

Nerve-Sparing Surgery Significantly Affects Long-Term Continence After Radical Prostatectomy

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OBJECTIVES	In this long-term prospective study we evaluated the factors affecting urinary continence after radical prostatectomy.
METHODS	In this study, we recruited 156 patients (mean age, 64.1 ± 6.7 years; follow-up, 7.8 ± 1.3 years; prostate-specific antigen [PSA] level, 9.57 ± 8.81 ng/mL) who underwent radical prostatectomy between 1995 and 1998. Long-term data were obtained on 152 patients, with 4 patients lost to follow-up. Incontinence was evaluated by the number of pads per day. Follow-up data were collected at 3, 6, 12, and 24 months and annually. The multivariate analysis included the following variables: preoperative PSA levels, nerve-sparing (NS) status (bilateral NS, unilateral NS, and non-NS), and age at the time of operation (≤ 65 or >65 years).
RESULTS	With a mean follow-up of 7.8 ± 1.3 years, the overall incontinence rate was 17.7% (27 of 152). The incontinence rates were significantly higher in the non-NS group (18 of 61) compared with the bilateral NS group (6 of 66; $P < 0.05$). No significant difference was seen between the unilateral NS and non-NS groups in terms of incontinence rates ($P > 0.05$). When stratified by the NS status, the bilateral NS group had a significant improvement in overall continence. The association between age and incontinence was significant: $P < 0.05$ for patients 65 years or younger (7 of 85) versus those older than 65 years (20 of 67). The association between the preoperative PSA levels and incontinence was not significant but showed a trend (the median PSA in the incontinence group was 8.75 ng/mL; in the continence group it was 5.9 ng/mL; $P = 0.0534$).
CONCLUSIONS	Nerve-sparing radical prostatectomy improves the time interval to regain continence and long-term continence rates. UROLOGY 70: 1127–1130, 2007. © 2007 Elsevier Inc.

Prostate cancer has been the second most common cause of cancer death in men after the age of 50 years. Radical prostatectomy (RP) has been the reference standard treatment for organ- or specimen-confined prostate cancer. Because cancer control is considerably improved with the operation, the quality-of-life issue has become the major concern among these patients. Incontinence has been the most important quality-of-life issue after RP.

The incidence of incontinence reported after RP in the published data varies between 2.5% and 87%.¹ This wide variation in reported published data has been attributed to the definition, methodology used for assessing the return of continence, time of reporting after surgery, and patient selection.² Modifications in

surgical techniques have improved the reported continence rates to 92% to 95%. However, several patient-reported series in recent times have revealed a completely different picture, with incontinence rates being as high as 50%.³ Walsh *et al.*⁴ reported that neurovascular bundle preservation has improved the potency rates after surgery, but the effect of nerve-sparing (NS) surgery on incontinence has not been well publicized in the literature.

Several earlier studies reported no association between neurovascular preservation and return of continence after surgery.^{5,6} However, the lack of significance in these studies was partly attributed to the limited follow-up period (12–24 months).⁷ This time interval is not pertinent in the era of prostate-specific antigen (PSA), when younger patients must return to work early and desire to be pad free.

In this study we assessed the overall effect of NS on long-term continence and the chronologic return of continence within the first year. We also investigated the effect of age, PSA level, and Gleason score on the return of continence.

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Table 1. Chronology of return of continence

Type of Operation	Duration (mo)				
	3	6	12	24	>60
Non-NS (n = 61)	24 (39)	36 (59)	42 (69)	47 (77)	43 (70.5)
Unilateral NS (n = 25)	14 (56)	19 (76)	23 (92)	24 (96)	22 (88)
Bilateral NS (n = 66)	39 (59)	51 (77)	57 (86)	62 (94)	60 (91)
Total (continent)	77 (50.7)	106 (69.7)	122 (80.3)	133 (87.5)	125 (82.2)

NS = nerve sparing.
Data are presented as n (%).

