Predictors of deviation in neurovascular bundle preservation during robotic prostatectomy

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Introduction: *Neurovascular bundle (NVB) preservation during robot-assisted radical prostatectomy (RARP) directly affects patient functional outcomes. Despite careful surgical planning, many NVB preservation techniques are changed intraoperatively from their preoperative plan. Our objective was to identify risk factors predicting intraoperative change in NVB preservation technique during RARP.*

Materials and methods: *Prospective data from 578 RARPs performed by a single surgeon between 2010 and 2017 at a tertiary care center. Side-specific NVB preservation technique was planned preoperatively. Surgical techniques were either complete nerve sparing (CNS), or incomplete nerve sparing (INS). Variables included age, tumor grade, prostate volume, number of lifetime biopsies, history of post-biopsy sepsis, and laterality. Variables were modeled in multivariable logistic regressions as potential predictors of deviation in surgical technique. Functional and oncological outcomes were also assessed.*

Results: *A total of 46.9% of cases underwent some intraoperative change in NVB preservation from their preoperative plan. A total of 37.7% of 880 prostate sides planned for CNS underwent unplanned INS. Older age, Gleason ≥ 3+4, post-biopsy sepsis, prostate volume, and left-sided dissections were significantly associated with unplanned INS. Number of lifetime biopsies was not a predictor of unplanned INS. Patients with an intraoperative change to INS had poorer potency and continence. Study limitations included the retrospective nature of analysis and lack of pathological assessment of NVB preservation.*

Conclusions: *Age, Gleason ≥ 3+4, post-biopsy sepsis, prostate volume, and laterality were significant predictors of unplanned INS during RARP, which should guide patient counseling when discussing risks and functional outcomes. The number of lifetime biopsies did not predict unplanned INS, a valuable finding for patients on active surveillance. Our findings highlight the importance of careful preoperative planning and novel adjuncts such as multiparametric MRI.*

Key Words: neurovascular bundle, radical prostatectomy

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Introduction

Radical prostatectomy (RP) has long been the gold standard treatment for localized prostate cancer. Neurovascular bundle (NVB) preservation during RP aims to achieve complete oncological resection, while maintaining the integrity of periprostatic nerves to optimize functional outcomes, namely potency and urinary continence.[1-3] The advent of robot-assisted radical prostatectomy (RARP) has aided in the precision of interfascial, or nerve sparing, and extrafascial techniques of NVB preservation. In 2012, Ficarra et al were the first to provide a systematic review and meta-analysis on this subject, showing a statistically significant advantage in functional outcomes using RARP versus retropubic RP and laparoscopic RP in terms of functional outcome.[4] Similarly, Coelho et al, as well as multiple others have demonstrated equal or improved functional and oncological outcomes of RARP.[5-9]

However, due to concerns regarding positive surgical margins (PSM), nerve sparing is sometimes difficult to achieve in patients with locally advanced prostate cancer invading the adjacent NVB. Careful surgical planning must be undertaken to ensure the use of an appropriate and individualized resection technique, while avoiding oncological complications.[10,11] Therefore, multiple nomograms have been developed and validated for planning NVB preservation in patients undergoing RARP based on preoperative risk factors, as well as side-specific risks for extracapsular extension (ECE).[12-15]

Despite the use of nomograms and careful patient counseling at our institution, our experience has shown that a significant proportion of NVB preservation techniques during RARP are changed intraoperatively. Reasons for deviation in technique can include challenging anatomical features (e.g. narrow pelvis, amount of fatty tissues), disrupted surgical planes, and other factors leading to more difficult resections. To the best of our knowledge, in the English language literature, no studies discuss risk factors for intraoperative deviation from preoperatively planned NVB preservation technique. The aim of our study is to identify patient and disease risk factors that may predict such intraoperative changes.

Materials and methods

We performed retrospective analysis of data obtained from a prospectively collected, IRB-approved Canadian database. A total of 578 RARPs performed by a single surgeon with an over 2000-case experience between January 2010 and September 2017 using side-specific NVB preservation techniques were reviewed. Preoperative planning of surgical technique was guided by the validated Kattan nomogram estimating the risk of ECE based on preoperative factors including clinical tumor stage, prostate-specific antigen (PSA) level, Gleason score on biopsy, and number of positive biopsy cores.[16] Other patient factors such as age, preoperative Sexual Health Inventory for Men (SHIM) score, and patient preference guided patient counseling and surgical planning.

