ± standard deviation or count (column percent). Percents were calculated excluding missing data.

[§]TURP indicates transurethral resection of the prostate.

[£]Tumor was not resectable via TURP, thus the real stage could not be evaluated.

were included in the analysis. There was no significant difference between two groups in terms of age, pre-operative serum level of creatinine, presence of hydronephrosis, or tumor stage and grade on transurethral resection of the prostate (TURP) ($P > .05$; Table 1).

Results of pathological examination of the cystectomy specimen in two groups are presented in Table 2. The pathological stage and grade were not significantly different between two groups. In the final pathology of the prostate in the CRC group, 2 cases of the adenocarcinoma with Gleason score of 6 and 3 were detected. While in the PSC group, one patient with adenocarcinoma with Gleason score of 5 was detected in the enucleated prostate adenoma. They underwent watchful waiting and experienced no recurrence at the end of the study. Only one patient in CRC group showed prostate stromal involvement with TCC, who was a 65-year-old man with history of a high-grade bladder tumor and pre-operative bilateral hydronephrosis. He was alive at 4-year follow-up with a local recurrence. There was no report of CIS in the final cystectomy specimen.

Mean follow-up period was 39 months in PSC group and 35 months in CRC group ($P = .65$). Mean follow-up for patients who were alive in the last follow-up was 53 months (range, 23 to 90 months) and 57 months (range, 17 to 110 months) in PSC and CRC groups, respectively. Mean survival time in the PSC and CRC groups was 27 months (range, 2 to 74 months) and 22 months (range, 1 to 52 months), respectively. Twenty-nine (58%) patients, including 12 (52%) patients in the PSC group and 17 (63%) in the CRC group, died during follow-up ($P = .39$). In 25 patients, the death cause was apparent; 22 deaths were caused by tumor or chemotherapy complications and 3 were due to myocardial infarction.

The overall 5-year survival was 47% and 30% in PSC and CRC groups, respectively. Median overall survival was estimated to be 48 months in PSC and 36 months in CRC group, using Kaplan-Meier survival analysis ($P > .05$; Figure). Two-year overall survival divided by stage was not significantly different between two groups (55% versus 52%; Table 3). The 5-year disease-free survival was estimated to be 35% in PSC and 13% in CRC group.

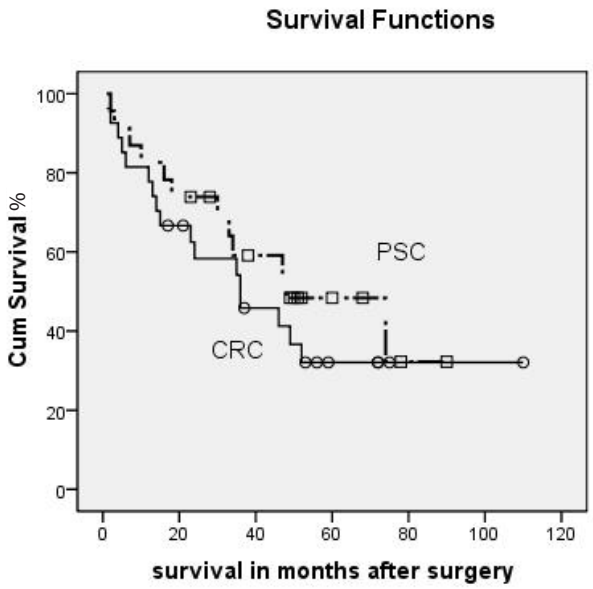
**Table 2.** Results of pathological evaluation of cystectomy specimen in two groups.[*§]

| Variable | Radical cystoprostatectomy | Prostate-sparing cystectomy | *P* |
|---|---|---|---|
| **Tumor stage,[£] n (%)** | | | |
| T0 | 0 (0.0) | 1 (4.3) | |
| T1 | 6 (22.2) | 7 (30.4) | .51 |
| T2a | 6 (22.2) | 5 (21.7) | |
| T2b | 6 (22.2) | 4 (17.4) | |
| T3a | 2 (7.4) | 4 (17.4) | |
| T3b | 5 (18.5) | 2 (8.7) | |
| T4 | 2 (7.4) | 0 (0.0) | |
| **Tumor grade, n (%)** | | | |
| I | 4 (14.8) | 1 (5.3) | |
| II | 5 (18.5) | 3 (15.8) | .54 |
| III | 18 (66.7) | 15 (78.9) | |
| **Prostate, n (%)** | | | |
| Normal | 18 (78.3) | 12 (85.7) | |
| **PI-TCC** | 1 (4.3) | 0 (0.0) | |
| Adenocarcinoma | 2 (8.7) | 1 (7.1) | .86 |
| HGPIN | 2 (8.7) | 1 (7.1) | |

[*]Percents were calculated excluding missing data.

