Perioperative predictors for post-prostatectomy urinary incontinence in prostate cancer patients following robotic-assisted radical prostatectomy: Long-term results of a Canadian prospective cohort

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Abstract

Introduction: We aimed to report the impact of perioperative factors that have not been well-studied on continence recovery following robotic-assisted radical prostatectomy (RARP).

Methods: We analyzed data of 322 men with localized prostate cancer who underwent RARP between October 2006 and May 2015 in a single Canadian centre. All patients were assessed at one, three, six, 12, and 24 months after surgery. We evaluated risk factors for post-prostatectomy urinary incontinence from a prospectively collected database in multivariate Cox regression analysis. The primary endpoint was continence, defined as 0 pad usage per day.

Results: 0-pad continence rates were 126/322 (39%), 187/321 (58%), 222/312 (71%), 238/294 (80%), and 233/257 (91%) at one, three, six, 12, and 24 months, respectively. Bladder neck preservation (hazard ratio [HR] 0.71; 95% confidence interval [CI] 0.5–0.99; p=0.04), and prostate size (HR 0.99; 95% CI 0.98–0.99; p=0.02) were independent predictors of continence recovery after RARP. Smoking at time of surgery predicted delayed continence recovery on multivariate analysis (HR 1.42; 95% CI 1.01–1.99; p=0.04). Neurovascular bundles preservation was associated with continence recovery after 24 months. No statistically significant correlation was found with other variables, such as age, body mass index, Charlson comorbidity index, preoperative oncological baseline parameters, presence of median lobe, or thermal energy use.

Conclusions: Our results confirmed known predictors of post-prostatectomy incontinence (PPI), namely bladder neck resection and large prostate volume. Noteworthy, cigarette smoking at the time of RARP was found to be a possible independent risk factor for PPI. This study is hypothesis-generating.

Introduction

Robotic surgery in organ-confined prostate cancer has rapidly evolved since 2002 and has achieved worldwide acceptance. Alongside oncological results, quality of life outcomes are of a major concern to patients after robotic-assisted radical prostatectomy (RARP). Several studies and systematic meta-analyses have examined the impact of various preoperative and intraoperative technical variables on post prostatectomy incontinence (PPI) recovery after RARP. Reported predictive variables for continence recovery include age, surgeon experience and hospital volume, prostate size, neurovascular bundle (NVB) preservation, preoperative erectile function, cancer characteristics, and preoperative urinary function. Herein, we sought to examine the impact of preoperative variables and potential intraoperative variables that may affect continence recovery post-RARP in a large Canadian cohort. Explicitly in the current report, we focused on the effect of current active smoking status and bladder neck (BN) preservation on urinary continence recovery after RARP.

Methods

Study population

After institutional review board approval, data were analyzed retrospectively from our prospectively collected database. The study included all consecutive 322 patients with organ-confined prostate cancer who underwent RARP from October 2006 to May 2015 by a single surgeon (AEH) at Hôpital du Sacré Cœur de Montréal. Patients were not preselected; any patient who was a surgical candidate was offered RARP. All men were followed by the same surgeon at one, three, six, nine, and 12 months, and then every six months for five years and yearly thereafter.
Data collection

Patient demographics and baseline parameters were collected, including age, prostate volume, prostate-specific antigen (PSA), Gleason score, and pathological stage. Detailed intraoperative data were recorded on a standardized abstraction sheet simultaneously during surgery. Postoperatively pads number were collected at each visit and recorded prospectively in the database.

Definition of continence

The primary endpoint of the study was time to continence, defined as 0 pad use. Continence was assessed by a modified question added to the usual International Prostate Symptom Score (IPSS): “How many pads per 24 hours on average did you use in the past month for urinary incontinence: zero, one security liner, one pad, two pads, three pads, four pads or more?” We used a strict definition of PPI whereby patients were considered incontinent if they reported the use of a security liner or any number of pads per day.

Covariates

Age at surgery, PSA, and prostate size were coded as continuous variables. Pathological stage was categorized into four groups: T2a–b, T2c, T3a, and T3b–T4, using TNM seventh edition classification system. Pathological Gleason grade was categorized into four groups: ≤6, 3+4, 4+3, and 8–10. Body mass index (BMI), Charlson comorbidity index (CCI), year of surgery, operative time, current smoking status at the time of RARP, presence of median lobe, perineal pressure during anastomosis (which is a surrogate for difficult pelvic anatomy; narrow and deep), thermal energy use during NVB dissection, BN-sparing, and NVB preservation were also included.

