

Nerve-sparing technique and urinary control after robot-assisted laparoscopic prostatectomy

Wesley W. Choi · Marcos P. Freire · Jane R. Soukup ·
Lei Yin · Stuart R. Lipsitz · Fernando Carvas ·
Stephen B. Williams · Jim C. Hu

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Abstract

Objectives To characterize determinants of 4-, 12-, and 24-month urinary control after robot-assisted laparoscopic prostatectomy (RALP).

Methods Adjusted comparative study using prospectively collected, patient self-reported urinary control for 602 consecutive RALPs. Urinary control defined as: (1) EPIC urinary function (UF) scored from 0 to 100 and (2) continence (zero pads per day).

Results Both UF (62.8 vs. 42.4, $P < 0.001$) and continence rates (47.2 vs. 26.7%, $P = 0.043$) were better for bilateral nerve-sparing (BNS) vs. non-nerve-sparing (NNS) at 4 months, but only UF scores were significantly better at 12- (80.9 vs. 70.7, $P = 0.014$) and 24-month (89.2 vs. 77.4, $P = 0.024$) post-RALP. No difference in positive margin rates was observed. In multivariate analysis, older age

(parameter estimate -0.42 , 95% CI -0.80 to -0.04) and increasing gland volume (-0.13 , CI -0.26 to -0.01) resulted in lower UF scores at 4 months, while higher pre-operative UF (0.25, CI 0.05–0.46), bladder neck-sparing technique (10.1, CI 3.79–16.35), BNS (19.1, CI 9.37–28.82), and unilateral nerve-sparing (19.00, CI 7.88–30.11) resulted in higher UF scores at 4 months. At 12 months, higher pre-operative UF (0.24, CI 0.083–0.40) and BNS (9.54, CI 1.92–17.16) resulted in higher UF scores. At 24 months, higher pre-operative UF (0.20, CI 0.06–0.33), bladder neck-sparing technique (7.80, CI 3.48–12.10), and BNS (7.86, CI 1.04–14.68) resulted in higher UF scores.

Conclusions BNS, bladder neck-sparing technique, and higher pre-operative UF score result in improved 24-month urinary control after RALP.

Keywords Radical prostatectomy · Continence · Outcomes · Nerve sparing

W. W. Choi and M. P. Freire are contributed equally.

W. W. Choi · M. P. Freire · L. Yin · F. Carvas ·
S. B. Williams · J. C. Hu
Division of Urologic Surgery, Brigham and Women's Hospital,
Harvard Medical School, Boston, MA, USA

S. B. Williams
e-mail: swilliams22@partners.org

J. R. Soukup · S. R. Lipsitz · J. C. Hu
Center for Surgery and Public Health, Brigham and Women's
Hospital, Harvard Medical School, Boston, MA, USA

J. C. Hu
Lank Center for Genitourinary Oncology,
Dana-Farber Cancer Institute, Boston, MA, USA

S. B. Williams · J. C. Hu (✉)
Division of Urology, Brigham and Women's Hospital,
45 Francis St, ASB-II, Boston, MA 02115, USA
e-mail: jhu2@partners.org

Introduction

Despite advancements in pelvic anatomy and refinement of surgical technique, loss of urinary control after radical prostatectomy remains a significant source of patient morbidity, diminishing quality of life [1, 2]. The prevalence of incontinence after radical prostatectomy varies widely from 2.5 to 87% [3], depending on the definition of urinary control, methodology of collecting outcomes, and surgical technique.

Several factors affecting post-operative urinary control have been studied without consistent results, and the role of neurovascular preservation for urinary control is particularly controversial [4]. Most results are based on large series of open radical retropubic prostatectomy (RRP) [5–7]. However, in the US, more than 75% of radical

prostatectomies are currently performed robotically [8]. A recent population-based study suggested that incontinence may be more commonly diagnosed following minimally invasive laparoscopic prostatectomy, with or without robotic assistance, vs. RRP [9]. The purpose of our study is to assess the effect of surgical technique on urinary control following RALP, adjusting for potential confounders such as age and risk of disease.

Materials and methods

Patients

From September 2005 to May 2009, 602 consecutive men with clinically localized prostate cancer underwent RALP by a single surgeon (JCH): 469 men underwent a bilateral nerve-sparing, 89 underwent a unilateral nerve-sparing, and 44 underwent a non-nerve-sparing technique. The nerve-sparing technique utilized was based on pre-operative erectile function and risk of disease. Because nerve-sparing technique may occur along a continuous spectrum vs. 3 distinct categories, we considered a neurovascular bundle “spared” if at least 70% of the bundle remained in situ. This type of subjective consideration to the extent of nerve preservation has been previously validated to correlate with EPIC outcomes [10]. We prefer an interfascial technique when attempting to spare 100% of the nerve bundle. Detailed descriptions of our nerve-sparing and bladder neck-sparing techniques have been previously described [11, 12].

