



Prostatic Capsule- and Nerve-sparing Cystectomy in Organ-confined Bladder Cancer: Preliminary Results

Gianni Martis, M.D., Gianluca D'Elia, M.D., Massimo Diana, M.D., Maurizio Ombres, M.D., Bruno Mastrangeli, M.D.

Department of Urology, S. Camillo Hospital, Viale Kennedy, 02100, Rieti, Italy

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Abstract. We present a novel radical cystectomy technique that allows bladder cancer control while maintaining urinary continence and reducing the risk of erectile dysfunction by sparing the prostatic capsule and the neurovascular bundles. Between September 1997 and December 2002, 85 men were candidates for cystectomy; 32 were selected for a prostatic capsule- and seminal-sparing cystectomy with orthotopic urinary diversion. All patients had clinical organ-confined bladder cancer (cT1 to cT3a). One patient died of unrelated causes. Of the remaining 31 patients, two with pT4, N+ disease underwent three cycles of adjuvant chemotherapy and are free of disease at 10 and 12 months postoperatively. Twenty-nine patients with organ-confined bladder cancer are free of disease after a mean follow-up of 32 months. At 24 months, 98% of the patients are completely continent during the day and 83% during the nighttime hours. In addition, 80% of the patients are able to complete sexual intercourse without auxiliary measures at a mean of 24 months postoperatively. Prostatic capsule- and nerve-sparing cystectomy permits en bloc removal of the bladder, of the adenomatous prostatic tissue, and of the seminal vesicles, thereby achieving local cancer control and preserving erectile function and urinary continence.

Introduction

Radical cystectomy represents the gold standard of treatment for infiltrating and high-grade, organ-confined, multifocal bladder cancer refractory to endovesical immunotherapy [1]. Radical cystectomy is a destructive operation, however, with inherent risks of incontinence and erectile dysfunction. Such a result has a huge impact on quality of life, especially for young patients. Studies performed on the neuroanatomy of the hypogastric nerve and on the location of the pelvic plexus have demonstrated that nerve-sparing cystectomy, while preserving erectile function, does not increase the risk of local relapse. Nor doesn't decrease tumor-related survival when compared to standard radical cystectomy [2, 3].

In addition, the maintainance of urinary continence is mandatory for the patient's quality of life. This could ideally be accomplished by sparing the prostatic capsule, such as in Millin's prostatic adenomectomy [4].

We present a surgical technique that allows bladder cancer control while maintaining urinary continence and reducing the risk of erectile dysfunction by sparing the prostatic capsule and the neurovascular bundles.

Materials and Methods

Between January 1997 and December 2002, 85 men with bladder tumor were candidates for cystectomy in our urology division. All patients were preoperatively assessed by voiding diary, International Prostatic Symptom Score (IPSS) [5, 6] and International Index of Erectile Function (IIEF-15) [7–9], as well as total and free prostate specific antigen (PSA). Patients were preoperatively staged by TUR-B with biopsies of the prostatic urethra, computed tomography (CT) of the abdomen, and pelvic and intravenous pyelography.

The selection criteria for a nerve- and prostatic capsule-sparing cystectomy with orthotopic ileal urinary diversion were a normal digital rectal examination with a PSA level < 4 ng/ml or PSA in the range 4–10 ng/ml, with a PSA ratio > 15%.

Transrectal sextant biopsies of the prostate were performed when digital rectal examination was suspicious for cancer and/or the PSA was > 10 ng/ml or PSA ratio < 15% in the PSA range 4–10 ng/ml. We considered only clinically organ-confined bladder cancer (cT1 to cT3a), without involvement of the trigone and/or prostatic urethra.

Preoperative clinical staging showed 9 patients with T1, 14 with T2, and 9 with T3a bladder cancer. The World Health Organization (WHO) grade was G2 in 17 cases and in G3 15. All 9 patients with T1 bladder cancer were G3, multifocal, and they relapsed after endovesical immunotherapy.