Surgical techniques included either interfascial, partial extrafascial, or wide extrafascial resection planes, and were previously described by our team.[15] Complete nerve sparing (CNS) was defined as purely interfascial technique (dissection at the avascular plane between the prostatic fascia and Denonvilliers' fascia), while partial extrafascial and wide extrafascial techniques (wider dissection into the NVB) were considered as incomplete nerve sparing (INS). Partial extrafascial technique (or partial nerve sparing) was included in a separate group from the purely interfascial technique to capture factors that would prevent our expert surgeon to achieve a completely nerve-sparing technique, which was the true intent when planning patients for periprostatic nerve sparing. Side-specific (left and right) planning was done, and compared to the final intraoperative technique to look for change in surgical technique on either side. Final NVB preservation status was determined by the surgeon's assessment intraoperatively, as described by our team.[15]

Multivariable logistic regression models were used to determine if different patient characteristics, disease, or biopsy-related variables were significant predictors of deviation in surgical technique. Preoperative variables included age, body mass index (BMI), SHIM score, PSA level, prostate volume on transrectal ultrasound (TRUS), disease stage and grade, number of previous lifetime biopsies, and history of post-TRUS biopsy sepsis. In addition to patient-specific analyses, prostate side-specific analyses were performed, and also included variables such as laterality, maximum percentage of disease in ipsilateral positive core biopsies, total number of ipsilateral positive core biopsies, and ipsilateral ECE on final pathology. Preoperative characteristics underwent initial univariate analyses, with significant ($p < 0.05$) and near-significant characteristics ($p < 0.10$) being selected for multivariate analyses.

We also assessed the impact of deviation in NVB preservation on functional outcomes, namely potency and urinary continence, and on oncological outcomes, more specifically PSM and biochemical recurrence (BCR). Urinary continence was defined using the number of daily protective pads used by the patient (either 1 protective pad per day at most, or strictly no pads), and potency was defined as the ability to penetrate, with a SHIM score of 17 or more (with at least a score of 3 on question number 2) and/or an

TABLE 1. **Sample preoperative characteristics based on preoperative plan**

	All patients (n = 578)	Bilateral CNS (n = 381/65.9%)	Unilateral CNS (n = 118/20.4%)	Bilateral INS (n = 79/13.7%)	p value
Mean age (years)	60.7 ± 6.7	60.0 ± 6.7	60.7 ± 6.6	63.7 ± 6.0	< 0.001
Mean BMI (kg/m^2)	27.2 ± 3.8	26.8 ± 3.4	27.3 ± 3.4	29.1 ± 5.4	< 0.001
Mean PSA (ng/mL)	6.4 ± 3.4	6.1 ± 3.3	6.3 ± 3.1	8.2 ± 4.2	< 0.001
Mean TRUS prostate volume (mL)	41.7 ± 19.2	41.3 ± 19.8	41.4 ± 16.8	43.8 ± 19.3	0.57
Biopsy Gleason score [n (%)]					< 0.001
6	149 (25.8%)	131 (34.3%)	17 (14.4%)	1 (1.3%)	
7	372 (64.4%)	241 (63.3%)	77 (65.3%)	54 (68.3%)	
8	44 (7.6%)	6 (1.6%)	19 (16.1%)	19 (24.1%)	
9	13 (2.2%)	3 (0.8%)	5 (4.2%)	5 (6.3%)	
Clinical tumor stage [n (%)]					< 0.001
T1b	1 (0.2%)	1 (0.3%)	0	0	
T1c	472 (81.7%)	347 (91.0%)	70 (59.3%)	55 (69.5%)	
T2a	76 (13.1%)	27 (7.1%)	33 (28.0%)	16 (20.3%)	
T2b	25 (4.3%)	5 (1.3%)	14 (11.9%)	6 (7.6%)	
T2c	3 (0.5%)	1 (0.3%)	1 (0.8%)	1 (1.3%)	
T3	1 (0.2%)	0	0	1 (1.3%)	
Pathological tumor stage [n (%)]					< 0.001
T2	330 (57.1%)	248 (65.1%)	50 (42.4%)	32 (40.5%)	
T3	248 (42.9%)	133 (34.9%)	68 (57.6%)	47 (59.5%)	
> 1 lifetime biopsy [n (%)]	120 (20.8%)	82 (21.5%)	22 (18.6%)	16 (20.3%)	0.79
Mean number of lifetime biopsy cores	12.2 ± 1.3	12.1 ± 1.4	12.3 ± 1.2	12.1 ± 0.8	0.38
Mean time from last biopsy to RARP (days)	163.6 ± 107.5	168.2 ± 107.8	157.3 ± 97.2	151.0 ± 120.3	0.34
Post-biopsy sepsis [n (%)]	20 (3.5%)	16 (4.2%)	1 (0.8%)	3 (3.8%)	0.22
Means preoperative SHIM score	19.0 ± 6.6	19.7 ± 6.2	19.2 ± 6.7	15.2 ± 7.3	< 0.001