Outcomes

Urinary control was evaluated using the expanded prostate cancer index composite (EPIC) urinary function short form [2, 13] at baseline, 4-, 12-, and 24-month post-operatively. The EPIC short form is scored continuously from 0 to 100, with higher scores indicating better urinary function. Since urinary control is often defined by pad use, we also examined the EPIC item: “How many pads or adult diapers per day did you usually use to control leakage during the last 4 weeks?” and defined continence as 0 pads per day. Patient demographic and pre-operative risk characteristics, nerve-sparing technique, pathologic outcomes, and EPIC responses were prospectively entered into a Microsoft Access (Microsoft, Redmond, WA, USA) database by research personnel uninvolved with patient care.

Statistical analysis

SAS version 9.1.2 (SAS, Cary, NC, USA) was used for the statistical analysis. To compare continuous demographic

characteristics, peri-operative and pathological results across the three nerve-sparing groups, the Wilcoxon rank-sum test was used for non-normal variables, while analysis of variance was used for normally distributed variables. For categorical variables, a Mantel–Haenszel trend test was used to compare the three groups. For the positive margins by stage, which had very small numbers, an exact trend test was used.

Differences in urinary function and continence among the three groups were adjusted for age, pre-operative urinary function, bladder neck-sparing, endovascular stapler use, gland volume, and BMI, using robust regression for urinary function and logistic regression for continence.

Results

Men undergoing bilateral nerve-sparing vs. unilateral nerve-sparing vs. non-nerve-sparing RALP were younger (57.8 vs. 59.0 vs. 60.5 years, $P = 0.013$) and more likely to present with clinical stage T1c (92.3 vs. 81.8 vs. 81.8%, $P = 0.002$) and Gleason grade 3 + 3 on biopsy (71.2 vs. 31.5 vs. 43.2%, $P < 0.001$) (Table 1).

Operative time and estimated blood loss did not vary by nerve-sparing approach (Table 2). Urinary retention was less frequent in the bilateral nerve-sparing group vs. unilateral nerve-sparing vs. non-nerve-sparing (1.9 vs. 6.7 vs. 4.6%, $P = 0.039$). There were no differences in utilization of a bladder neck-sparing approach, endovascular stapler use for DVC control, or pathologic gland size. Independent of nerve-sparing approach, the overall positive margin rate was 12.8%, occurring in 10.6% of pT2, 22.2% of pT3a, and 40.9% of pT3b disease.

Bilateral nerve-sparing vs. non-nerve-sparing RALP resulted in higher mean urinary function scores at 4 (62.8 vs. 42.4, $P < 0.001$), 12 (80.9 vs. 70.7, $P = 0.014$), and 24 months (89.2 vs. 77.4, $P = 0.024$), and higher continence rates at 4 months (47.2 vs. 26.7, $P = 0.043$). Unilateral nerve-sparing vs. non-nerve-sparing RALP resulted in a higher mean urinary function scores at 4 months (63.6 vs. 42.4, $P < 0.001$) only and no difference in continence rates at any time point (Table 3).

In multivariate analysis for urinary function, older age (parameter estimate [PE] -0.42 , 95% CI -0.80 to -0.04) and increasing gland volume (PE -0.13 , 95% CI -0.26 to -0.01) were associated with a lower urinary function score at 4 months, while higher pre-operative urinary function (PE 0.25, 95% CI 0.05–0.46), bladder neck-sparing technique (PE 10.1, 95% CI 3.79–16.35), unilateral nerve-sparing (PE 19.00, 95% CI 7.88–30.11), and bilateral nerve-sparing (PE 19.1, 95% CI 9.37–28.82) resulted in higher urinary function scores at 4 months (Table 4). At 12 months, higher pre-operative urinary function (PE 0.24, 95% CI 0.083–0.40)