We excluded Candidates with an IIEF-15 score indicative of erectile dysfunction.

Applying these criteria, we did not include in our study 18 candidates with sextant transrectal biopsies positive for prostate cancer, 11 with PSA > 10 ng/ml, and 7 with a PSA ratio < 15% in the PSA range 4–10 ng/ml.

Twenty five patients had bladder cancer that was not clinically organ confined, 9 had tumors involving the trigone; and 6, the prostatic urethra. We excluded 9 patients with preoperatively IIEF-15 scores positive for erectile dysfunction. All patients se-

lected were continent before surgery. We performed a nerve- and prostatic capsule-sparing cystectomy on the 32 remaining patients. The mean age of these men was 59 years (range: 52–72 years). The average follow-up was 32 months (range: 6–60 months). Erectile function was evaluated postoperatively through the IIEF-15 score and, on a subjective basis, through a patient's ability to autonomously reach a valid erection capable of completing sexual intercourse in a satisfying way. Continence was evaluated after catheter removal at 6, 12, and 24 months through voiding diary, IPSS score, and a 1-hour pad test [5, 10], and was defined as the absence of urine leakage and no need for use of pads.

Surgical Technique

We perform an ascending cystectomy with preservation of the prostatic capsule and of the neurovascular bundles. As in Millin's retropubic adenomectomy, we leave about 2.5 cm of prostatic capsule and remove the adenomatous prostatic tissue within (Fig. 1A and 1B). In this way the dissection doesn't affect either the pubo-prostatic ligaments or the dorsal venous complex. The latter is not preventively ligated or dissected, and hemostasis is achieved by placing a running suture on the dissection edge of the prostatic capsule. Oncologic radicality is assured by removing the bladder, the seminal vesicles, the prostatic urethra, and the surrounding adenomatous prostatic tissue.

We create a modified Studer's ileal neobladder with two horns for ureteral anastomosis (Fig. 2). The left ureter is not passed through the mesentery and the left lateral horn of the neobladder is placed extraperitoneally. The neobladder-prostatic capsule anastomosis is done with hemi-running sutures of the posterior wall of the lateral edges, and of the anterior wall.

Results

We did not discover any incidental prostatic tumor in this series of patients, and there was no intraoperative mortality. Mean operative time was 200 minutes (range: 180–280 minutes). Mean blood loss was 250 cc (range: 90–700cc). The catheter was removed on average on the eighteenth postoperative day (range: 14–27 days). Mean hospital stay was 18 days (range: 16–28 days). Procedure-related complications were three uretero-neobladder stenoses treated with endourological balloon dilation, one dehiscence of the ileo-ileal anastomosis treated conservatively, and four urinary fistulas treated with prolonged catheterization.

Histopathological examination showed 4 pT1, N0 (13%), 11 pT2, N0 (35%), 14 pT3a, N0 (43%), 1 pT3b, N0 (3%), and 2 pT4, N+ (6%). The WHO grade was G2 in 13 patients (34%) and G3 in 19 (66%). The urethral margin was negative in all cases.

One patient with pT3b cancer died 2 months after surgery after a cerebrovascular accident.

Two patients with pT4, N+ underwent three cycles of adjuvant M-VAC (methotrexate, vinyblastine, adriamycin, cisplatin) chemotherapy and are free of disease at 10 and 12 months postoperatively. The remaining patients with organ-confined bladder cancer are free of disease after a mean follow-up of 32 months.