CNS = complete nerve sparing; INS = incomplete nerve sparing; BMI = body mass index; PSA = prostate-specific antigen; TRUS = transrectal ultrasound; RARP = robot-assisted radical prostatectomy; SHIM = sexual health inventory for men

Erection Hardness Scale score ≥ 3 with or without phosphodiesterase type 5 inhibitors. PSM was defined as the presence of cancer at the inked margin, while BCR was defined as a rising PSA > 0.20 ng/mL.

Results

Table 1 summarizes the different preoperative characteristics of the 578 patients included in this study based on the preoperative surgical plan for NVB preservation. In our sample, 381 (65.9%), 118 (20.4%), and 79 (13.7%) patients were planned for bilateral CNS, unilateral CNS, and bilateral INS, respectively. As expected, patients with a plan for bilateral CNS were significantly younger, had lower PSA levels, had lower clinical and pathological tumor stage, and had lower biopsy Gleason grade disease compared to patients with planned bilateral INS ($p < 0.001$ for all). Patients with planned bilateral CNS had also significantly lower BMIs ($p < 0.001$) than other groups.

As outlined in Table 2, intraoperative deviation in surgical technique occurred in 271 men (46.9%). Of those planned for bilateral CNS, 176 (46.2%) underwent at least one unplanned INS (unilateral or bilateral). A total of 375 (32.4%) of the 1156 prostate sides analyzed underwent a change from preoperative plan, with 332 (37.7%) of the 880 sides planned for CNS undergoing unplanned INS.

Table 3 describes the binary logistic regressions performed on variables as potential predictors of patients experiencing at least one unplanned INS on either side, or as predictors of bilateral unplanned INS. On multivariate analysis, older age (OR 1.07 [95%CI

TABLE 2. **Patterns in deviation in neurovascular bundle preservation technique**

Patient-specific	
All (n = 578)	
Any change	271 (46.9%)
Any bilateral change	104 (18.0%)
Any unilateral change only	167 (28.9%)
At least one unplanned INS	234 (40.5%)
Bilateral unplanned INS	98 (17.0%)
Unilateral unplanned INS only	133 (23.0%)
At least one unplanned CNS	40 (6.9%)
Bilateral unplanned CNS	3 (0.5%)
Unilateral unplanned CNS only	34 (5.9%)
Unilateral unplanned INS and CNS	3 (0.5%)
Planned bilateral CNS (n = 381)	
At least one unplanned INS	176 (46.2%)
Bilateral unplanned INS	98 (25.7%)
Unilateral unplanned INS only	78 (20.5%)
Planned unilateral CNS (n = 118)	
Any change	80 (67.8%)
Any bilateral change	3 (2.5%)
Any unilateral change only	77 (65.3%)
At least one unplanned INS	58 (49.2%)
Unilateral unplanned INS only	55 (46.6%)
At least one unplanned CNS	25 (21.2%)
Unilateral unplanned CNS only	22 (18.6%)
Planned bilateral INS (n = 79)	
At least one unplanned CNS	15 (19.0%)
Bilateral unplanned CNS	3 (3.8%)
Unilateral unplanned CNS only	12 (15.2%)
Prostate side-specific	
All (n = 1156)	
Any change	375 (32.4%)
Unplanned INS	332 (28.7%)
Unplanned CNS	43 (3.7%)
Planned CNS (n = 880)	
Unplanned INS	332 (37.7%)
Planned INS (n = 276)	
Unplanned CNS	43 (15.6%)

INS = incomplete nerve sparing; CNS = complete nerve sparing

1.04-1.11]; p < 0.001) and Gleason score ≥ 3+4 (OR 2.33 [95%CI 1.48-3.68]; p < 0.001) were associated with a higher probability of at least one unplanned INS. Older age (OR 1.09 [95%CI 1.05-1.14]; p < 0.001) and having a history of post-TRUS biopsy sepsis (OR 4.16 [95%CI 1.56-11.09]; p = 0.004) were significant predictors of unplanned bilateral INS in multivariate analyses. There were no significant predictors of unplanned CNS at the patient level in multivariate analyses.