MATERIALS AND METHODS

We identified 156 patients who underwent RP between 1995 and 1998 in the Cleveland Clinic Foundation. Long-term data were available for 152 patients, with 4 patients lost to follow-up. Baseline data obtained included age, PSA, and the Gleason score of the preoperative biopsy. The NS status was collected from the operative record. The procedure was deemed as a non-NS procedure if the operative report did not specifically mention neurovascular preservation. All cases were clinical stage T1 to T3. The mean age of these patients was 64.1 ± 6.7 years, and the mean PSA level was 9.57 ± 8.81 ng/mL. Patients receiving postoperative radiotherapy were also included in the study.

Continence Status Assessment

The catheter was removed 10 to 14 days after surgery in all patients. All patients were followed up at 3, 6, and 12 months and then annually with a minimum follow-up of at least 5 years. A self-administered institutional questionnaire was our instrument for assessing continence. The questionnaire included the number of pads used at that follow-up period, how many months after surgery the patient was completely pad free, and any operations received for incontinence (sling, artificial sphincter, or injections). Continence was defined as completely pad free or wearing a single pad for protection (dry pad). Patients whose urine leaked into one or more pads were considered as incontinent. The primary outcome of the study was the return of continence. The time of the continence and the number of pads were assessed during each visit: at 3, 6, 12, and 24 months and then annually. The questionnaire was personally given at each follow-up visit or mailed at regular intervals. All patients were stratified according to NS status as reported in the operative notes. All these patients were reassessed after a minimum follow up of 5 years with the same questionnaire.

Of all 152 patients, 8 developed strictures necessitating dilatation. Six of these 8 patients were incontinent after repeated treatments. Patients who received treatment for incontinence (artificial urinary sphincter, sling, or collagen injections) during the follow-up period were included in the incontinence group. Quality of life was assessed on the scale of 0 to 6 (0, delighted; 1, pleased; 2, mostly satisfied; 3, mixed satisfaction; 4, mostly dissatisfied; 5, unhappy; 6, terrible).

Statistical Analysis

Age, PSA, and Gleason score are expressed as mean and SD. Age was classified as 65 years or younger (group 1; n = 85) or older than 65 years (group 2; n = 67); the Gleason score was expressed as greater than 6 or 6 or less. Univariate analysis was performed between the incontinence and the individual factors. Statistical significance between the groups was assessed with a

Fisher's exact test. A two-tailed $P < 0.05$ was considered as statistically significant. Multivariate analysis was performed by using logistic regression analysis. Computations used SAS software (version 8.1; SAS Institute, Cary, NC).

RESULTS

After a mean follow-up of 7.8 ± 1.3 years, 27 (17.7%) of 152 patients were incontinent. These patients were further analyzed according to NS status, age at the time of operation, biopsy Gleason score, and preoperative PSA level.

Return of Continence

A questionnaire on the return of continence was administered at 1, 3, 6, 12, and 24 months. Continence was regained in 35 (23.1%) of 152 at 1 month, 77 (50.6%) of 152 at 3 months, 106 (69.7%) of 152 at 6 months, 122 (80.2%) of 152 at 12 months, and 133 (87.5%) of 152 at 24 months. With a mean follow-up of 7.8 ± 1.3 years, 125 (82.2%) of 152 remained continent (Table 1). When reviewing the chronologic return of continence, those who had a bilateral NS operation had significantly higher return of continence compared with the non-NS operation at 3 months (39 [59%] of 66 versus 24 [39%] of 61; $P = 0.03$), 6 months (51 [77%] of 66 versus 36 [59%] of 61; $P = 0.04$), 12 months (57 [86%] of 66 versus 42 [69%] of 61; $P = 0.02$), and 24 months (62 [94%] of 66 versus 47 [77%] of 66; $P = 0.01$).

Eight patients became incontinent after they regained complete continence. The reasons included recurrent stricture disease requiring dilatation (n = 6) and salvage radiation for increasing PSA (n = 2). Six patients underwent artificial urinary sphincter insertion, 3 patients underwent a sling procedure (1 later underwent a sphincter procedure), and 2 patients received collagen injections (both underwent sphincter procedures after dissatisfaction with the injections).