Seventy-six percent of the patients had a negative 1-hour pad test at 6 months, and 98% had that result at 24 months. Regarding the use of pads, 68% of the patients were not using pads at 6 months and 98% at 24 months. At night, 51% are completely

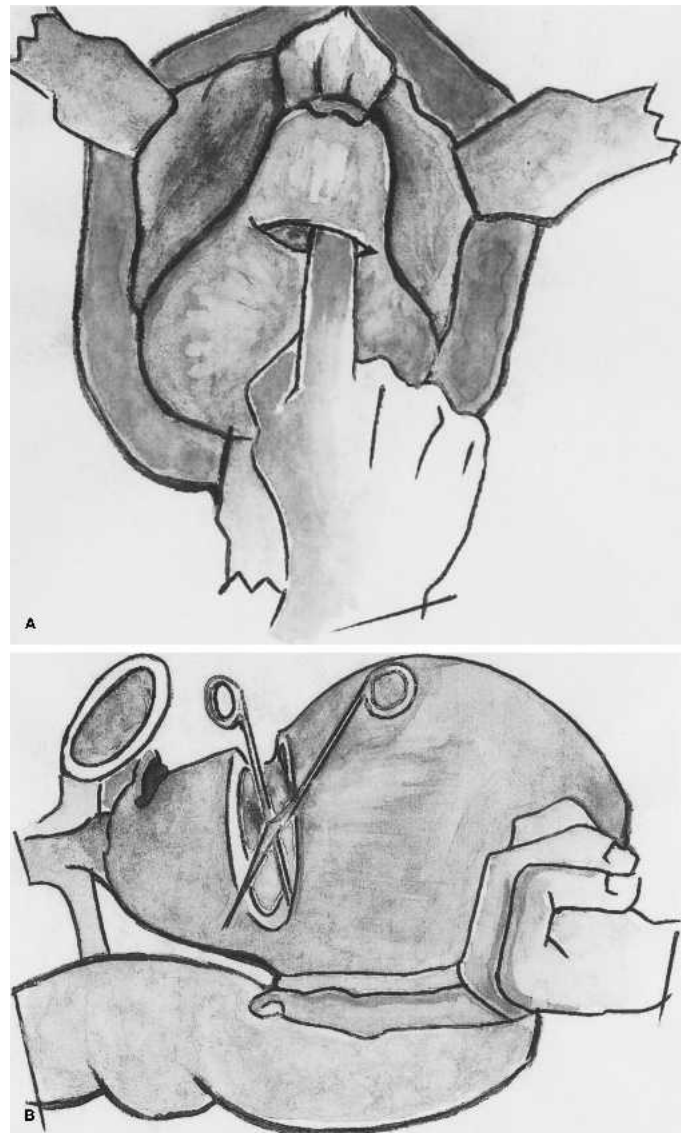


Fig. 1. (A, B). As in Millin's retropubic adenomectomy, about 2.5 cm of prostatic capsule is preserved and the adenomatous prostatic tissue is removed in our capsule- and nerve-sparing cystectomy.

continent at 6 months and 83% at 24 months. Eighteen patients (55%) had an IIEF domain score greater than 26 and were able to complete sexual intercourse without auxiliary measures at 6 months postoperatively. That increased to 25 (80%) after 24 months.

Discussion

In patients with organ-confined bladder cancer, radical cystectomy should achieve oncological radicality while obtaining a good quality of life [11]. Tumor-specific survival depends on pathological stage rather than the type of surgery performed. The rate of pelvic recurrence in organ-confined tumors ranges between 3.9% and 11%, regardless of the technique used [1, 12].

The relationship between the neurovascular bundles and Denonvillier's fascia has been adequately studied and their course



Fig. 2. Postoperative intravenous pyelography of patient No. 14, showing a non-dilated upper urinary tract at 24 months

traced from the origin to the pelvic plexus and more distally to the urethra [13, 14]. It has been shown that nerve-sparing cystectomy does not increase the incidence of local recurrence, nor does it decrease tumor-specific survival when compared with conventional radical cystectomy in patients with organ-confined disease pT1-pT3a, or node-positive disease [15–17].