Table 4 describes the binary logistic regressions performed for predictors of side-specific deviation in surgical technique. Older age (OR 1.07 [95%CI 1.05-1.10]; p < 0.001), larger prostate volume on TRUS (OR 1.01 [95%CI 1.00-1.02]; p = 0.04), history of post-biopsy sepsis (OR 2.34 [95% CI 1.18-4.65]; p = 0.02), Gleason ≥ 3+4 (OR 1.87 [95%CI 1.30-2.68]; p = 0.01), and left-sided dissections (OR 1.34 [95%CI 1.02-1.76]; p = 0.04) were significant predictors of side-specific unplanned INS.

TABLE 3. **Patient-specific binary logistic regressions for unplanned incomplete nerve sparing**

At least one unplanned incomplete nerve sparing				
	Univariate		**Multivariate**	
	OR [95% CI]	**p value**	**OR [95% CI]**	**p value**
Age (years)	1.09 [1.06-1.12]	< 0.001	1.07 [1.04-1.10]	< 0.001
BMI (kg/m^2)	1.00 [0.96-1.05]	0.91	-	-
PSA (ng/mL)	1.05 [0.99-1.10]	0.06	1.01 [0.96-1.07]	0.66
TRUS prostate volume (mL)	1.01 [1.00-1.02]	0.01	1.01 [1.00-1.02]	0.12
cStage (cT2 vs. cT1)	1.68 [1.09-2.57]	0.02	1.22 [0.77-1.95]	0.40
pStage (pT3 vs. pT2)	1.56 [1.11-2.19]	0.01	1.21 [0.83-1.77]	0.32
Gleason score ≥ 3+4	3.10 [2.01-4.77]	< 0.001	2.25 [1.42-3.57]	< 0.001
Preoperative SHIM score	0.97 [0.95-0.99]	0.01	1.00 [0.97-1.03]	0.85
Post-biopsy sepsis	1.84 [0.75-4.50]	0.18	-	-
Biopsy to RARP (days)	1.00 [0.99-1.00]	0.61	-	-
More than 1 lifetime biopsy	1.06 [0.71-1.60]	0.77	-	-
Number of lifetime cores	1.15 [1.00-1.32]	0.06	1.10 [0.95-1.29]	0.21
Unplanned bilateral incomplete nerve sparing				
	Univariate		**Multivariate**	
	OR [95% CI]	**p value**	**OR [95% CI]**	**p value**
Age (years)	1.11 [1.07-1.16]	< 0.001	1.09 [1.05-1.14]	< 0.001
BMI (kg/m^2)	1.04 [0.98-1.10]	0.19	-	-
PSA (ng/mL)	1.05 [0.99-1.11]	0.14	-	-
TRUS prostate volume (mL)	1.01 [1.00-1.02]	0.01	1.01 [1.00-1.02]	0.19
cStage (cT2 vs. cT1)	1.53 [0.82-2.87]	0.18	-	-
pStage (pT3 vs. pT2)	1.06 [0.68-1.66]	0.80	-	-
Gleason score ≥ 3+4	1.96 [1.11-3.48]	0.02	1.41 [0.77-2.58]	0.27
Preoperative SHIM	0.94 [0.92-0.97]	< 0.001	0.97 [0.94-1.00]	0.06
Post-biopsy sepsis	3.47 [1.38-8.72]	0.008	4.16 [1.56-11.09]	0.004
Biopsy to RARP (days)	1.00 [0.99-1.00]	0.75	-	-
More than 1 lifetime biopsy	1.58 [0.96-2.60]	0.07	1.51 [0.90-2.54]	0.12
Number of lifetime cores	1.06 [0.92-1.22]	0.45	-	-

BMI = body mass index; PSA = prostate-specific antigen; TRUS = transrectal ultrasound; cStage = clinical tumor stage; pStage = pathological tumor stage; SHIM = sexual health inventory for men = RARP = robot-assisted radical prostatectomy

Similarly, older age (OR 0.95 [0.91-0.99]; p = 0.03) and dissections on the left side (OR 0.52 [0.28-0.99]; p = 0.05) were associated with a decreased probability of unplanned side-specific CNS.

