

## **Chapter 7a:**

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### **Clinical Outcomes after Sexuality Preserving Cystectomy and Neobladder (Prostate-Sparing Cystectomy) in 44 Patients**

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*Journal of Urology* 2005; 174(1): 97-102  
*Journal of Urology* 2008;179(5suppl):S38-38



## Abstract

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**Purpose:** To describe the functional outcome on erectile function, continence and voiding, and local and distant cancer recurrence rates in 44 patients after sexuality preserving cystectomy and neobladder (prostate-sparing cystectomy).

**Materials and Methods:** 44 males underwent cystectomy with preservation of the prostate, seminal vesicles and vasa deferentia, after which a Studer type neobladder was anastomosed to the prostate. Oncological outcome (disease specific survival, distant and local recurrence rates) and functional results (continence, voiding, erectile function) were determined.

**Results:** At a median follow-up of 42 months, 13 (30%) patients died of cancer. All 13 experienced widespread disease, in 3 patients combined with a pelvic recurrence (pelvic recurrence rate: 6.9%). The 3-year survival according to pathological stage was 86% for pT $\leq$ 2N0, 63% pT3N0, and 39% for node positive tumours (anyT Npos). Prostate cancer was diagnosed in 1 patient 5 years after treatment, and recurrent carcinoma in situ in the prostatic urethra in another patient. Complete day- and nighttimes continence was achieved in 95.3% and 74.4% respectively. Incontinence during day and night could be managed by one pad per day/night in 4.7% and 20.9% respectively, while 4.7% needed more than 1 pad per night.

Erectile function could be determined in 40 patients; potency was maintained in 77.5%, impaired in 12.5%, and absent in 10%.

**Conclusions:** functional results with regard to erectile function and urinary continence after prostate-sparing cystectomy are good. Oncological results until now are promising, but need to be confirmed after longer follow-up, and in larger trials.

## Introduction

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Standard radical cystectomy for bladder cancer consists of removal of the bladder, prostate, seminal vesicles and vasa deferentia in males. In this procedure the autonomic nerves, which are essential for a normal sexual response are often removed or damaged. Walsh described the anatomy of the pelvic innervation and showed how the neurovascular bundles containing cavernous nerves could be preserved during prostatectomy<sup>1,2</sup>. In analogy the nerve sparing cystoprostatectomy was developed<sup>3-5</sup>, after which various modified cystectomy-techniques followed. Spitz described a cystectomy with partial prostatectomy while preserving vasa deferentia, seminal vesicles and posterior prostate<sup>6</sup>, Muto combined cystectomy with an adenoma enucleation according to Millin<sup>7</sup>, and Colombo and Vallancien described extirpation of the bladder preceded by transurethral resection (TUR) of prostatic tissue and prostatic urothelium with preservation of the prostatic capsule<sup>8,9</sup>. At our institute the bladder neck, prostate, and prostatic urethra are sampled extensively before prostate-sparing cystectomy, but no effort is done to remove all prostatic urothelium<sup>10</sup>. Besides improved sexual function, both nerve sparing cystoprostatectomy and prostate-sparing cystectomy are associated with enhanced urinary continence after orthotopic bladder substitution<sup>2,4,7-10</sup>. At our institute the prostate-sparing cystectomy was introduced in 1994 as sexuality preserving cystectomy and neobladder (SPCN). The indications, technical aspects and early oncological results have been published before on 10 males<sup>10</sup>. The aim of this study was to determine the long term functional and oncological results, and untoward sequelae of this procedure in 44 successive males, with a median follow-up that has now surpassed 40 months.