It is questionable, however, whether nerve-sparing cystectomy alone significantly reduces the incidence of erectile dysfunction. The relationship with the seminal vesicles and the weak injury points during radical cystoprostatectomy in the dissection of the seminal vesicles and of the vascular pedicles has been highlighted in the past [3]. The studies performed by Vallancien et al. confirmed that the major risk of injury of the bundles during radical cystoprostatectomy is during posterior and lateral dissection. In his report on 100 patients, the feasibility of prostatic capsule-, seminal vesicles-, and nerve-sparing cystectomy with a z-type ileal reservoir after transurethral resection of the prostate (TURP) and subsequent neobladder–prostatic capsule anastomosis was shown. In these patients, TURP ruled out involvement of the prostatic urethra. Erectile function and urinary continence were preserved in the great majority of patients [4].

In 1998 Muto and Moroni [18] reported on 42 patients who underwent radical cystectomy for organ-confined disease, sparing the neurovascular bundles, the seminal vesicles and the prostatic capsule by performing Millin's adenomectomy. Colombo et al. [19] published in 2001 a study on radical cystectomy sparing the

vas deferens, seminal vesicles, and neurovascular bundles in eight patients with organ-confined bladder cancer. A prostatic capsule–W-shaped ileal neobladder anastomosis was performed. Daytime and nighttime continence was achieved in the vast majority of patients early after catheter removal. Erectile function was maintained in all cases.

In 2004 Botto reported on 42 patients selected for a prostatic capsule- and seminal-sparing cystectomy with orthotopic urinary diversion. All patients had clinically organ-confined tumors. The first step was to perform a transurethral resection of the prostate. After a mean follow-up of 26 months, seven patients (21%) had recurrence; one developed a local recurrence, there were widespread metastases in six (18%), and five had histologically confirmed organ-confined tumor. Rates for daytime and night-time continence were 90% and 85%, and in 29 patients sexual potency was unchanged [20].

In 2004 Muto et al. published a report on seminal-sparing cystectomy performed in 63 patients with superficial bladder cancer resistant to conservative therapies and in 5 patients with invasive bladder cancer that was monofocal and located away from the bladder neck. Their seminal-sparing cystectomy was a modification of standard radical cystectomy in which the posterior bladder dissection is anterior to the seminal vesicle plane to preserve the vasa deferens, seminal vesicles, prostatic capsule, and neurovascular bundles. Ablation of the whole bladder and the prostatic urothelium with surrounding hypertrophic tissue is guaranteed, and injury to the pelvic nerve plexus that provides autonomic innervation to the corpora cavernosa is avoided. All patients had normal sexual function. The mean follow-up was 68 months. Normal erectile function was preserved in 58 patients (95%). All patients had normal sexual function preoperatively, and normal erectile function was preserved in 58 patients (95%) postoperatively. Complete daytime continence was reached in 58 patients (95%) and night-time continence was achieved in 19 patients (31%). A total of 55 patients (90.2%) were alive and 6 patients (9.8%) died, 5 of cancer progression. [21].

In 2004 Colombo et al. assessed postoperative clinical outcomes such as day and nighttime urinary continence and overall sexual function in patients who underwent nerve- and seminal-sparing cystectomy with ileocapsuloplasty compared with patients after standard cystoprostatectomy with a similar orthotopic urinary reservoir. Nerve- and seminal-sparing cystectomy provides better outcomes in terms of urinary and urodynamic parameters compared to standard cystoprostatectomy. Furthermore, fully normal postoperative erectile function and satisfactory overall sexual quality of life were documented at early and follow-up delayed follow-up in all patients [22].

In 2004 Saidi et al. published their study on long-term functional and oncological results of prostate-sparing cystectomy [11]. A total of 25 patients underwent prostate-sparing cystectomy. The investigators excluded patients with invasion of the prostatic urethra and associated prostatic adenocarcinoma. Transurethral resection of the prostate was performed preoperatively to evaluate the prostatic urethra. All patients had a PSA < 4 ng/ml or negative prostatic needle biopsies. Seven patients (28%) died, all from their cancer.