Figure 1 shows the percentage of patients who were planned for unilateral or bilateral CNS and did not undergo any unplanned INS according to age group and Gleason score. It highlights a significant downward trend in successful CNS with increasing age, as well as a lower success rate in Gleason ≥ 3+4 for all age groups. Similarly, Figure 2 shows the percentage of successfully planned side-specific CNS techniques according to age and history of post-biopsy sepsis, showing the same downward trend with increasing age and the negative impact of sepsis on success rates for all age groups, except one. Figure 3 presents the percentage of successfully planned side-specific CNS techniques based on prostate volume and laterality (right and left), showing a significant decrease in larger prostates, and the consistently lower success rates in left-sided dissections compared to the right side.

TABLE 4. **Prostate side-specific binary logistic regressions for deviation in neurovascular bundle preservation technique**

Side-specific unplanned incomplete nerve sparing	**Univariate**		**Multivariate**	
	OR [95% CI]	**p value**	**OR [95% CI]**	**p value**
Age (years)	1.09 [1.07-1.11]	< 0.001	1.07 [1.05-1.10]	< 0.001
BMI (kg/m²)	1.02 [0.98-1.05]	0.39	-	-
PSA (ng/mL)	1.04 [1.01-1.08]	0.02	1.01 [0.98-1.06]	0.49
TRUS prostate volume (mL)	1.01 [1.01-1.02]	0.01	1.01 [1.00-1.02]	0.04
cStage (cT2 vs. cT1)	1.19 [0.86-1.64]	0.30	-	-
pStage (pT3 vs. pT2)	1.27 [0.98-1.65]	0.07	0.92 [0.65-1.29]	0.63
Gleason score ≥ 3+4	2.50 [1.78-3.51]	< 0.001	1.87 [1.30-2.68]	0.01
Preoperative SHIM score	0.96 [0.94-0.98]	< 0.001	0.99 [0.97-1.01]	0.18
Post-biopsy sepsis	2.32 [1.23-4.38]	0.01	2.34 [1.18-4.65]	0.02
Biopsy to RARP (days)	1.00 [1.00-1.00]	0.56	-	-
More than 1 lifetime biopsy	1.23 [0.90-1.67]	0.20	-	-
Number of lifetime cores	1.08 [0.99-1.19]	0.09	1.06 [0.96-1.17]	0.27
Laterality (left vs. right)	1.31 [1.02-1.69]	0.04	1.34 [1.02-1.76]	0.04
Ipsilateral max % positive in cores	1.00 [1.00-1.01]	0.75	-	-
Number of ipsilateral positive cores	0.99 [0.92-1.05]	0.66	-	-
Ipsilateral ECE on pathology	1.42 [1.05-1.94]	0.02	1.29 [0.86-1.92]	0.22

Side-specific unplanned complete nerve sparing	**Univariate**		**Multivariate**	
	OR [95% CI]	**p value**	**OR [95% CI]**	**p value**
Age (years)	0.95 [0.91-0.99]	0.03	0.95 [0.91-0.99]	0.03
BMI (kg/m²)	0.95 [0.87-1.03]	0.22	-	-
PSA (ng/mL)	1.05 [0.97-1.13]	0.24	-	-
TRUS prostate volume (mL)	0.98 [0.96-1.00]	0.11	-	-
cStage (cT2 vs. cT1)	0.88 [0.39-2.00]	0.76	-	-
pStage (pT3 vs. pT2)	1.29 [0.70-2.37]	0.42	-	-
Gleason score ≥ 3+4	1.15 [0.56-2.37]	0.70	-	-
Preoperative SHIM score	1.03 [0.98-1.08]	0.32	-	-
Post-biopsy sepsis	0 [0-0]	1.0	-	-
Biopsy to RARP (days)	1.00 [1.00-1.00]	0.47	-	-
More than 1 lifetime biopsy	1.01 [0.48-2.14]	0.98	-	-
Number of lifetime cores	1.02 [0.83-1.26]	0.83	-	-
Laterality (left vs. right)	0.52 [0.28-0.99]	0.05	0.52 [0.28-0.99]	0.05
Ipsilateral max % positive in cores	1.00 [0.99-1.01]	0.45	-	-
Number of ipsilateral positive cores	1.02 [0.87-1.20]	0.79	-	-
Ipsilateral ECE on pathology	1.40 [0.70-2.83]	0.34	-	-

BMI = body mass index; PSA = prostate-specific antigen; TRUS = transrectal ultrasound; cStage = clinical tumor stage; pStage = pathological tumor stage; SHIM = sexual health inventory for men = RARP = robot-assisted radical prostatectomy; ECE = extracapsular extension