Univariate Analysis

Effect of NS Status. At 24 months, of the 152 patients, 66 underwent bilateral NS, 25 underwent unilateral NS, and 61 underwent non-NS RP. The incontinence rates were 4 (6%) of 66 in the bilateral NS group, 1 (4%) of 25 in the unilateral NS group, and 14 (23%) of 61 in the non-NS group. A significant association was found in incontinence rates between the bilateral NS and non-NS

Table 2. Relationship of variables with nerve-sparing status

Variable	Age, y (mean ± SD)	PSA, ng/mL (mean ± SD)	Incontinence (>5 y f/u), n (%)	Quality of Life		
				Q2, n (%)	Q3, n (%)	Q4, n (%)
Bilateral NS (n = 66)	62.1 ± 6.1	6.3875 ± 3.2	6 (9)*	62 (93.8)	3 (4.7)	1 (1.5)
Unilateral NS (n = 25)	63.5 ± 8.4	6.92 ± 14.4	3 (12)	20 (80)	4 (16)	1 (4)
Non-NS (n = 61)	66.6 ± 6.0	14.35 ± 12.13	18 (29.5)	47 (77.1)	10 (18.2)	4 (6.6)
Total (n = 152)	64.1 ± 6.7	9.57 ± 8.81	27 (17.7)	129 (84.8)	17 (11.3)	6 (3.9)

PSA = prostate-specific antigen; f/u = follow-up; Q2 = mostly satisfied; Q3 = mixed satisfaction; Q4 = mostly dissatisfied; NS = nerve sparing.

groups ($P = 0.0096$; Table 1). After 5 years, the incontinence rates were 6 (9%) of 66 in the bilateral NS RP group, 3 (12%) of 25 in the unilateral NS RP group, and 18 (29.5%) of 61 in the non-NS RP group. A significant association was found in incontinence rates between the bilateral NS and non-NS groups ($P = 0.0356$). No significant difference was observed between the unilateral NS and non-NS or the bilateral NS and unilateral NS RP groups (Table 2).

We also evaluated the effect of the NS status on quality of life pertaining to the urinary function. Of all 152 patients, 129 (84.8%) were mostly satisfied with the results of surgery; only 6 (3.9%) were mostly unsatisfied, and remaining 17 (11.3%) had mixed satisfaction. Nearly 100% (62 [93.8%] of 66) of patients who underwent bilateral NS surgery reported being mostly satisfied with RP, compared with 47 (77%) of 61 in the non-NS group who reported being mostly satisfied.

Effect of Age and the Gleason Score. Patients older than 65 years ($n = 67$) at operation have a significantly increased risk of incontinence compared with patients 65 years or younger ($n = 85$; 20 versus 7; $P < 0.05$). Patients with a Gleason score greater than 6 had significantly higher incontinence rates (16 [28%] of 57) compared with patients with a Gleason score of 6 or less (11 [12%] of 95; $P = 0.015$).

Multivariate Analysis

Incontinence showed a significant relationship with NS status ($P = 0.009$) and Gleason score ($P = 0.025$). However, the patient's age and PSA level did not show a significant association. This reflects the fact that patients older than 65 years typically have non-NS operations.

COMMENT

Urinary incontinence is one of the major quality-of-life issues after RP. The incontinence rates reported in the published data vary with the duration after surgery, definition of incontinence, and surgical technique. Walsh *et al.*⁴ reported that the pelvic plexus and branches that provide autonomic innervation to the sphincter may contribute to the return of continence. In cadaveric anatomic studies, Narayan *et al.*⁸ identified that the external urethral sphincter receives part of its innervation through special branches originating from the dorsal

nerve of the penis and they are in close proximity to the prostatic apex. Wei *et al.* reported that NS RP significantly decreases the interval for the return of continence. In this article, the investigators suggest that NS procedures preserve the motor innervation of the urethral sphincter. However, no further direct neurophysiologic evidence exists for their hypothesis.⁹ Similarly, in our study we found a significant association between incontinence and NS status at 24 months and during long-term follow-up.