At 3 years, 93.7% of patients had normal daytime continence; 75% of patients were continent at night, 37.5% of patients reported normal erections, 37.5% of patients reported partial

erections, and 25% of patients reported major erectile dysfunction [11].

Madersbacher et al. in 2004 analyzed several studies of nerve-sparing cystectomy, showing that the oncological outcome is not compromised by such a technique; in particular the rate of local recurrences is not enhanced. They described the importance for the lower urinary tract function, including continence status, after orthotopic bladder substitution and erectile function [23].

In our study we used the IPSS score, voiding diary, and 1-hour pad test to assess continence, and the IIEF-15 score to evaluate sexual function pre- and postoperatively. All patients selected showed a very good result in these quality of life assessments.

In 2004 Moore et al. [5] evaluated continence in men awaiting radical prostatectomy through a 24-hour pad test and their IPSS score. Lepor and co-workers and Cooperberg et al. determined the impact of radical retropubic prostatectomy on continence and lower urinary tract symptoms by means of the American Urological Association (AUA) symptom index [24, 25].

Hu et al. in 2004 predicted quality of life after radical prostatectomy with the Physical and Mental Component Summaries of the RAND 36-Item Health Survey and with the Sexual and Urinary Function scales of the UCLA Prostate Cancer Index [26].

Tosti et al. in 2004 evaluated variations in sexual and erectile function by administering the abridged 5-item version of the International Index of Erectile Function (IIEF-5) [7], whereas both Blander et al. and Cappelleri and colleagues used the IIEF-15 score [8, 9].

Montorsi, et al. Eardley et al., and Schulman et al. used Sexual Encounter Profile (SEP) diary erectile dysfunction, and the International Index of Erectile Function (IIEF) [27–29].

Our technique decreases the risk of damaging the neurovascular bundles compared to standard radical cystectomy due to the sparing of the distal portion of the prostatic capsule. The sparing of about 2.5 cm of prostatic capsule allows easy identification of the neurovascular bundles, and the risk of injury at this level is minimized. In addition, sparing the neurovascular bundles is facilitated by the use of an ascending dissection technique. In this way the course of the bundles can be followed under direct vision without the risk of damaging them. This is reflected in our 80% potency rate without auxiliary measures at 24 months postoperatively.

Continence is obtained by sparing part of the prostatic capsule and by the anatomical integrity of the external urinary sphincter and of the pubo-prostatic ligaments, which are not affected by the dissection. This translates in to our early continence rate of 68% at 6 months and 98% at 24 months. Furthermore, because since the dorsal venous complex is not dissected and tied, bleeding is kept to a minimum, and placement of a suture along the dissected capsule is sufficient to achieve accurate hemostasis. Regarding oncological radicality, the rationale for this technique is based on the fact that the distal urethra is covered by cylindrical epithelium. All 29 patients with organ-confined disease are free of disease after a mean follow-up of 32 months. The removal of all urothelial tissue of entodermic origin and the accurate selection of patients is mandatory to achieve oncological radicality.

We had no cases of prostate cancer after surgery, and the urethral margin was negative in all cases.

In our study candidates were highly selected for prostatic capsule-sparing cystectomy. They were preoperatively staged by TUR-B with biopsies of the prostatic urethra. Only men with a

normal digital rectal examination with PSA level 4 ng/ml or PSA in the range 4–10 ng/ml with PSA ratio > 15% were included. Transrectal sextant biopsies of the prostate were performed when digital rectal examination was suspicious for cancer and/or PSA was > 10 ng/ml or the PSA ratio was < 15% in the PSA range 4–10 ng/ml. We excluded 18 candidates with sextant transrectal biopsies positive for prostate cancer, 11 with PSA > 10 ng/ml, and 7 with a PSA ratio < 15% in the PSA range 4–10 ng/ml, 25 patients with bladder cancer not clinically organ confined, 9 with tumors involving the trigone, and 6 with tumors involving the prostatic urethra.