[§] PI-TCC indicates prostate involvement with transitional cell carcinoma; and HGPIN, high-grade prostate intra-epithelial neoplasia.

[£]Tumor stage was based on TNM tumor staging system; Sobin, L. H. and I. D. Fleming:"TNM Classification of Malignant Tumors, fifth edition (1997)".




Kaplan-Meier survival rate plot by surgery type.
PSC indicates prostate-sparing cystectomy; and CRC, conventional radical cystectomy.

**Table 3.** Two-year survival data divided by final pathological stage.

| | Prostate-sparing cystectomy | | Radical cystoprostatectomy | |
|---|---|---|---|---|
| **Stage** | no. | 2-year survival | no. | 2-year survival |
| T1 | 7 | 53% | 6 | 67% |
| T2 | 9 | 71% | 12 | 55% |
| T3 | 6 | 33% | 7 | 29% |
| All patients* | 23 | 55% | 27 | 52% |

*Including one patient with stage T0 and two with T4.

The recurrence data were available for 38 patients, including 18 patients in PSC and 20 patients in CRC group. Twenty-two (57.9%) patients developed tumor recurrence at follow-up (61.1% in PSC and 55% in CRC group; $P > .05$).

Twenty-four patients, including 12 patients in each group who were completely potent and able to have intercourse pre-

**Table 4.** Functional results of available patients in two groups.

| Variable | Radical cystoprostatectomy | Prostate-sparing cystectomy | *P* |
|---|---|---|---|
| **Potency, n (%)** | | | |
| Impotent | 10/12 (83.3) | 2/12 (16.6) | .002 |
| Potent | 2/12 (16.6) | 10/12 (83.3) | |
| Erection, no penetration[a] | 2/12 (16.6) | 3/12 (25.0) | |
| Penetration, no ejaculation[b] | 0/12 (0) | 3/12 (25.0) | |
| Penetration and ejaculation[c] | 0/12 (0) | 4/12 (33.3) | |
| **Continence, n (%)** | | | |
| Totally incontinent | 1/13 (7.6) | 1/16 (6.2) | NS |
| Continent but Bed wetting[d] | 4/13 (30.7) | 2/16 (12.5) | |
| Continent with CIC[e] | 1/13 (7.6) | 5/16 (31.2) | |
| Continent, no CIC | 7/13 (53.8) | 8/16 (50.0) | |
| **Stricture[f], n (%)** | | | |
| No | 11/13 (84.6) | 16/16 (100) | NS |
| **Yes** | 2/13 (15.3) | 0/16 (0) | |

[a] There was erection, but not enough for intercourse.

[b] Strong enough erection and ability for penetration, but dry ejaculation.

[c] As b, also complete normal ejaculation.

[d] No pad and no CIC in the daytime, but only bed wetting.

[e] These patients were dependent on CIC.

[f] Patients with any evidence of local or urethral tumor recurrence were excluded.

[*] CIC indicates clean intermittent catheterization.

operatively (IIEF score >20), cooperated for potency status interview. Of twelve patients in the CRC group, 10 (83.3%) showed severe erectile dysfunction (no erection), but in the PSC group, only 2 (16.6%) patients had no erection ($P$ = .002; Table 4). Regarding the IIEF-5 questionnaire results, mean score of the PSC group was 19.8 compared with 5.7 in the CRC group ($P$ = .003).

Data regarding postoperative continence status were collected in 29 patients (16 in PSC and 13 in CRC group). As Table 4 shows, only one patient in each group was completely incontinent. Eight (50%) patients in PSC and 7 (53.8%) patients in CRC group did not need to do clean intermittent catheterization (CIC) to become continent ($P$ > .05). Bed wetting was seen more frequently in CRC group, but the difference was not significant. In contrast, dependence on CIC for the bladder emptying was less in CRC group. After excluding patients with any evidence of local or urethral tumor recurrence, only 2 (15.3%) patients in CRC group showed stricture at the urethral anastomosis ($P$ > .05).

