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Address for Correspondence:

Sung Gu Kang, MD, PhD

Department of Urology, Anam Hospital, Korea University College of Medicine, 73, Incheon-ro, Seongbuk-gu, Seoul 02841, Korea.
Email: kkangsung76@daum.net

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ORCID iDs

Ji Sung Shim

<https://orcid.org/0000-0002-6745-1776>

Jong Hyun Tae

<https://orcid.org/0000-0001-5826-3469>

Tae Il Noh

<https://orcid.org/0000-0002-5278-7672>

Seok Ho Kang

<https://orcid.org/0000-0002-1524-5233>

Jun Cheon

<https://orcid.org/0000-0002-3000-6329>

Jeong Gu Lee

<https://orcid.org/0000-0002-0467-4913>

Vipul R. Patel

<https://orcid.org/0000-0002-8802-9734>

Sung Gu Kang

<https://orcid.org/0000-0001-7289-1269>

Toggling Technique Allows Retrograde Early Release to Facilitate Neurovascular Bundle Sparing During Robot-Assisted Radical Prostatectomy: A Propensity Score-Matching Study

Ji Sung Shim ¹, Jong Hyun Tae ¹, Tae Il Noh ¹, Seok Ho Kang ¹, Jun Cheon ¹, Jeong Gu Lee ¹, Vipul R. Patel ², and Sung Gu Kang ¹

¹Department of Urology, Anam Hospital, Korea University College of Medicine, Seoul, Korea

²Global Robotics Institute, Florida Hospital-Celebration Health Celebration, University of Central Florida School of Medicine, Orlando, FL, USA

ABSTRACT

Background: This study aimed to present the surgical facilitation of neurovascular bundle (NVB) sparing using the toggling technique (30° lens down/up switching) and to evaluate erectile dysfunction (ED) recovery after robot-assisted radical prostatectomy (RARP).

Methods: We assessed 144 patients (group with toggling, n = 72; group without toggling, n = 72) who underwent RARP with bilateral NVB sparing using propensity score matching. Inclusion criteria were ≥ 1 year follow-up and preoperative potency as per the Sexual Health Inventory for Men (SHIM) questionnaire (≥ 17 points). Recovery of ED after RARP was defined as return to baseline sexual function or self-assessment regarding successful intercourse. The subjective surgeon's nerve sparing (SNS) score and tunneling success rates were used to evaluate surgical facilitation. The recovery rate of ED between the groups was analyzed using Kaplan-Meier analysis.

Results: A better ED recovery trend was confirmed according to the SNS score ($R^2 = 0.142$, $P = 0.004$). In the analysis of NVB sparing ease, the toggling group showed higher SNS scores (on right/left side: $P = 0.011$ and < 0.001 , respectively) and overall tunneling success rates (87% vs. 74%, $P = 0.001$) than the group without toggling. Overall, ED recovery rates were 82% (59/72) and 75% (54/72) in the groups with and without toggling, respectively, at the 1-year follow-up ($P = 0.047$), and the toggling group showed a faster ED recovery rate at 3 months (47% vs. 35%, $P = 0.013$). In a specific analysis of the potent cohort (< 60 years, bilateral full NVB spared, SHIM score ≥ 22), the ED recovery rate reached 87% (14/16) in the toggling group.

Conclusion: The retrograde early release with the toggling technique improves the facilitation of NVB sparing, leading to improved ED recovery.

Keywords: Prostate Cancer; Prostatectomy; Robotics

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Disclosure

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: Kang SG. Data curation: Tae JH. Formal analysis: Noh TI. Methodology: Patel R. Vipul. Supervision: Kang SG. Validation: Lee JG, Cheon J, Kang SH. Writing - Writing - review & editing: Kang SG, Shim JS

INTRODUCTION

Erectile dysfunction (ED) is one of the most relevant functional complications following radical prostatectomy. Recovery of potency in large representative trials has been reported to be 51–95% in one year.¹⁻⁸ Such significant variability could be attributed to the different definitions and tools adopted to evaluate potency, as well as the physician's proficiency in performing the procedure.

Since the introduction of open radical prostatectomy, urologists have continually tried to improve the functional outcomes while maintaining oncological safety. Regarding surgical techniques, avoiding electrocautery near the neurovascular bundle (NVB) or mechanical stretching of the neural tissue during the procedure could affect ED recovery.⁹⁻¹¹ Moreover, the anatomic nerve-sparing approach and securing the NVB itself could maximize the ED recovery.¹²

The concept of precise nerve sparing has become clearer after robot-assisted radical prostatectomy (RARP) was first reported in 2001.¹³ RARP has not only shown improved functional outcomes, but also enabled more accurate periprostatic fascial layer identification to conserve neurovascular tissue to five different degrees.^{14,15} Nevertheless, the neurovascular anatomy is often difficult to recognize for inexperienced surgeons, leading to less optimal NVB preservation or abandonment. Furthermore, the anatomy could be variable or hidden.