Although these findings need to be confirmed in a larger patient population, when respecting rigorous patient selection criteria and careful postoperative surveillance, nerve- and capsule-sparing cystectomy seems to offer satisfactory clinical and functional outcomes.

In their study, Muto et al. reported only three patients with high-grade prostatic intraepithelial cancer and 1 with prostatic cancer. These patients had a normal PSA before operation and a serum PSA less than 0.2 ng/ml at a mean follow-up of 19 months. No positive margins were identified on permanent histological analysis of the specimens, nor were local pelvic recurrences observed. A complete clinical evaluation (with PSA, digital rectal examination, and transrectal ultrasound) to exclude concomitant prostate cancer was performed [21].

Saidi et al. noted only one patient with prostatic adenocarcinoma that developed after 36 months, which was treated by external beam radiotherapy. In their series TURP was performed preoperatively to evaluate the prostatic urethra. All patients had a PSA < 4 ng/ml or negative prostatic needle biopsies. Six patients (24%) developed a pelvic recurrence, and 2 patients (8%) developed an urethral recurrence [11]. In their series Botto et al. used transurethral resection of the prostate to exclude prostate cancer. Only one of their patients was positive for prostate carcinoma after surgery [20].

Conclusions

Prostatic capsule- and nerve-sparing cystectomy permits en bloc removal of the bladder, of the adenomatous prostatic tissue, and of the seminal vesicles, achieving local cancer control and preserving erectile function and urinary continence [30].

Limitations of our study are the small number of patients and the short follow-up. Nevertheless, the excellent surgical and functional results obtained led us to perform prostatic capsule- and nerve-sparing cystectomy routinely in selected patients with organ-confined bladder cancer.

References

1. Solsona E, Iborra I, Rubio J, et al. Late oncological occurrences following radical cystectomy in patients with bladder cancer. *Eur. Urol.* 2003;43:489
2. Schlegel PN, Walsh PC. Neuroanatomical approach to radical cystoprostatectomy with preservation of sexual function. *J Urol.* 1987;138:1402
3. Tewari A, Peabody JO, Fischer M, et al. An operative and anatomic study to help in nerve sparing during laparoscopic and robotic radical prostatectomy. *Eur. Urol.* 2003;43:444
4. Vallancien G, El Fettouh HA, Cathelineau X, et al. Cystectomy with prostate sparing for bladder cancer in 100 patients: 10-year experience. *J Urol.* 2002;168:2413