Table 1 Patient demographics and tumor characteristics

	BNS (<i>n</i> = 469)	UNS (<i>n</i> = 89)	NNS (<i>n</i> = 44)	<i>P</i> -value
Follow-up (days), median (range)	562 (71–1,386)	512 (73–1,362)	523 (80–1,432)	0.390
Age (years), mean \pm SD	57.8 \pm 6.6	59.0 \pm 6.6	60.5 \pm 7.0	0.013
Race, no. (%)				0.971
White	446 (95.1)	84 (94.4)	42 (95.4)	
Black	16 (3.4)	3 (3.4)	1 (2.3)	
Other	7 (1.5)	2 (2.2)	1 (2.3)	
Charlson comorbidity index, no. (%)				0.134
None	39 (83.6)	71 (79.8)	34 (77.3)	
One	59 (12.6)	12 (13.5)	7 (15.9)	
Two or more	18 (3.8)	6 (6.7)	3 (6.8)	
Pre-operative UF, median (range)	100 (30.3–100)	100 (30.3–100)	100 (69.3–100)	0.470
BMI, median (range)	28.0 (15.6–48.0)	27.9 (18.0–37.6)	28.5 (22.0–52.1)	0.366
PSA, median (range)	4.8 (0.4–23.0)	4.9 (1.3–20.0)	5.0 (1.9–26.7)	0.534
Clinical stage, no. (%)				0.002
T1c	431 (92.3)	72 (81.8)	36 (81.8)	
T2	36 (7.7)	16 (18.2)	8 (18.2)	
Gleason grade on biopsy, no. (%)				<0.001
3 + 2	3 (0.6)	0	1 (2.3)	
3 + 3	332 (71.2)	28 (31.5)	19 (43.2)	
3 + 4	92 (19.7)	34 (38.2)	12 (27.3)	
4 + 3	32 (6.9)	14 (15.7)	7 (15.9)	
4 + 4	5(1.1)	12 (13.5)	3 (6.8)	
3 + 5	2(0.4)	1 (1.1)	0	
4 + 5	0	0	1 (2.3)	
5 + 4	0	0	1 (2.3)	

BNS bilateral nerve-sparing, UNS unilateral nerve-sparing, NNS non-nerve-sparing, UF urinary function

and bilateral nerve-sparing (PE 9.54, 95% CI 1.92–17.16) resulted in higher urinary function scores. At 24 months, higher pre-operative urinary function (PE 0.20, 95% CI 0.06–0.33), bladder neck-sparing technique (PE 7.80, 95% CI 3.48–12.10), and bilateral nerve-sparing (PE 7.86, 95% CI 1.04–14.68) resulted in higher urinary function scores.

Comment

Despite advancements in surgical technique, loss of urinary control is not uncommon after radical prostatectomy. Patient factors such as age [5], body mass index, and prostate gland volume [14] and surgical factors such as bladder neck-sparing technique [11], neurovascular bundle preservation, puboprostic ligament preservation [15], DVC control technique, and maximizing urethral length [16] have been implicated in affecting urinary control after RRP, but without consistent results [4].

Our study has several important findings. First, bilateral nerve-sparing during RALP improves post-operative urinary function. At each of the study time points, bilateral nerve-sparing RALP improved urinary function by at least 10 points, indicating a clinically significant improvement in patient's quality of life [17]. Multivariate analysis also confirmed that bilateral nerve-sparing improved urinary function at 4 (PE 19.1, 95% CI 9.37–28.82), 12 (PE 9.54, 95% CI 1.92–17.16), and 24 months (PE 7.86, 95% CI 1.04–14.68), and that bilateral nerve-sparing improved urinary function more than any other factor at all time points. When examining continence (0 pads per day), bilateral nerve-sparing was associated with improved continence at 4 months ($P = 0.043$), but not at 12 or 24 months. This discordance has been evaluated by Krupski et al. who found various definitions of continence based on pad use to be impractical due to patient heterogeneity and concluded that composite scores more accurately reflected health-related quality of life [18].