Recently, Patel et al.¹⁶ mentioned a technique that makes retrograde NVB sparing more effective. With the use of Da Vinci Xi (Intuitive Surgical, Sunnyvale, CA, USA), they dissected the prostate by a toggling technique, which means changing the camera angle from 30° down to up. Using this technique, the NVB can be released easily from below, achieving a good avascular plane between the prostate fascia and NVB. Tunneling is the process of connecting a space created by separating the NVB from the anterior prostate surface with the previously created Denonvillier's space. This facilitation of retrograde early release is expected to improve the completeness of the operation and help in better ED recovery, but there have been no clinical studies on this aspect.

The objective of this study was to describe the key surgical step of retrograde early release by using the toggling technique and to compare the ED recovery rates between the groups with and without toggling using propensity score matching.

METHODS**Study population**

We analyzed 427 consecutive patients who underwent RARP with bilateral NVB sparing at Korea University Hospital between March 3, 2015, and December 31, 2017. In total, 49 patients with incomplete data and 27 who were lost to follow-up were excluded from the analysis. As a rule, the NVB sparing procedure was performed in patients with prostate cancer of clinical stage T1–T2, biopsy Gleason score 6–7, and preoperative Sexual Health Inventory for Men (SHIM) score ≥ 17 . NVB sparing was modified and performed athermally with an early retrograde release.¹⁷ Additionally, those who underwent wide resection on any side were excluded.

Basic characteristics and group distribution

Two groups were compared after propensity matching: group with toggling technique (n = 72), and group without toggling technique (n = 72). Descriptive variables, such as age, body mass

index (BMI), prostate-specific antigen (PSA) level, prostate volume, pathologic stage, Gleason score, positive surgical margin according to pathologic stage, and preoperative SHIM score were analyzed. All operations were performed by a single surgeon (SG Kang) who had overcome the RARP learning curve by operating on more than 150 cases prior to the beginning of this series.

Surgical technique

All cases were performed using a six-port transperitoneal approach. We used the Da Vinci surgical system Xi or Si (Intuitive Surgical) in all cases.

Sequentially, the key steps of the surgical technique were as follows:

1. A zero-degree lens was used from the beginning of the surgery. An incision was made on the anterior peritoneum to access the Retzius space, followed by dorsal vein ligation and placement of a periurethral suspension stitch (anchoring of periosteum) in all patients.¹⁸
2. Thereafter, the surgery was performed using a 30° down lens. The anterior bladder neck was incised between the bladder and prostate to expose the vas deference and seminal vesicle.
3. After dissection of the vas deference and seminal vesicle without thermal ligation, the posterior plane could be accessed through the interfascial plane (**Fig. 1A**). Here, it was important for the assistant to symmetrically hold the seminal vesicle in the antero-cranial aspect with the 4th robotic arm.
4. After some degree of detachment, the lens was switched from 30° down to 30° up by toggling (**Fig. 1B**). The proper dissection of the interfascial plane with exposure of the medial side of the NVB is a good sign of nerve sparing. When the bilateral NVB is dissected carefully with scissors while maintaining the interfascial plane, the surgeon may sense that nerve sparing is almost complete.
5. The 30° down lens was used again. The levator fascia over the prostate was opened sharply to expose the NVB. The NVB can be easily separated even with a little dissection, and surgeon may find successful tunneling present below (**Fig. 1C**). The plane was then continued in a retrograde direction toward the base of the prostate to detach the NVB from the prostatic pedicle completely. "Tunneling" is defined as a connection between the prostatic anterior aspect and Denonvillier's fascia following the separation of the NVB (**Fig. 1C**).
6. The plane was then continued toward the apex by detaching the prostate from the NVB.
7. All cases underwent bladder neck and posterior reconstruction as described in a previous study.¹⁶