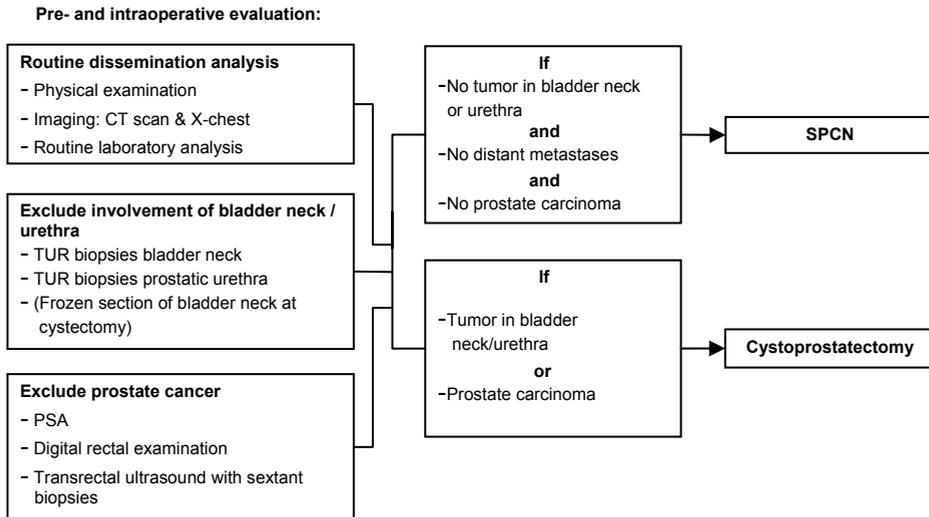
## Patients and methods

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Between 1994 and 2003 a sexuality preserving cystectomy and neobladder (prostate-sparing cystectomy) was performed in 44 men (out of a total of 189 male cystectomy patients). The operation technique and indications are described in our previous paper<sup>10</sup>. In summary, inclusion criteria are stage T1-3 bladder cancer not amenable to bladder preserving strategies, and patient motivation for preserving sexual function. Also patients with a non-functional bladder could be included. Excluded are tumours growing into the bladder neck or prostatic urethra (sampled by transurethral biopsies), and patients with prostate carcinoma (sampled by prostate specific antigen measurement, rectal ultrasound and sextant prostate biopsies). The diagnostic work up is summarized in figure 1.

A pelvic lymph node dissection (lymph nodes between ureter crossing of the vessels, genitofemoral nerve, bladder wall, lateral pelvic wall, and obturator nerve) is done and a cystectomy is performed, while the seminal vesicles, the vasa deferentes and the prostate are left in situ. A Studer type neobladder is anastomosed to the outer rim of the prostate. On indication, the margin (bladder neck) of the resected specimen was examined by frozen section to exclude tumour involvement during cystectomy.

**Figure 1:** Algorithm of inclusion/exclusion and diagnostic work up



All tumours were staged before cystectomy according to the UICC classification rules 2002, pathological-stage (pT) was assigned according to highest stage after diagnostic TUR or cystectomy<sup>11</sup>. Patients with positive lymph nodes were treated with adjuvant or neoadjuvant MVAC according to EORTC trials open at time of diagnosis. Oncological follow-up consisted of regular physical examination, endoscopic evaluation, urine cytology, PSA evaluation, chest X-ray and CT scan of the pelvis and abdomen. Pelvic (or local) recurrences were defined as any bladder cancer recurrence below the iliac bifurcation within the pelvic soft tissue.

Voiding function and continence were evaluated by interviews on continence and pad use, the international prostate symptom score (I-PPS), and post void residual measurements by ultra sound or transurethral catheterization. Indications for clean intermittent catheterization were residual volume of at least 150 cc if this was accompanied with infection or frequency or incontinence, otherwise residual urine up to 250 cc was accepted. Complete continence was defined as no urinary loss, satisfactory day/night continence as incontinence requiring one pad or less per day/night, poor continence as requiring more than one pad per day/night.

Sexual function was evaluated by interviews on erection and ejaculatory function, and the international index of erectile function (IIEF) questionnaire. All patients with adequate nightly erections and/or erections adequate for intercourse after cystectomy were considered to have maintained erectile function. Since the aim was to evaluate whether the prostate-sparing cystectomy could spare potency, the best post cystectomy erectile function in time was considered end value.