Surgical technique

All cases were performed using our previously reported RARP surgical technique.9 BN preservation was defined as tight BN dissection that allowed minimal but sufficient visualization of the bladder interior mucosa and ureteral orifices, with preservation of circular BN fibers. BN preservation was performed whenever feasible based on preoperative oncological characteristics and intraoperative anatomy. NVB preservation was performed when oncologically appropriate even in patients with documented erectile dysfunction. A risk-stratified graded approach to nerve-sparing was used similar to the Pasadena consensus.10 Pedicile control was performed with Hem-o-lok® clips and minimal or no thermal energy around the NVBs. Maximal urethral stump length preservation was attempted in all cases. Bidirectional, continuous anastomotic suture was used with mucosa-to-mucosa apposition. All men had single running anastomotic layer without a separate posterior or anterior reconstruction. All anastomoses were tested with 120–180 ml of normal saline to rule out leak prior to case completion. A 20 Fr silicone urethral catheter was inserted with removal on postoperative day 7 without cystogram.

Statistical analyses

Descriptive statistics were used to report patients’ baseline characteristics and proportions of different risk factors. The Mann-Whitney test and Chi-square test were used to compare differences in medians and proportions, respectively. Multivariate Cox logistic regression analysis was performed to examine the association between status of urinary continence and the factors described above. All statistical tests were performed using R software environment for statistical computing and graphics (Vienna, Austria, version 3.0.1). All tests were two-sided with a significance level set at p<0.05.

Results

Baseline clinical and pathological characteristics (n=322) are summarized in Table 1. Overall continence recovery rates (0 pad) were 39.1% (126/322), 58.2% (187/321), 71.1% (222/312), 80.9% (238/294), and 90.7% (233/257) at one, three, six, 12, and 24 months, respectively. Mean followup ± standard deviation (SD) was 49±25 months, and 80% of men had ≥24-month followup.

Within our cohort, 44 (13.7%) and 90 (27.9%) patients were active smokers and ex-smokers, respectively. Among the ex-smokers, 81.1% of patients withheld smoking more than 10 years prior to surgery. Median lobe was present in 45 (13.9%) patients. BN-sparing was performed in 245 (76%), and 18 (5.6%) patients required BN reconstruction, either with separate interrupted stitches laterally at the 3 and 9 o’clock positions or with continuous anterior running suture. Nerve-sparing was performed in 285 (88.5%) patients: unilaterally in 85 (26.4%) and bilaterally in 200 (62.1%). Thermal energy use around NVBs was reported in 99 (30.7%) patients. Perineal pressure during anastomosis was required in 27 (8.3%) patients. There was one anastomotic stricture treated with direct vision internal urethrotomy, and one self-contained urine leak managed with prolonged Jackson-Pratt drainage for one week. No patient in this cohort had surgical intervention for PPI.

Patients’ baseline characteristics stratified according to current smoking and BN status are shown in Table 2. There were no significant differences between active smokers and non-smokers (ex-smokers and never-smokers). BN preservation...
Continence recovery is a major concern in patients treated with RARP for clinically localized prostate cancer.\textsuperscript{11} In general, urinary continence following prostatectomy is multifactorial in origin. Several perioperative risk factors have been studied extensively.\textsuperscript{12} More specifically, pelvic floor integrity, including neural and vascular integrity, seems to play a crucial role for urinary function recovery.\textsuperscript{13} Reeves et al reported the incidence of urinary function improvement in nerve-sparing prostatectomy in a large meta-analysis.\textsuperscript{4} Overall, 42.2%, 64.8%, 88.9%, and 83.9% of patients with NVB preservation were continent at six weeks, three months, six months, and 12 months, respectively. Our overall continence rates are in keeping with those results, considering that 88.5% of patients had either unilateral or bilateral nerve-sparing.

Identifying perioperative predictors of delayed functional recovery allows appropriate counselling and implementation of rehabilitation programs to hasten recovery. Traditionally recognized risk factors do not discriminate sufficiently between patients; therefore, any additional independent, new predictive factor will contribute to better prognostication and personalization of patient care. In our cohort, we documented three independent prognostic risk factors responsible for delayed continence recovery, including current cigarette smoking (hazard ratio [HR] 1.42; 95% confidence interval [CI] 1.01–1.88; \(p=0.04\)), BN resection (HR 1.41; 95% CI 95% 1.01–1.96; \(p=0.04\)), and larger prostate size (HR 0.99; 95% CI 0.98–0.99; \(p=0.02\)) at different intervals post-RARP up to 24 months. We further studied other potential operation-specific factors, such as thermal energy uses around NVB and perineal pressure during vesico-urethral anastomosis; neither demonstrated statistically significant relation.