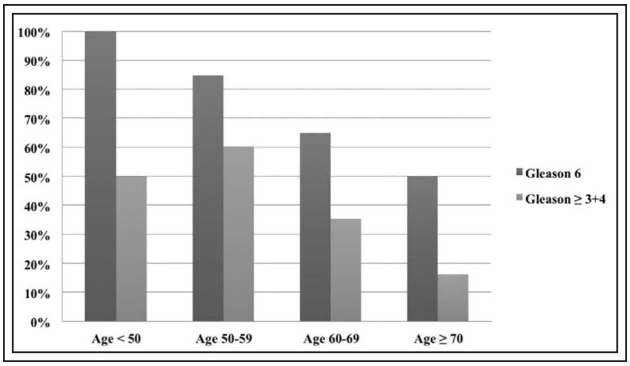

Figure 1. Proportion of patients with fully successful planned complete nerve sparing by age group and Gleason score ($p < 0.001$).

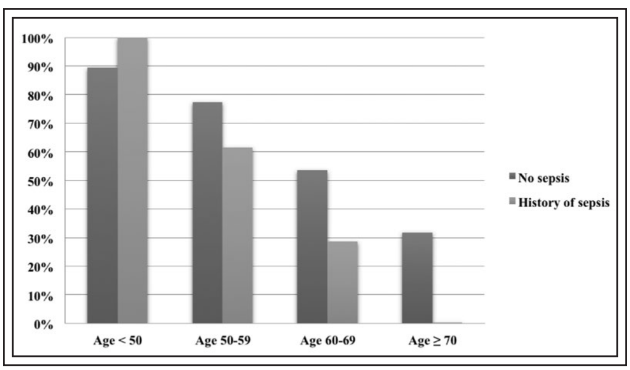

Figure 2. Proportion of side-specific successful planned complete nerve sparing by age group and history of post-biopsy sepsis ($p < 0.001$).

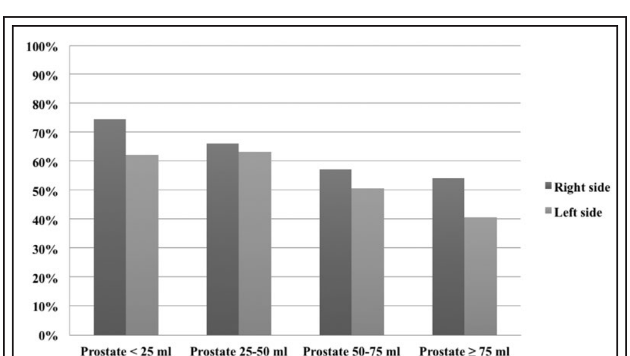

Figure 3. Proportion of side-specific successful planned complete nerve sparing by prostate volume on transrectal ultrasound and laterality ($p = 0.005$).

We provide here additional data not presented in tables or figures. In men with no history of post-TRUS biopsy sepsis, 24.7% of planned bilateral CNS were changed to bilateral INS intraoperatively. A significant difference was seen in patients with a history of post-TRUS biopsy sepsis, as 50.0% of those with bilateral CNS underwent bilateral INS ($p = 0.02$). Unplanned INS occurred in 40.4% of left-sided dissections, compared to 35.0% on the right side ($p = 0.10$). While prostate volume was included as a continuous variable in regression models, prostates greater than 50 mL in volume on TRUS were found to have side-specific unplanned INS in 47.8% of cases, whereas unplanned INS occurred in 34.7% of sides in prostates less than 50 mL ($p = 0.001$). On average, patients who underwent side-specific unplanned CNS were significantly younger than patients without such deviation (58.5 ± 6.8 versus 63.2 ± 6.1 years of age; $p < 0.001$).

Of note, number of previous lifetime core biopsies, time from biopsy to RARP, and BMI were not significant predictors of unplanned INS in multivariate analyses. Also, while only Gleason ≥ 3+4 is reported here, other Gleason scores were tested as potential thresholds to predict deviation in surgical technique (including 4+3), with only Gleason ≥ 3+4 versus Gleason 6 showing a statistically significant effect on univariate analysis in all models.