Table 2 Peri-operative and pathologic outcomes by nerve-sparing technique

	BNS (<i>n</i> = 469)	UNS (<i>n</i> = 89)	NNS (<i>n</i> = 44)	<i>P</i> -value
Estimated blood loss (ml), mean ± SD	203.3 ± 105.4	203.24 ± 103.6	195.93 ± 93.2	0.905
Operative time (min), mean ± SD	169.8 ± 44.9	162.75 ± 43.2	174.36 ± 59.6	0.310
Length of stay (days), median (range)	1.0 (0–9)	1.0 (1–13)	1.0 (0–6)	0.604
Length of catheterization (days), median (range)	7.0 (4–35)	7.0 (4–21)	7.0 (0–21)	0.176
Urinary retention, no. (%)	9 (1.9%)	6 (6.7%)	2 (4.6%)	0.039
Anastomotic stricture, no. (%)	4 (0.9)	1 (1.1)	0	0.723
Delayed urine leak/urinoma, no. (%)	4 (0.9)	1 (1.1)	0	0.723
Ureteral injury, no. (%)	1 (0.2%)*	0	0	0.621
Bladder neck-sparing, no. (%)	254 (54.2)	52 (58.4)	28 (63.6)	0.177
None, no. (%)	215 (45.8)	37 (41.6)	16 (36.4)	
Stapler, no. (%)	183 (39.0)	31 (34.8)	15 (34.1)	0.372
None, no. (%)	286 (61.0)	58 (65.2)	29 (65.9)	
Gland size (pathology), median (range)	50.0 (24–175)	49.0 (26–133)	53.5 (30–148)	0.278
Pathologic Gleason grade, no. (%)				<0.0001
3 + 2	3 (0.6)	0	0	
3 + 3	227 (48.8)	18 (20.2)	13 (30.2)	
3 + 4	164 (35.3)	39 (43.8)	16 (37.2)	
3 + 5	2 (0.4)	0	1 (2.3)	
4 + 3	55 (11.8)	15 (16.9)	9 (20.9)	
4 + 4	10 (2.2)	11 (12.4)	0	
4 + 5	4 (0.9)	5 (5.6)	4 (9.3)	
5 + 3	0	1 (1.1)	0	
Pathologic stage				0.0003
pT2	410 (88.2)	67 (75.3)	35 (81.4)	
pT3a	45 (9.7)	16 (18.0)	2 (4.6)	
pT3b	10 (2.1)	6 (6.7)	6 (14.0)	
Positive margins, no. (%)				
pT2	43 (10.5)	8 (11.9)	3 (8.6)	0.911
pT3a	9 (20.0)	5 (31.2)	0	0.779
pT3b	5 (50.0)	2 (33.3)	2 (33.3)	0.615
Positive margins (overall), no. (%)	57 (12.2)	15 (16.8)	5 (11.4)	0.628

BNS bilateral nerve-sparing, UNS unilateral nerve-sparing, NNS non-nerve-sparing

* Presence of duplicated system on side of injury

Importantly, at 24 months, men undergoing a bilateral nerve-sparing RALP have higher urinary function scores than those undergoing a non-nerve-sparing RALP. Previous RALP studies [19, 20] show that neurovascular bundle preservation improves urinary control present data at 12 months only, prior to the point at which further improvements in urinary control plateau [1, 2]. Our data imply there is no “catchup” in urinary function outcomes; in the long term, nerve regeneration and pelvic floor exercises in men undergoing non-nerve-sparing RALP do not improve urinary function to the level that initial bilateral nerve-sparing does. Also, by using positive margin rate as a proxy, we show that oncologic control is not compromised with

neurovascular bundle preservation, echoing the results of many large series [21].

Our result of bilateral nerve-sparing improving urinary control is consistent with multiple, large, retrospective RRP analyses [5, 22–26]. These results are also supported by electrophysiological studies showing that stimulation of the neurovascular bundle leads to increased intraurethral pressures [27], suggesting urinary control is at least partially a result of autonomic innervation. However, a better understanding of the neuroanatomy of the rhabdosphincter, correlated with additional neurophysiological evidence, is needed to reconcile results that have found no association between bilateral nerve-sparing and urinary control [6, 7, 28].

Table 3 Urinary control (urinary function and continence) outcomes stratified by nerve-sparing approach and time

Post-operative time	Sample size			EPIC urinary function (0–100)				
	BNS	UNS	NNS	BNS	UNS	NNS	<i>P</i> -value BNS vs. NNS	<i>P</i> -value UNS vs. NNS
4 months (<i>n</i> = 479)	377	72	30	62.8 ± 25.8	63.6 ± 22.5	42.4 ± 20.1	0.0001*	0.0008*
12 months (<i>n</i> = 381)	303	52	26	80.9 ± 18.6	71.8 ± 21.6	70.7 ± 24.5	0.014*	0.970*
24 months (<i>n</i> = 186)	146	27	13	89.2 ± 14.1	81.0 ± 14.0	77.4 ± 23.2	0.024*	0.592*

Post-operative time	Continence [#] rate (%)			<i>P</i> -value BNS vs. NNS	<i>P</i> -value UNS vs. NNS
	BNS (%)	UNS (%)	NNS (%)		
4 months	47.2	48.6	26.7	0.043*	0.084*
12 months	84.6	73.1	76.9	0.431*	0.705*
24 months	94.5	92.6	92.3	0.742*	0.974*