With regards to smoking, there is paucity of data on its role in post-prostatectomy incontinence. To our knowledge, our study is the first to report negative effect of active smoking on continence recovery in RARP patients. Mao et al studied three-month continence recovery in 446 patients who underwent open radical prostatectomy in a recent retrospective cohort. In their study, age, preoperative pelvic floor muscle exercise, and BMI were predictors of continence recovery, but smoking was not.\textsuperscript{14} Similarly, a decade ago, Wille et al did not show a significant role for smoking on continence recovery in univariate analysis after open radical prostatectomy in a cohort of 742 patients.\textsuperscript{12}

The absence of tactile feedback made BN dissection a more challenging step during RARP. It has been reported that operation time for all steps of the surgery decreased quickly after 12–50 cases, but BN dissection and NVB preservation showed the slowest decrease.\textsuperscript{15} Freire et al demonstrated the value of BN-sparing on continence recovery four months after RARP.\textsuperscript{16} In their cohort, they studied 619 patients who underwent RARP in a prospectively collected database and they compared BN-sparing with standard technique. Continence recovery at four, 12, and 24 months were 65.6% vs. 26.5% (\(p<0.001\)), 86.4% vs. 81.4% (\(p=0.303\)), and 100% vs. 96.1% (\(p=0.308\)), respectively. Gacci et al conducted a multicenter, prospective study on 1972 patients who underwent radical prostatectomy (including open ret-

**Discussion**

Continence recovery is a major concern in patients treated with RARP for clinically localized prostate cancer. In general, urinary continence following prostatectomy is multifactorial in origin. Several perioperative risk factors have been studied extensively. More specifically, pelvic floor integrity, including neural and vascular integrity, seems to play a crucial role for urinary function recovery. Reeves et al reported the incidence of urinary function improvement in nerve-sparing prostatectomy in a large meta-analysis. Overall, 42.2%, 64.8%, 88.9%, and 83.9% of patients with NVB preservation were continent at six weeks, three months, six months, and 12 months, respectively. Our overall continence rates are in keeping with those results, considering that 88.5% of patients had either unilateral or bilateral nerve-sparing.

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| Table 1. Baseline characteristics |
|---------------------------------|
| Variables                       | n (%)            |
| Age, year                      |                  |
| Mean (median)                  | 60.8 (61)        |
| IQR                            | 56–66            |
| Charlson comorbidity index     |                  |
| 0–2                            | 124 (38.5)       |
| ≥3                             | 198 (61.5)       |
| Body mass index                |                  |
| Normal (\(≤25\) kg/m\(^2\))   | 62 (19.3)        |
| Overweight (>25–30 kg/m\(^2\))| 134 (41.6)       |
| Obese (>30 kg/m\(^2\))        | 70 (21.7)        |
| Unknown                        | 56 (17.4)        |
| Year of surgery                |                  |
| 2006–2010                      | 140 (43.5)       |
| 2011–2015                      | 182 (56.5)       |
| PSA                            |                  |
| Mean (median)                  | 6.8 (5.7)        |
| IQR                            | 4.58–7.65        |
| Prostate volume, g             |                  |
| Mean (median)                  | 49.6 (47)        |
| IQR                            | 38–57            |
| Pathological stage             |                  |
| T2a–b                          | 73 (22.7)        |
| T2c                            | 169 (52.5)       |
| T3a                            | 61 (18.9)        |
| T3b–T4                         | 19 (5.9)         |
| Pathological Gleason score     |                  |
| 3+3                            | 50 (15.5)        |
| 3+4                            | 201 (62.4)       |
| 4+3                            | 28 (8.7)         |
| ≥8                             | 43 (13.4)        |

IQR: interquartile range; PSA: prostate-specific antigen
ropubic, perineal, laparoscopic, and robotic approaches). In a multivariate analysis, they showed significant effect of BN-sparing on continence recovery at one month after surgery (p=0.003). Also, a randomized, controlled, single-blind study was reported by Nyarangi-Dix et al showing the significant effect of BN-sparing without compromising the oncological outcome at zero, three, six, and 12 months (p<0.001).