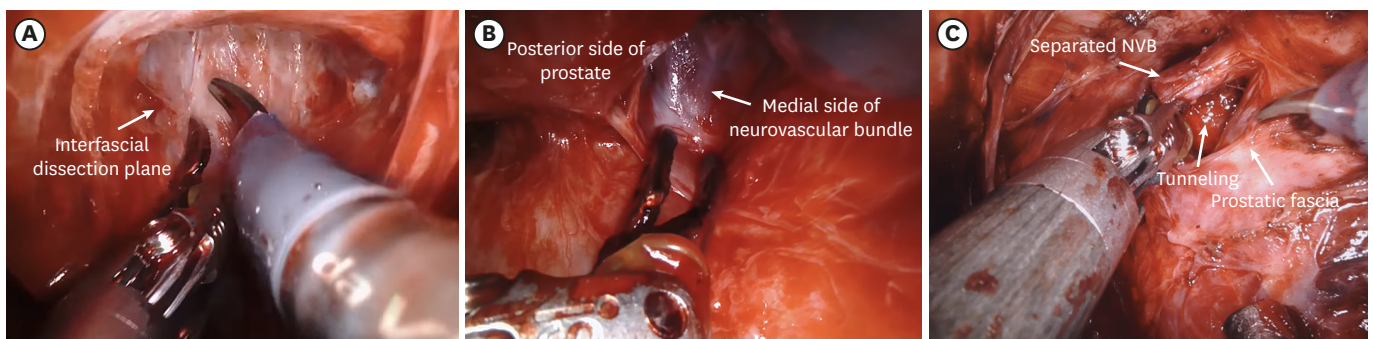


Fig. 1. Key surgical steps for retrograde early release using toggling technique. **(A)** 30° down view: The appropriate dissection approach into the interfascial plane is important in this step. The deeper dissection plane between the prostate fascia and the neurovascular bundle is rarely seen in this view. **(B)** 30° up view: After the proper dissection of the interfascial plane followed by toggling, the medial side of the neurovascular bundle is visible. The accomplishment of this process guarantees sparing of the whole neurovascular bundle. **(C)** 30° down view: After toggling again, the final step of the neurovascular bundle sparing process is performed anteriorly. Tunneling, defined as a connection between the anterior aspect of the prostate and the Denonvillier's fascia following separation of the neurovascular bundle, can be observed here.

NVB = neurovascular bundle.

Main outcome measures

Patients with ≥ 1 year of follow-up and preoperative potency as determined by the SHIM questionnaire (≥ 17) were included. Recovery of ED after RARP was defined as return to baseline sexual function as determined by the SHIM responses (SHIM response options 2 and 3: achieve and maintain erection satisfactory for intercourse for more than half the time, with or without the use of oral phosphodiesterase type 5 inhibitors [PDE-5 inhibitors])

Facilitation of NVB sparing: correlation test and subjective nerve sparing score

We performed univariate linear regression analysis to assess the correlation between the erectile function recovery period and bilateral sum of subjective surgeon's nerve sparing (SNS) score. Thereafter, we investigated the SNS score for measuring surgical ease. To classify the extent of nerve resection in RARP patients, we utilized a five-point nerve sparing score, as described previously.¹⁹ Each nerve was assigned a nerve sparing score intraoperatively by the surgeon. In addition, we analyzed successful tunneling rates to assess the surgical facilitation. We defined successful tunneling as creation of a space between the anterior prostate and Denonvillier's fascia at mid-prostate level after retrograde early release by using the toggling technique.

Recovery rate of ED between groups: Kaplan-Meier analysis

Baseline sexual functions of the patients were assessed before RARP by themselves. All patients were prescribed a PDE-5 inhibitor (tadalafil 5 mg daily) for early penile rehabilitation starting 7 days postoperatively, until recovery of sexual function. Erectile function was measured by the SHIM score preoperatively and postoperatively (1, 3, 6, 9, 12 months). Even if there was successful intercourse, patients who used a vacuum erection device, penile injection/prosthesis were judged not to be potent while patients taking PDE-5 inhibitors to achieve successful intercourse were considered potent.

Statistical analysis

Descriptive statistics were used to report patient demographic variables and percentage of patients between the two groups. The student's *t*-test and χ^2 analysis were used to test the significance of categorical variables. Linear regression analysis was used to represent the relationship between the SNS score and time of ED recovery. To reduce the effects of selection bias and potential confounding factors, propensity matching was performed using various clinicopathological characteristics: age, BMI, PSA, prostate volume, pT stage, Gleason score, surgical margin and preoperative SHIM score. The Kaplan-Meier curve was used to depict the recovery rate of ED. All analyses were performed using Statistical Package for the Social Sciences software (version 20.0; SPSS Inc., Chicago, IL, USA). Results were considered statistically significant if *P* value was < 0.05 .

Ethics statement

This study was approved by the Institutional Review Board of Korea University Medical Center (approval number: 2018AN0339) and informed patient consent for research was waived. All research and data collection adhered to the tenets of the Declaration of Helsinki.