Table 5 presents patient oncological and functional outcomes at different follow up times based on deviation in surgical technique, suggesting less favorable outcomes in both potency and urinary continence for those undergoing unplanned INS. PSM and BCR were not significantly affected by deviation in surgical technique, except for patients undergoing at least one unplanned CNS, which was actually associated with decreased PSM (not side-specific) compared to those without such deviation (12.5% versus 32.5%; $p = 0.01$). We also performed side-specific analysis comparing deviation in surgical technique to ipsilateral PSM. Both side-specific unplanned INS (6.6% versus 8.9%; $p = 0.22$) and unplanned CNS (4.7% versus 13.7%; $p = 0.10$) were associated with a decreased rate of ipsilateral PSM compared to patients without such deviation, but neither association was statistically significant (data not presented in tables).

Discussion

RARP represents the main surgical procedure in North America for the treatment of localized prostate cancer. Complete oncological resection with maximal functional outcomes remains the primary, challenging

TABLE 5. Functional and oncological outcomes of patients undergoing deviation in neurovascular bundle preservation technique

	Any unplanned INS		Bilateral unplanned INS		Any unplanned CNS	
Follow up	**%**	**p value**	**%**	**p value**	**%**	**p value**
Potency						
6 months	14.7% vs. 56.6%	< 0.001	8.5% vs. 53.4%	< 0.001	42.9% vs. 8.6%	< 0.001
12 months	23.9% vs. 63.6%	< 0.001	10.2% vs. 62.4%	< 0.001	34.6% vs. 18.8%	0.08
24 months	32.2% vs. 69.2%	< 0.001	15.9% vs. 69.6%	< 0.001	38.1% vs. 23.9%	0.20
Urinary continence (1 protective pad, or no pads per day)						
6 months	88.2% vs. 94.2%	0.03	83.1% vs. 93.8%	0.01	89.3% vs. 81.2%	0.31
12 months	93.7% vs. 95.1%	0.56	88.3% vs. 96.0%	0.03	92.3% vs. 87.1%	0.47
24 months	93.4% vs. 95.1%	0.55	88.6% vs. 96.3%	0.05	85.7% vs. 93.1%	0.29
Urinary continence (Strictly no pads per day)						
6 months	72.6% vs. 81.6%	0.03	74.6% vs. 78.8%	0.47	75.0% vs. 69.2%	0.55
12 months	83.5% vs. 89.7%	0.09	78.3% vs. 90.5%	0.01	84.6% vs. 78.2%	0.47
24 months	88.4% vs. 90.9%	0.51	81.8% vs. 92.5%	0.04	85.7% vs. 81.9%	0.69
PSM						
-	19.7% vs. 26.3%	0.08	18.4% vs. 22.3%	0.41	12.5% vs. 32.5%	0.01
BCR						
-	7.6% vs. 8.4%	0.77	7.8% vs. 6.3%	0.62	8.1% vs. 13.5%	0.38

INS = incomplete nerve sparing; CNS = complete nerve sparing; PSM = positive surgical margins; BCR = biochemical recurrence

objective of such a treatment modality. The use of validated preoperative tools for predicting ECE aids surgeons to appropriately stratify patients for surgical planning, patient counseling, and reduction of adverse outcomes. Despite the use of such tools and surgeon experience, a substantial number of operations undergo intraoperative change with regards to their preoperative plan. As this remains an underreported phenomenon, this study provides the first analysis of preoperative risk factors in relation to intraoperative adjustments in NVB preservation technique.

Firstly, we found that deviation in surgical technique was common, occurring in 46.9% of cases, with 18.0% of men undergoing a bilateral change in technique. Our results highlight that age is a significant risk factor in the deviation of CNS to INS. As illustrated in Figure 1 and Figure 2, a clear downward trend is seen regarding the proportion of successfully planned CNS with increasing age. In a recent study of 35,968 men, Pereira et al highlighted that increasing age independently predicted perioperative complications.[17] In addition to perioperative events, Mandel et al have shown an important, independent negative effect of age on functional outcomes including the recovery of continence and potency after prostatectomy.[18] With this knowledge, surgeon bias may exist with older surgical patients during difficult dissections, resulting in wider planes to ensure complete oncologic resection, with less consideration for function. These findings highlight the importance of age in preoperative counseling, regardless of erectile function.

As expected, we demonstrated the negative impact of unplanned INS on functional outcomes in Table 5. Patients with the same surgical plan for NVB preservation had poorer urinary continence and potency rates across follow up times if they had unplanned INS. While these findings are more likely due to final NVB preservation status rather than deviation in surgical technique, they highlight the well-known negative impact of INS on functional outcomes, as well as the importance of identifying patterns and risk factors for deviation to such technique. With regards to oncological outcomes, PSM and BCR were not significantly affected by deviation in surgical technique, except for patients undergoing unplanned CNS, who were found to have lesser PSM rates. This can be explained by the fact that these patients had likely more favorable surgical planes, leading to easier, better prostatic and capsular dissections.