In fact, our results showed superior improvement in continence recovery in BN-sparing up to 12 months after surgery on multivariate analysis with a strict definition of continence. However, the presence of median lobe did not correlate with delayed continence recovery in our study. Similarly, Jenkins et al noted that median lobe had no effect on continence recovery after RARP in a cohort of 345 patients.

The effect of prostate size on urinary continence post-RARP is mixed according to available studies. In a retrospective study by Skolarus et al, recovery of continence in larger prostates (>100 g) was delayed compared to patients with smaller prostates (<50 g); the three-month continence rate after RARP was 44.0% compared to 62.2%, respectively (p=0.03). The latter results were limited by the low number of large prostates and short followup. Interestingly, in our cohort, the cutoff for prostate size that was found to correlate with delayed continence recovery was 47 g, which is in keeping with previous reports. In another retrospective analysis of a large cohort by Kumar et al, the one-year continence rate in 280 patients with prostate weight of ≥80 g was 85.8% compared to 95.1% in 2447 controls, but was not statistically different. However, time to continence (SD) was delayed to 3.3±4.4 months compared to 2.4±3.2 months (p<0.001). On the other hand, Link BA et al retrospectively analyzed 1847 patients who underwent RARP and subdivided them into four groups: prostate size <30 g, 30–50 g, 50–70 g, and >70 g.

Table 2. Baseline patients’ characteristics stratified according to current smoking and bladder neck (BN) status

| Variables                  | Non-smokers (and ex-smokers) n=278 | Active smokers n=44 | p   | BN resection n=77 | BN preservation n=245 | p   |
|----------------------------|-------------------------------------|---------------------|-----|------------------|-----------------------|-----|
| Age, years                 |                                     |                     |     |                  |                       |     |
| Mean (median)              | 60.9 (61)                           | 60 (60)             | 0.3 | 61.6 (62)        | 60.6 (61)             | 0.2 |
| IQR                        | 57–66                               | 56–65               |     | 59–66            | 56–66                 |     |
| Charlson comorbidity index, n (%) |                                  |                     |     |                  |                       |     |
| 0–2                        | 103 (37.1)                          | 21 (47.7)           | 0.2 | 20 (26)          | 104 (42.4)            | 0.01|
| ≥3                         | 175 (62.9)                          | 23 (52.3)           |     | 57 (74)          | 141 (57.6)            |     |
| Body mass index, n (%)     |                                     |                     |     |                  |                       |     |
| Normal (<25 kg/m²)         | 50 (18)                             | 12 (27.3)           |     | 9 (11.7)         | 53 (21.6)             |     |
| Overweight (25–30 kg/m²)   | 115 (41.4)                          | 19 (43.2)           | 0.4 | 37 (48.1)        | 97 (39.6)             | 0.2 |
| Obese (>30 kg/m²)          | 62 (22.3)                           | 8 (18.2)            |     | 18 (23.4)        | 52 (21.2)             |     |
| Unknown                    | 51 (18.3)                           | 5 (11.4)            |     | 13 (16.9)        | 43 (17.6)             |     |
| Year of surgery, n (%)     |                                     |                     |     |                  |                       |     |
| 2006–2010                  | 123 (44.2)                          | 17 (38.6)           | 0.6 | 30 (39)          | 110 (44.9)            | 0.4 |
| 2011–2015                  | 155 (55.8)                          | 27 (61.4)           |     | 47 (61)          | 135 (55.1)            |     |
| PSA                        |                                     |                     |     |                  |                       |     |
| Mean (median)              | 6.9 (5.8)                           | 6 (5.5)             | 0.5 | 6.6 (6.2)        | 6.9 (5.6)             | 0.1 |
| IQR                        | 4.6–7.7                             | 4.5–6.9             |     | 4.9–7.9          | 4.6–7.5               |     |
| Prostate volume, g         |                                     |                     |     |                  |                       |     |
| Mean (median)              | 49 (46)                             | 53.4 (49)           | 0.2 | 60 (56)          | 46 (44)               | <0.001|
| IQR                        | 38–57                               | 40–58               |     | 44–74            | 37–54                 |     |
| Pathological stage, n (%)  |                                     |                     |     |                  |                       |     |
| T2a–b                      | 60 (21.6)                           | 13 (29.5)           |     | 16 (20.8)        | 57 (23.3)             |     |
| T2c                        | 153 (55)                            | 16 (36.4)           | 0.1 | 39 (50.6)        | 130 (53.1)            | 0.8 |
| T3a                        | 49 (17.6)                           | 12 (27.3)           |     | 16 (20.8)        | 45 (18.4)             |     |
| T3b–T4                     | 16 (5.8)                            | 3 (6.8)             |     | 6 (7.8)          | 13 (5.3)              |     |
| Pathological Gleason score, n (%) |                              |                     |     |                  |                       |     |
| 6                          | 42 (15.1)                           | 8 (18.2)            | 0.8 | 13 (16.9)        | 37 (15.1)             | 0.4 |
| 3+4                        | 176 (63.3)                          | 25 (56.8)           |     | 49 (63.6)        | 152 (62)              |     |
| 4+3                        | 23 (8.3)                            | 5 (11.4)            |     | 3 (3.9)          | 25 (10.2)             |     |
| ≥8                         | 37 (13.3)                           | 6 (13.6)            |     | 12 (15.6)        | 31 (12.7)             |     |