Kaplan-Meier survival estimates were used in survival data analysis and follow up.

## Results

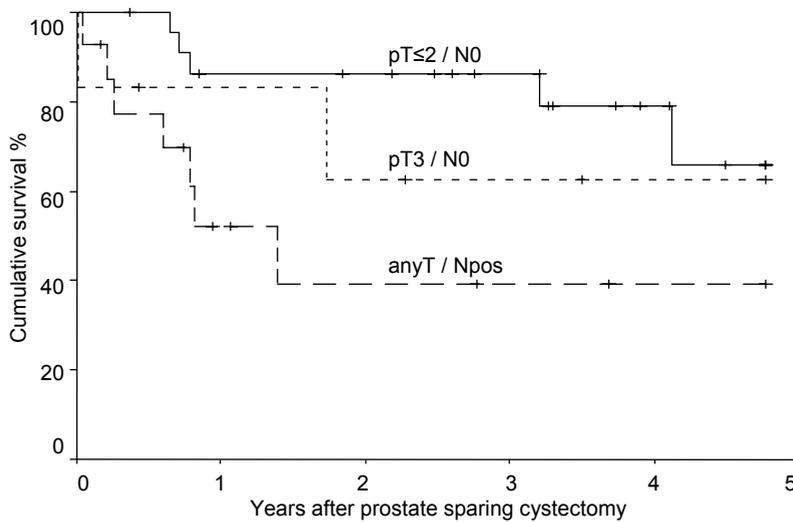
One patient underwent cystectomy because of a dysfunctional bladder. This patient was excluded from evaluation of survival and recurrence rates. Table 1 lists the relevant patient's characteristics. Ten patients were treated with neoadjuvant methotrexate, vinblastine, doxorubicin and cisplatin (MVAC); 9 because of tumour positive lymph nodes (identified by lymph node dissection or aspiration-cytology after CT-scan) and 1 to improve resectability of the primary (cT3) tumour. All patients underwent subsequent cystectomy, after a complete (n=9) or partial (n=1; residual cT1 bladder tumour) clinical response. Two patients were treated with adjuvant MVAC for positive lymph nodes found at histopathology of the resected specimen. At a median follow-up of 42 months (range 3 – 104 months) 13 patients have died because of widespread disease, of whom 3 with a local recurrence (local recurrence rate: 6.9%). Two patients died of non-cancer related causes. The median time from surgery until disease related death was 11 months (range 3 – 52 months). Pelvic recurrences were found in patients with tumour stage pT1N0, pT3N1, and pT2N1 after 20, 5 and 7 months respectively. None of these recurrences involved the remnant bladder neck or prostate. One patient however developed recurrent carcinoma in situ (CIS) in the prostatic urethra after a follow-up of 41 months. Prostate cancer was experienced 5 years after bladder removal by another patient. The 3-year disease specific survival rate according to pT was 86% for organ confined, node negative tumours (pT≤2N0), 63% for non-organ confined, node negative tumours (pT3N0), and 39% for node positive tumours (anyT Npos) (figure 2).

**Table 1:** patient characteristics

Patient characteristics		No.	(%)
Mean age (±SD) in year (±9)		57	
<b>Clinical stage</b>			
T0	(glandular cystitis)	1	
T Ca in situ	N0	1	
TaT1	N0	11	
T2	N0	18	
T3	N0	4	
anyT	Npos	9	
<b>Pathological stage*</b>			
T0	(glandular cystitis)	1	
T Ca in situ	N0	1	
TaT1	N0	10	
T2	N0	12	
T3	N0	6	
anyT	Npos	14	
<b>Carcinoma in situ</b>			
Yes		9	
No		35	
<b>Pathological grade</b>			
G0	(glandular cystitis)	1	
G2		6	
G3		37	
<b>Daytime continence (%)</b>			
Unknown**	(early death)	1	-
Complete	(no pads)	41	(95.3)
Satisfactory	(1 pad/day)	2	(4.7)
Poor	(>1 pad/day)	0	
<b>Nighttime continence (%)</b>			
Unknown**	(early death)	1	-
Complete	(no pads)	32	(74.4)
Satisfactory	(1 pad/day)	9	(20.9)
Poor	(>1 pad/day)	2	(14.7)
<b>Need to catheterise</b>			
Unknown** (early death)		1	-
No		31	(72.1)
For post-void residual urine		9	(20.9)
No spontaneous voiding		3	(7.0)
<b>Erectile function</b>			
Unknown**		4	-
Complete		31	(77.5)
Impaired		5	(12.5)
Impotent		4	(10.0)