Secondly, we found that post-biopsy sepsis was a significant risk factor for unplanned INS across age groups, as shown in Figure 2. Our results are in accordance with reports of difficult procedures following post-biopsy sepsis, and can be attributed to the significant inflammatory changes that occur, including fibrosis and adhesions, which disrupt the differentiation of surgical planes.[19]

In addition, our results show that without the presence of sepsis, the number of biopsies proves no correlation to an increase in INS. Similarly, Rosenbaum et al have found that patients undergoing repeated biopsies show comparable functional outcomes to those only undergoing a single biopsy.[20] These results have important implications for patient counseling, in particular for those under active surveillance, as there appears to be no increase in risk of intraoperative changes or adverse functional outcomes due to repeated biopsies. However, patients who have experienced post-biopsy sepsis should be counseled on their increased intraoperative and postoperative risks.

Thirdly, our results suggest that Gleason 3+4 and above is associated with more unilateral unplanned INS, regardless of the affected side. As seen in Figure 1, such disease consistently led to less successfully planned CNS than lower-grade disease across all age groups. These results may be explained again by some component of surgeon bias, stemming from fear of PSM with higher-grade disease, regardless of the affected side.

Larger prostates are known to lead to longer operative time and more difficult prostatectomy cases, and it has been shown that RARP does not reduce this impact.[21,22] As outlined in Figure 3, a consistent and significant decrease in successful side-specific CNS was seen with increasing prostate volume, which may suggest that large prostate also lead to more challenging dissection of the NVB. Moreover, our analyses showed that left-sided dissections were associated with more unplanned INS and less unplanned CNS than on the right side. This may be explained by the fact that the surgeon in our study is right-handed, leading to a more difficult precision in left-sided dissections because of the dominant robotic arm having to reach to the other side, and more challenging access to surgical planes. Further studies should try to compare these findings to those with an experienced, left-handed surgeon.

Finally, our study did not find any correlation between shorter time from biopsy to surgery and deviation in NVB preservation technique. Although no other intraoperative studies were found, Martin et al demonstrated that RARPs performed sooner after TRUS biopsy (4 week and 6 week thresholds) were associated with more postoperative complications.[23] While residual inflammation was offered as a possible explanation, our sample did not reveal a similar intraoperative correlation, possibly since very few patients had RARP within 6 weeks of their last biopsy.

Overall, our findings highlight the limitations of existing nomograms in surgical planning of RARP and support the recent push in the literature for the use of multiparametric MRI (mpMRI) in surgical planning to better assess ECE, pelvic anatomy, and tumor characteristics and location. Most studies have reported sensitivities and specificities of around 35%-60% and 90%, respectively, for ECE detection, which helps better plan NVB preservation in most cases.[24-26] Recent studies and reviews have recognized the value of mpMRI as an important tool and adjunct when planning RARP that may lead to better operative decisions and improve patient outcomes.[27,28]

Limitations

Our study is the first of its kind to analyze preoperative risk factors for deviation in NVB preservation surgical planning in RARP. However, it is not devoid of limitations. First, it relies on retrospective data reported and performed by a single surgeon at a single institution. Second, final NVB preservation status was determined subjectively without pathological assessment. Nonetheless, with an over 2000-case experience, surgeon assessment of NVB preservation status can be accepted with confidence.[29] Third, although the use of preoperative nomogram tools provided guidance into NVB preservation technique selection, we recognize the lack of strict criteria use for surgical planning and the possible subjectivity of each case. However, the consideration of other patient factors not included in the nomogram may be beneficial as it allows personalization of the surgical experience for each patient and their unique situation. This limitation is also unlikely to have affected our results, as we strictly aimed at comparing surgeon intent to final outcome.

Conclusion

In conclusion, we found that older age, Gleason ≥ 3+4, post-biopsy sepsis, larger prostate volume on TRUS, and side-specific laterality were significant predictors of unplanned INS during RARP, which was associated with poorer functional outcomes. Interestingly, the number of lifetime biopsies was not a significant predictor of unplanned INS, a particularly novel and valuable finding for patients under active surveillance. While CNS, if in accordance with patient preference and disease factors, should remain an objective for surgeons, our data provides new insight that should help preoperative counseling, and set patient expectations with regards to functional outcomes and the risk for deviation. ☐

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