IQR: interquartile range; PSA: prostate-specific antigen.
Impact of perioperative factors on continence recovery after RARP

Table 3. Predictive factors and continence rates (n [%]) of all patients at different time intervals during the first two years of followup

| Variables                  | 1 month (n=322) | 3 months (n=321) | 6 months (n=312) | 12 months (n=294) | 24 months (n=257) |
|----------------------------|-----------------|------------------|------------------|-------------------|-------------------|
|                            | C (n=126)       | I (n=196)        | C (n=187)        | I (n=134)         | C (n=228)         |
| Smoker                     |                 |                  |                  |                   |                   |
| No                         | 114 (90.5)      | 164 (83.7)       | 165 (88.2)       | 112 (83.6)        | 197 (88.7)        |
| Yes                        | 12 (9.5)        | 32 (16.3)        | 22 (11.8)        | 22 (16.4)         | 25 (11.3)         |
| BN preservation            |                 |                  |                  |                   |                   |
| No                         | 20 (15.9)       | 57 (29.1)        | 34 (18.2)        | 42 (31.3)         | 44 (19.8)         |
| Yes                        | 106 (84.1)      | 139 (70.9)       | 153 (81.8)       | 92 (68.7)         | 178 (80.2)        |
| NVB preservation           |                 |                  |                  |                   |                   |
| No                         | 8 (6.3)         | 29 (14.8)        | 17 (9.1)         | 20 (14.9)         | 22 (9.9)          |
| Unilateral                 | 36 (28.6)       | 49 (25)          | 49 (26.2)        | 35 (26.1)         | 60 (27)           |
| Bilateral                  | 82 (65.1)       | 118 (60.2)       | 121 (64.7)       | 79 (59)           | 140 (63.1)        |
| Prostate size (g)          |                 |                  |                  |                   |                   |
| ≤47                        | 77 (61.1)       | 87 (44.4)        | 109 (58.3)       | 55 (41)           | 129 (58.1)        |
| >47                        | 49 (38.9)       | 109 (55.6)       | 78 (41.7)        | 79 (59)           | 93 (41.9)         |
| Thermal use                |                 |                  |                  |                   |                   |
| No                         | 90 (71.4)       | 133 (67.9)       | 133 (71.1)       | 90 (67.2)         | 153 (68.9)        |
| Yes                        | 36 (28.6)       | 63 (32.1)        | 54 (28.9)        | 44 (32.8)         | 69 (31.1)         |
| Perineal pressure          |                 |                  |                  |                   |                   |
| No                         | 116 (92.1)      | 179 (91.3)       | 174 (93)         | 120 (89.9)        | 205 (92.3)        |
| Yes                        | 10 (7.9)        | 17 (8.7)         | 13 (7)           | 14 (10.4)         | 17 (7.7)          |
| Median lobe                |                 |                  |                  |                   |                   |
| No                         | 112 (88.9)      | 165 (84.2)       | 164 (87.7)       | 112 (83.6)        | 191 (86)          |
| Yes                        | 14 (11.1)       | 31 (15.8)        | 23 (12.3)        | 22 (16.4)         | 31 (14)           |