BNS bilateral nerve-sparing; UNS unilateral nerve-sparing; NNS non-nerve-sparing

* Adjusted for age, pre-operative urinary function, bladder neck-sparing technique, endovascular stapler for DVC control, prostate gland volume, and BMI

[#] Continence defined as 0 pads/day

Table 4 Multivariate analysis for urinary function at 4, 12, and 24 months

Parameter	4 months				12 months				24 months			
	Estimate	95% Confidence limits	<i>P</i> -value		Estimate	95% Confidence limits	<i>P</i> -value		Estimate	95% Confidence limits	<i>P</i> -value	
Age	-0.420	-0.797	-0.044	0.029	-0.147	-0.452	0.157	0.343	0.131	-0.156	0.419	0.371
Preop UF	0.252	0.046	0.457	0.016	0.242	0.083	0.400	0.003	0.197	0.063	0.332	0.004
BN sparing	10.066	3.787	16.345	0.002	2.566	-2.091	7.222	0.280	7.790	3.480	12.099	0.0004
BNS	19.095	9.367	28.823	0.0001	9.540	1.917	17.162	0.014	7.860	1.037	14.683	0.024
UNS	18.991	7.875	30.106	0.0008	0.170	-8.799	9.139	0.970	-2.200	-10.253	5.853	0.592
NNS (0)	-	-	-	-	-	-	-	-	-	-	-	-
Stapler	3.194	-3.287	9.674	0.334	4.260	-0.244	8.765	0.064	0.036	-4.731	4.802	0.988
Gland volume	-0.132	-0.258	-0.005	0.041	-0.010	-0.101	0.081	0.823	-0.064	-0.137	0.008	0.082
BMI	-0.515	-1.087	0.056	0.089	0.029	-0.451	0.508	0.906	-0.026	-0.452	0.400	0.906

Preop UF pre-operative urinary function, BN bladder neck, BNS bilateral nerve-sparing, UNS unilateral nerve-sparing, NNS non-nerve-sparing, BMI body mass index

Second, we determined that men with higher pre-operative urinary function scores resulted in improved urinary function across all time points. Higher pre-operative urinary function may indicate the absence of baseline detrusor instability and/or obstruction. While obstructive symptoms are relieved after RALP, irritative symptoms from detrusor instability may persist, resulting in worse urinary function after RALP for men with lower pre-operative urinary function scores. In addition, men undergoing bladder neck preservation had higher 4- and 24-month urinary function scores, consistent with prior reports [11].

Third, return of urinary function at 4 months was also improved by unilateral nerve-sparing, but delayed by older patient age and larger prostate gland volume. The effect of

unilateral nerve-sparing appears to be short-lived, as no long-term benefit of unilateral nerve-sparing on urinary control was observed. Other authors have concluded that patient’s age affects return of urinary control [4, 5], but we found this limited to 4 months only. Further, an analysis of CaPSURE™ revealed that larger baseline prostate gland size predicts lower levels of urinary control at 2 years, presumably secondary to subclinical bladder dysfunction [14]. However, we found prostate gland size to be predictive only at 4 months, which may be a reflection of prolonged recovery of urinary control after an anatomically challenging operation.

Our findings must be interpreted in the context of the study design. Our limitations are similar to most studies

examining this topic, which may help explain the heterogeneity of data. First, there is no exact definition of “continence,” mostly due to its subjective nature; different conclusions can be made in the same study population depending on which definition is used [18]. For these reasons, we report urinary function using the EPIC score and, for the sake of comparison to other studies, also disclose results dichotomizing continence as 0 vs. 1 or more pads per day. Although we found no difference in 24-month pad usage, we found a clinically significant difference in EPIC urinary function score when bilateral nerve-sparing technique is employed. Second, the quality of a particular neurovascular bundle sparing effort is subjective and not quantifiable. Some have argued that urinary control results should be correlated with return of erectile function (as a proxy for successful neurovascular bundle preservation) [28]. However, that is assuming there is a simple direct relationship among neurovascular bundle preservation, erectile function, and urinary control. Others have used intraoperative electrophysiological testing to confirm the preservation of a neurovascular bundle [24]. Third, there may be unrecognized differences in apical dissection technique, which may also explain our findings. Although unlikely, less trauma may be inflicted upon the rhabdosphincter and pudendal nerve fibers during bilateral nerve-sparing RALP vs. non-nerve-sparing resulting in better urinary control [29].

Conclusion

Bilateral neurovascular bundle preservation, bladder neck-sparing technique, and higher pre-operative urinary function score result in improved 24-month urinary control after RALP without an increase in positive margin rates.

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Conflict of interest The authors declare that they have no conflict of interest.

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