## DISCUSSION

Kaplan-Meier analysis has not shown lower overall and disease-free survival rates for the patients who underwent PSC in comparison with the CRC group. Overall 5-year survival rate of patients after radical cystectomy reportedly is 50% to 66%.[11-14] In a research by Rozet and colleagues, this rate was 67% in 107 patients selected for PSC. They reported long-term follow-up period of the largest group of PSC patients, and compared the survival results of their cohort with the literature data on the 5-year survival after CRC. They concluded that the results were comparable and *"prostate-sparing cystectomy is an additional option for treating high-*

*ly selected patients who want to be offered curative therapy with minimal side effects."*[15]

In a recently published study, de Vries and associates evaluated the long-term survival of 63 men who underwent PSC. The 5-year disease-specific survival rate was 66% compared with 64% in the CRC group. They concluded that this procedure is safe and could be offered to selected patients.[16] In our study, the overall 5-year survival rate was 30% in the CRC group and 47% in the PSC group. The lower survival of our patients compared with the survival rate in the literature may be due to delayed diagnosis and treatment of the patients in our country. It seems while PSC results in significantly better functional recovery in selected patients, the tumor control and survival are not significantly different.

In long-term follow-up (mean of 54 months) of 108 patients after PSC by Rozet and coworkers, they found only 6 patients with prostate adenocarcinoma in their final pathology of TURP specimen, and 3 patients out of 102 during later follow-up. All of them had a Gleason score of 6 and were treated effectively by brachytherapy, high-intensity focused ultrasound, or androgen deprivation therapy. The authors concluded that concomitant prostate carcinoma does not have significant effect on survival of these patients in contrast with TCC.[15] Furthermore, the risk of prostate adenocarcinoma is significantly different in various races[17] and the amount of this risk should be regarded while considering prostate-sparing for the treatment of the bladder TCC.

de Veries and colleagues showed an incidence of 18% for incidental prostate adenocarcinoma in cystoprostatectomy specimens. They reported two patients with adenocarcinoma out of 63 patients who had undergone PSC; one died due to TCC recurrence and the other was alive at 50-month follow-up.[16] In our study, only one (4.3%) patient in the PSC group and 2 (7.4%) patients in the CRC group had prostate adenocarcinoma on final pathology. No one showed a Gleason grade of more than 3; all of them selected watchful waiting. One of them died due to the recurrence of bladder tumor and others were alive with no evidence of prostate adenocarcinoma recurrence. Furthermore, none of other patients in PSC group was suspicious for the prostate cancer during the postoperative follow-up. Our data show that in selected patients of Iranian population, prostate adenocarcinoma is not a significant factor against PSC.

It is accepted that PSC has better functional results than CRC.[5,8,15,18,19] Similarly, we observed an apparently better sexual function in patients in PSC group while continence results were not significantly different. Although nonsignificant, patients in PSC group showed lower rate of bed wetting than CRC group, while their need to CIC for the bladder emptying was a little more. Similarly, some authors have indicated that in spite of lower rate of bed wetting, overcontinence may be an imperfection for PSC.[7] We think this shortcoming is not significant compared to the major advantages of this technique. Finally, urethral anastomosis stricture occurred in 2 patients in CRC group without tumor recurrence. This complication did not take place in PSC group, which may be due to a wider anastomosis with the neobladder,

**Limitations**

Although the patients in the CRC group were matched by age, stage, and other available clinical staging findings, we are aware that it is a retrospective study and selection bias may be present. Furthermore, because some patients did not cooperate tensely in the follow-up, they died without a distinct diagnosis of the site of recurrence or functional status. However, the vast majority of missed follow-up for functional evaluation seems to be related to patients' death due to the proven fatal nature of the disease and its low 5-year overall survival. Finally, it would be better to compare functional results of patients who had undergone PSC with a group of nerve-sparing conventional cystectomy patients.

## CONCLUSION

When selected patients are included, patients who underwent PSC did not show decreased overall and disease-free survival rates compared to CRC. Tumor recurrence rate was not associated with the type of surgery. Potency results were significantly better after PSC than CRC; however, continence results were not different. A randomized clinical trial is needed to disclose the truth about the safety of this functional preserving modality.

## CONFLICT OF INTEREST

None declared.

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