| Variables                  | 1 month (n=222) | 3 months (n=228) | 6 months (n=219) | 12 months (n=201) | 24 months (n=165) |
|----------------------------|-----------------|------------------|------------------|-------------------|-------------------|
|                            | C (n=90)        | I (n=90)         | C (n=90)         | I (n=90)          | C (n=90)          |
| Smoking                    |                 |                  |                  |                   |                   |
| No                         | 20 (22.2)       | 36 (40)          | 20 (22.2)        | 35 (38.8)         | 51 (28.6)         |
| Yes                        | 77 (77.8)       | 64 (60)          | 70 (77.8)        | 62 (61.2)         | 123 (71.4)        |
| BN preservation            |                 |                  |                  |                   |                   |
| No                         | 6 (6.6)         | 10 (11)          | 7 (7.7)          | 6 (6.6)           | 13 (7.7)          |
| Unilateral                 | 97 (87.4)       | 104 (114)        | 97 (87.4)        | 94 (87.4)         | 184 (107.7)       |
| Bilateral                  | 84 (75.4)       | 91 (82.2)        | 84 (75.4)        | 81 (75.4)         | 155 (90)          |
| Prostate size (g)          |                 |                  |                  |                   |                   |
| ≤47                        | 77 (66.7)       | 78 (68)          | 77 (66.7)        | 74 (68.4)         | 129 (71.8)        |
| >47                        | 49 (33.3)       | 51 (32)          | 49 (33.3)        | 46 (31.6)         | 93 (28.2)         |
| Thermal use                |                 |                  |                  |                   |                   |
| No                         | 90 (71.4)       | 133 (67.9)       | 133 (71.1)       | 90 (67.2)         | 153 (68.9)        |
| Yes                        | 36 (28.6)       | 63 (32.1)        | 54 (28.9)        | 44 (32.8)         | 69 (31.1)         |
| Perineal pressure          |                 |                  |                  |                   |                   |
| No                         | 116 (92.1)      | 179 (91.3)       | 174 (93)         | 120 (89.9)        | 205 (92.3)        |
| Yes                        | 10 (7.9)        | 17 (8.7)         | 13 (7)           | 14 (10.4)         | 17 (7.7)          |
| Median lobe                |                 |                  |                  |                   |                   |
| No                         | 112 (88.9)      | 165 (84.2)       | 164 (87.7)       | 112 (83.6)        | 191 (86)          |
| Yes                        | 14 (11.1)       | 31 (15.8)        | 23 (12.3)        | 22 (16.4)         | 31 (14)           |

50–70 g, and ≥70 g. One-year continence rates were not statistically different across all groups. In another retrospective study by Labanaris et al from a high-volume centre in Germany, 85 men had a pathological prostate specimen weight ≥100 g. A matched-pairs analysis was performed using a 4000-case RARP database to identify men with a pathological prostate specimen weight ≤50 g. Patients with larger glands had no difference regarding continence rates when compared to patients with smaller glands but exhibited significantly lower potency rates. The authors concluded that these results may not be generalized to a lower-volume centre. All the aforementioned studies considered various cutoffs for prostate volume grouping in a categorical manner. In multivariate analysis, we used prostate volume as a continuous variable. Our results showed that prostate volume is an independent predictor of continence recovery, statistically improving continence recovery throughout the first year.

Fig. 1. (A) Current smoker status has inferior continence recovery at all followup time points and reaches significant difference at six months. (B) Bladder neck (BN)-sparing statistically improves continence recovery throughout the first year.
Table 4. Multivariable Cox regression analysis