5. Moore K, Allen M, Voaklander DC. Pad tests and self-reports of continence in men awaiting radical prostatectomy: establishing baseline norms for males. *Neurourol. Urodyn.* 2004;23:623–626
6. Quek KF, Chua CB, Razack AH, et al. Construction of the Mandarin version of the International Prostate Symptom Score inventory in assessing lower urinary tract symptoms in a Malaysian population. *Int. J. Urol.* 2005;12:39–45
7. Tosti A, Pazzaglia M, Soli M, et al. Evaluation of sexual function with an international index of erectile function in subjects taking finasteride for androgenetic alopecia. *Arch. Dermatol.* 2004;140:857–858
8. Blander DS, Sanchez-Ortiz RF, Broderick GA. Sex inventories: can questionnaires replace erectile dysfunction testing? *Urology* 1999; 54:719–723
9. Cappelleri JC, Rosen RC, Smith MD, et al. Diagnostic evaluation of the erectile function domain of the International Index of Erectile Function. *Urology* 1999;54:346–351
10. Pycha A, Klingler CH, Haitel A, et al. Implantable microballoons: an attractive alternative in the management of intrinsic sphincter deficiency. *Eur. Urol.* 1998;33:469
11. Saidi A, Nahon O, Daniel L, et al. Prostate-sparing cystectomy: long-term functional and oncological results in a series of 25 cases *Prog. Urol.* 2004;14:172–177
12. Hardeman SW, Soloway MS. Urethral recurrence following radical cystectomy. *J. Urol.* 1990;144:666
13. Walsh PC, Mostwin JL. Radical prostatectomy and cystoprostatectomy with preservation of potency. Results using a new nerve sparing technique. *Br. J. Urol.* 1984;56:694
14. Pritchett TR, Schiff WM, Klatt E. The potency-sparing radical cystectomy: does it compromise the completeness of the cancer resection? *J. Urol.* 1988;140:1400
15. Brendler CB, Steinberg GD, Marshall FF. Local recurrence and survival following nerve-sparing radical cystoprostatectomy. *J. Urol.* 1990;144:1137
16. Revelo MP, Cookson MS, Chang SS, et al. Incidence and location of prostate and urothelial carcinoma in prostates from cystoprostatectomies: implications for possible apical sparing surgery. *J. Urol.* 2004;171:646–651
17. Moutzouris G, Barbatis C, Plastiras D, et al. Incidence and histological findings of unsuspected prostatic adenocarcinoma in radical cystoprostatectomy for transitional cell carcinoma of the bladder. *Scand. J. Urol. Nephrol.* 1999;33:27–30
18. Muto G, Moroni M. Seminal-sparing cystectomy and ileocapsuloplasty. *Acta Urol. Ital.* 1998;12:47
19. Colombo R, Bertini R, Salonia A, et al. Nerve and seminal-sparing radical cystectomy with orthotopic urinary diversion for selected patients with superficial bladder cancer: an innovative surgical approach. *J. Urol.* 2001;165:51
20. Botto H, Sebe P, Molinie V, et al. Prostatic capsule- and seminal-sparing cystectomy for bladder carcinoma: initial results for selected patients. *BJU Int.* 2004;94:1021–1025
21. Muto G, Bardari F, D'Urso L, et al. Seminal sparing cystectomy and ileocapsuloplasty: long-term followup results. *J. Urol.* 2004;172: 76–80
22. Colombo R, Bertini R, Salonia A, et al. Overall clinical outcomes after nerve and seminal sparing radical cystectomy for the treatment of organ confined bladder cancer. *J. Urol.* 2004;171:1819–1822
23. Madersbacher S, Hochreiter W, Studer UE. Tips and tricks for nerve-sparing cystectomy. *Urologe A.* 2004;43:151–155
24. Lepor H, Kaci L, Xue X. Continence following radical retropubic prostatectomy using self-reporting instruments. *J. Urol.* 2004; 171:1212–1215
25. Cooperberg MR, Master VA, Carroll PR. Health related quality of life: significance of single pad urinary incontinence following radical prostatectomy. *J. Urol.* 2003;170:512–515
26. Hu JC, Elkin EP, Pasta DJ, et al. Predicting quality of life after radical prostatectomy: results from CaPSURE. *J. Urol.* 2004;171:703–707 discussion 707–708
27. Montorsi F, Hellstrom WJ, Valiquette L, et al. North American and European Vardenafil Groups. Vardenafil provides reliable efficacy over time in men with erectile dysfunction. *Urology* 2004;64: 1187–1195
28. Schulman CC, Shen W, Stothard DR, et al. Integrated analysis examining first-dose success, success by dose, and maintenance of success among men taking tadalafil for erectile dysfunction. *Urology* 2004;64:783–788
29. Eardley I, Gentile V, Austoni E, et al. Efficacy and safety of tadalafil in a Western European population of men with erectile dysfunction. *BJU Int.* 2004;94:871–877
30. Kessler TM, Burkhard FC, Perimenis P, et al. Attempted nerve sparing surgery and age have a significant effect on urinary continence and erectile function after radical cystoprostatectomy and ileal orthotopic bladder substitution. *J. Urol.* 2004;172:1323–1327