\* pT is assigned according to highest stage after TUR or cystectomy.

\*\* Patients with unknown functional results were not included in calculation of percentages.

**Figure 2:** Disease specific survival according to pathological tumour stage

Functional results on continence and voiding function could be determined in all but one patient. This patient experienced rapid brain metastasis and death, so 43 patients remain. In 3 patients preoperative urodynamics showed obvious obstruction, and an additional Freyer type adenoma enucleation was performed during cystectomy. Complete daytime continence was achieved in 41 / 43 patients (95.3%), satisfactory daytime continence in the other two patients (4.7%). Complete continence at night was realized in 32 / 43 (74.4%) patients, while 9 (20.9%) patients attained satisfactory nighttime's continence. Urinary loss was not abundant and managed by one single pad per night in these patients, and with a nighttime's voiding regimen the frequency of incontinence improved in most of them. Two patients (4.7%) had poor nighttime's continence, and required two or more pads per night. Nightly voiding occurred once in 9 patients, and 2 to 4 times in 14 patients. Post-void residual volume was insignificant in 31 patients (72.1%), 9 patients started clean intermittent catheterization for post-void residual urine, and 3 patients had no spontaneous voiding at all and were completely CIC dependent. Three patients experienced a period of poor emptying of the neobladder combined with obvious bladder outlet obstruction. Two of them could completely stop CIC after transurethral resection of prostatic tissue, one still needs to catheterize once per day because of post-void residual urine. In two patients a period of poor bladder emptying was successfully treated with antibiotics for a urinary tract infection.

Erectile function could be determined in 40 out of 44 patients. Four patients experienced recurrent disease before resuming sexual activity. Potency was maintained in 31 / 40 patients (77.5%), of whom 4 used sildenafil with success, suggesting that the nervi erigentes were preserved during cystectomy. One patient used intracavernous injections (ICI) effectively during the first year after

treatment, but has adequate erections without ICI now. Four patients are impotent (10.0%), and 5 (12.5%) reported impaired erectile function after cystectomy. Information on ejaculation was available in 32 patients. In total 11 patients reported antegrade ejaculation, two reported antegrade and retrograde ejaculation different in time, and 19 have retrograde ejaculation.

### Discussion

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Injury of the autonomic innervation of the corpora cavernosa at deep pelvic resection has been demonstrated to result often in sexual dysfunction<sup>1,2</sup>. In order to preserve erectile function and improve continence and bladder emptying, different modifications of cystectomy have been proposed, either as nerve sparing radical cystoprostatectomy<sup>3-5,12</sup> or as cystectomy with preservation of (part of) the prostate<sup>6-10</sup>. Cystectomy with prostate preservation comprises the risk of developing prostate cancer and transitional cell cancer or carcinoma in situ in the remnant prostatic urethra. Furthermore the concern has been expressed that prostate-sparing cystectomy increases the risk of subsequent pelvic recurrence.