The published data have contradictory reports regarding the effect of NS surgery and the return of continence.¹⁰ Eastham *et al.*¹¹ believed that neurovascular preservation definitely influences the continence status and that resection of even one neurovascular bundle significantly influences the return of postoperative continence. We were not able to identify significant differences between the unilateral and non-NS groups, mostly because of the small number of patients in the unilateral group. Conversely, Catalona *et al.*¹² reported that the return of continence was not influenced by NS surgery. In this article, Catalona *et al.* found that 92% of the study population was continent (no pads) after a follow-up of 18 months, but only 7% had non-NS surgery in that series. In our series, 87.5% were continent 24 months after surgery. Although the mean age may be similar in both series, the high proportion (40%) of non-NS operations might be a cause for the higher incontinence rates in our series.

It is interesting to note that Talcot *et al.*⁷ found that the NS group used significantly more pads at 3 months than the non-NS groups, although this difference was not seen at 12 months. However, this study had a small population in the non-NS group, and the follow-up period was limited up to 12 months. The published data might have contradictory findings regarding the role of neurovascular preservation in the return of continence, but our multivariate analysis supported the fact that the return of continence in the long term depends on neurovascular preservation.

Studies concentrating on long-term continence were sparse in the published data. Most studies report incontinence rates between 12 and 18 months. The factors affecting long-term continence status (>5 years) have not been evaluated. However, we found that NS status still influences continence rates on a long-term basis.

None of the patients reported any recovery of continence after 24 months. In fact, we found that 8 patients—those were continent at 24 months—had become incontinent after 60 months. The reason for this incontinence was long-term treatment of urethral and bladder neck strictures in 6 patients and salvage radiation in the other 2 patients. Recently, Penson *et al.*, reviewing the data of the Prostate Cancer Outcome Study, reported that at 24 months, the proportion of men reporting frequent leakage or no control was 10.4%, and this increased to 13.9% at 60 months. Similarly, in our series 12.5% patients reported incontinence at 24 months, which increased to 17.7% after a mean follow-up of 7.8 ± 1.3 years.¹³ The most common reason for the increase in incontinence in long-term follow-up was treatment of complications such as urinary strictures.

Other than NS status, only the Gleason score was significant in multivariate analysis; age at the time of operation and initial PSA level were not significant. Clinically this reflects that non-NS operations were performed in most patients older than 65 years and in most patients with high Gleason score. We found that on univariate analysis, incontinence rates were significantly higher (30%) in patients who underwent RP after the age of 65 years versus patients younger than 65 years (8%), but the older population had significantly more non-NS operations. Whether incontinence rates in the older patients are reflective of age or type of NS surgery is not documented well in the published data. Catalona *et al.*¹¹ reported that a younger age was the only factor reported to affect the return of continence in their series. Fowler *et al.*¹⁴ reported that 63% of men who underwent RP after 65 years had daily urinary leakage. Similarly, in a cross-sectional study, Litwin *et al.*⁶ showed that 40% had urinary leakage but that only 23% had NS surgery with a mean age of 63 years. Thus, these data raise an interesting question: irrespective of age and potency status, should bilateral NS surgery be performed in all patients? It is interesting to note that few studies reported no association with incontinence rates and age. This lack of association can be explained by exceptionally low overall incontinence rates, yielding too few patients to identify a significant risk factor, or few elderly patients, making identifying a risk factor in any group extremely difficult.^{10,15} An earlier return of continence is a significant issue in the modern PSA era because the younger population must return to work earlier and desires to be pad free, and they are less tolerant to any urinary leakage and use of pads.

CONCLUSIONS

Nerve-sparing RP improves the interval to regain continence and long-term continence rates. This study suggests that all patients, irrespective of potency status and age, would benefit from NS procedures when this is clinically feasible.

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