| Variable                        | HR (95% CI) | p     |
|--------------------------------|-------------|-------|
| Age                            | 0.99 (0.96–1.02) | 0.3   |
| Charlson comorbidity index     |             |       |
| 0–2                            | Reference   |       |
| ≥3                             | 1.12 (0.79–1.59) | 0.5   |
| BMI                            |             |       |
| ≤25                            | Reference   |       |
| >25–30                         | 0.99 (0.7–1.39) | 0.9   |
| >30                            | 0.83 (0.56–1.22) | 0.3   |
| Unknown                        | 0.85 (0.56–1.28) | 0.4   |
| PSA                            | 0.99 (0.96–1.02) | 0.5   |
| Prostate size                  | 0.99 (0.98–0.99) | **0.02** |
| Pathological stage             |             |       |
| T2a–b                          | Reference   |       |
| T2c                            | 1.06 (0.78–1.43) | 0.7   |
| T3a                            | 0.93 (0.61–1.41) | 0.7   |
| T3b–T4                         | 1.41 (0.73–2.72) | 0.3   |
| Gleason score                  |             |       |
| 6                              | Reference   |       |
| 3+4                            | 0.82 (0.58–1.17) | 0.3   |
| 4+3                            | 0.83 (0.48–1.46) | 0.5   |
| ≥8                             | 0.96 (0.55–1.67) | 0.9   |
| Operative time                 | 1.001 (1.001–1.01) | **0.03** |
| Smoking history                |             |       |
| No                             | Reference   |       |
| Yes                            | 1.42 (1.01–1.99) | **0.04** |
| Median lobe                    |             |       |
| No                             | Reference   |       |
| Yes                            | 1.18 (0.82–1.69) | 0.4   |
| Perineal pressure              |             |       |
| No                             | Reference   |       |
| Yes                            | 1.1 (0.68–1.77) | 0.7   |
| Thermal use                    |             |       |
| No                             | Reference   |       |
| Yes                            | 0.9 (0.69–1.19) | 0.5   |
| BN sparing                     |             |       |
| No                             | Reference   |       |
| Yes                            | 1.41 (1.01–1.96) | **0.04** |
| NVB preservation               |             |       |
| No                             | Reference   |       |
| Unilateral                     | 1.53 (0.96–2.44) | 0.08  |
| Bilateral                      | 1.41 (0.91–2.2) | 0.1   |

Bold numbers=statistically significant difference (p<0.05). BMI: body mass index; BN: bladder neck; CI: confidence interval; HR: hazard ratio; NVB: neurovascular bundles; PSA: prostate-specific antigen.

Albeit the effect was small (HR 0.99; 95% CI 0.98–0.99; p=0.02). In further subanalysis, we found that large prostate size and BN resection are two closely related variables and they act as confounders for each other, but each can delay continence recovery as an independent predictor in a multivariate analysis.

Older age is a commonly reported risk factor for urinary incontinence post-prostatectomy. Different studies described the increasingly risk of urinary incontinence following radical prostatectomy with older age. On the other hand, other studies showed that aging was not associated with delayed continence recovery. In our study, the majority of patient were young, with a mean age of 60 years, and narrowly distributed, with an interquartile range of 56–66 years. Therefore, age was not found to be an independent predictor.

Future perspectives should include special investigations, such as urodynamic studies to better understand the pathophysiology PPI in active smokers undergoing RARP. Those investigations may differentiate whether the mechanism behind this particular type of incontinence is at the level of the bladder wall, sphincter level, pelvic support system, or a combination of the above. Further studies are also needed to assess if smoking cessation for a certain period before the intervention would mitigate the detrimental effect. In general, better understanding of risk factors may improve counselling and help patients prepare, cope, and work harder to recuperate functional outcomes. Implementation of pre- and postoperative rehabilitation strategies may be of particular benefit in patients at risk.

Our study is complementary to existing literature. It has examined new variables over a longer followup. However, it is not without limitations. This is a single-centre, single-surgeon observational study, with a retrospective analysis of, albeit prospectively collected, data. The sample size under investigation is small and the case load per year is limited by scarce resources in the Canadian public health system. Continence was assessed by non-validated questionnaire, although definition used (0 pad) is commonplace. PPI was not further characterized (urge vs. stress) with urodynamic studies and no pad weight was noted. We also did not record the use of overactive bladder medications. Furthermore, we could not calculate a dose effect of smoking on PPI due to missing data on the amount of smoking per patient. Lastly, the definition of some intraoperative variables was inherently subjective, including BN-sparing and extent of NVB preservation. In an effort to minimize inconsistency, the lead investigator recorded all intraoperative variables prospectively on an established data collection sheet in a real-time manner.

**Conclusion**

The association between active smoking and postoperative urinary incontinence has not been well-documented following RARP. Our results demonstrate that smoking might be an independent risk factor for delayed continence recovery after RARP. Active smokers who have other risk factors for delayed continence recovery, such as large prostate glands and non-BN-sparing should be counselled about the increased risk of urinary incontinence postoperatively. Other studies are required to further investigate the pathophysiological mechanisms involved in post-prostatectomy urinary incontinence in relation with smoking.
Impact of perioperative factors on continence recovery after RARP

Competing interests: Dr. Zorn has received honoraria as proctor/lecturer for Boston Scientific, and participated in the WATER II clinical trial with Aquablation supported by PROCEPT BioRobotics. The remaining authors report no competing personal or financial interests related to this work.

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