In literature incidental prostate carcinoma is found in up to 40% of the cystoprostatectomy specimens, with the minority being considered as clinically significant<sup>13,14</sup>. These percentages do apply to unselected patients, while in prostate-sparing studies maximal efforts are made to exclude associated prostate cancer. Besides pre-operative diagnostics, the margin of the resected specimen (bladder neck) at cystectomy was examined by frozen section on indication to exclude prostatic and transitional cell cancer in our procedure. In addition, a strict follow-up with digital examination and PSA measurements leads to early de novo prostate cancer detection and treatment. Patients with tumour growth in/near the bladder neck were excluded, and pre-operative transurethral samples were taken to minimize the risk of urethral/prostatic transitional cell recurrence. This is different from Vallancien et al, who removes all prostatic urothelium by TUR prior to cystectomy<sup>9</sup>. However, the reliability of sampling has been established before<sup>15</sup>, and per-operative frozen section of the urethra is considered a good predictive factor for late urethral recurrences<sup>15-17</sup>. CIS in the bladder (without presence of CIS in the bladder neck or urethra) is not considered a contraindication for the procedure, as CIS of the bladder not involving the bladder neck is not associated with urethral recurrent cancer<sup>17</sup>. Despite this, urethral CIS recurred in the prostatic urethra in one patient with previous CIS located in the bladder. This patient was treated with trans-urethral resection and additional bacillus Calmette-Guerin instillations.

The average rate of pelvic recurrences after standard radical cystoprostatectomy is 10%, but this figure increases with higher pathologic stages of bladder cancer<sup>18</sup>. In nerve sparing radical cystoprostatectomy follow-up is now long enough to be conclusive about pelvic recurrence, and the procedure appears not to compromise local cancer control<sup>3,12</sup>. In our series, pelvic recurrence rate is low with 6.9% after a median follow-up of 42 months. However, of the surviving patients 7 have a follow-up of less than two years, which is the period in which local recurrences show up<sup>18</sup>. Muto et al, Colombo et al (most

patients), and Spitz et al reported on prostate-sparing cystectomy in patients with high risk superficial bladder cancer or without urothelial malignancies<sup>6-8</sup>. In this series however invasive and node positive patients were also included (after treatment with systemic chemotherapy), analogous to the study described by Vallancien et al<sup>9</sup>. With pelvic recurrence rates of 5% (Vallancien) and 6.9% (our series) the procedure provides good local control to date. With a median follow-up exceeding three years in both studies the critical period for cancer recurrence is surpassed in the majority of patients, but longer follow-up is still needed.

Functional results of prostate-sparing techniques have been excellent until now. Day- and nighttimes time continence rates vary from 95% to 100%, and 31% to 100% respectively, while erectile function is preserved in 82% to 100% of the patients operated upon<sup>6-9</sup>. Our results are in accordance with the results previously reported, although erectile function is slightly worse. Two patients however were complete impotent after the use of systemic chemotherapy. Additionally, age plays an important role in the recovery of potency<sup>3</sup>, and possibly attributes to the difference with the excellent results of Colombo et al (100% potency). Their series included younger patients. Still, the presented percentages after prostate-sparing cystectomy are better than after nerve sparing cystoprostatectomy; they vary between 42% and 64%<sup>3,5,12</sup>. The need to catheterize was high with 28% in our series, compared to 0 –2% in other studies after prostate-sparing cystectomy<sup>7-9</sup>. Meinhardt et al reported that, according to urodynamics, the remaining prostate does not interfere with micturation in the majority of patients<sup>19</sup>. Also no strictures of the anastomosis were seen at cystoscopy. CIC rates improved in three patients after TUR of benign prostatic hyperplasia, but in the majority no obvious cause could be determined.

Although the presented study consists of a limited number of patients and has a moderate follow-up, our experience may indicate that this type of surgery is safe and satisfactory in terms of function and local cancer control, provided that patient selection is based on meticulous pre-operative diagnostics. To date, we have no oncological arguments to exclude muscle invasive bladder cancer patients from this procedure, although follow-up and patient numbers are not yet sufficient to draw firm conclusions.

## **Conclusions**

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Functional results with regard to erectile function and urinary continence after SPCN / prostate-sparing cystectomy are good. Oncological results until now are promising, but need to be confirmed after longer follow-up, and in larger trials.

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