RESULTS

The baseline characteristics of patients are shown in **Table 1**. The mean age of the patients was 62.8 ± 4.9 years (range, 43–70 years). There were no significant differences in age, BMI,

Table 1. Baseline demographics and clinical data of patients with ≥ 1 year follow-up of the two groups

Parameters	Before matching			After matching		
	With toggling (n = 259)	Without toggling (n = 92)	P value	With toggling (n = 72)	Without toggling (n = 72)	P value
Age, yr	61.4 ± 4.4	62.9 ± 3.0	0.796	62.2 ± 5.7	63.8 ± 3.0	0.182
BMI, kg/m ²	24.2 ± 2.8	23.7 ± 4.2	0.259	24.1 ± 2.8	23.9 ± 1.6	0.822
PSA level, ng/mL	7.9 ± 4.1	8.5 ± 2.7	0.588	7.7 ± 3.6	8.8 ± 3.7	0.215
Prostate volume, mL	32.1 ± 11.3	36.0 ± 8.7	0.151	31.9 ± 12.9	37.0 ± 15.0	0.138
Pathologic stage			0.230			0.508
≤ pT2	218 (84)	73 (79)		63 (87)	58 (81)	
≥ pT3a, pT3b	41 (16)	19 (19)		9 (13)	14 (19)	
Specimen Gleason score			0.035			0.691
≤ 6	186 (72)	39 (42)		50 (64)	42 (58)	
7	57 (22)	32 (35)		21 (27)	20 (27)	
8	16 (6)	21 (23)		7 (9)	10 (15)	
Positive surgical margin			0.294			0.589
Overall	36 (14.0)	16 (17.3)		12 (15.6)	14 (19.4)	
In pT2 cancers	25/229 (11.0)	8/73 (13.9)		9/65 (13.8)	8/58 (13.8)	
In pT3 cancers	11/30 (36.7)	8/19 (42.1)		3/7 (42.9)	6/14 (42.8)	
Preoperative SHIM score	19.3 ± 1.1	19.6 ± 2.6	0.577	19.7 ± 2.1	19.3 ± 2.4	0.412
22–25	43 (17)	19 (21)	0.254	12 (17)	16 (22)	0.760
17–21	216 (83)	73 (79)		60 (83)	56 (78)	

Data are shown as mean ± SD or number (%).

BMI = body mass index, PSA = prostate specific antigen, SHIM = Sexual Health Inventory for Men (22–25, no erectile dysfunction; 17–21, mild erectile dysfunction; 12–16, mild-to-moderate erectile dysfunction; 8–11, moderate erectile dysfunction; and 5–7, severe erectile dysfunction).

PSA level, prostate volume, pathologic stage, and positive surgical margin rates between the groups with and without toggling except Gleason score before propensity matching. After matching, the preoperative SHIM scores of the groups with and without toggling were 19.7 ± 2.1 and 19.3 ± 2.4, respectively, and there was no difference in the proportion of patients in the “no ED” (SHIM score 17–21) and “mild ED” (SHIM score 22–25) cohorts (*P* = 0.760).

Table 2 shows the NVB tunneling success rates. In the toggling group, the tunneling success number was 125 out of 144 trials, with an overall success rate of 87%. In the group without toggling, it was 106 out of 144 trials, and the overall success rate was 74% with a significant difference (*P* < 0.001). The rate of successful bilateral tunneling reached 76% in the toggling group and 24% of the cases failed bilaterally, whereas the success rate was 42% bilaterally in the group without toggling.

To investigate the correlation between SNS scores and ED recovery period, we performed univariate linear regression analysis. The ED recovery period showed a significant positive association with the sum of bilateral SNS scores ($Y = 41.768 - 3.072 \times X$, $R^2 = 0.142$, *P* = 0.004).

In surgical facilitation analysis of the right and left sides, the toggling group showed higher SNS scores than the group without toggling (right side: 4.7 ± 0.7 vs. 3.7 ± 1.5, *P* = 0.011; left side: 4.6 ± 0.6 vs. 3.2 ± 1.5, *P* < 0.001) (**Fig. 2**).

Table 2. Neurovascular bundle tunneling success rate between the two groups

Parameters	With toggling (n = 72)	Without toggling (n = 72)	P value
NVB tunneling ^a success No.			
None	3 (2)	12 (15)	
Unilateral	16 (22)	30 (42)	
Bilateral	53 (76)	30 (42)	
Overall tunneling ^a rate	87 (125/144)	74 (106/144)	< 0.001

Values are presented as number (%).

NVB = neurovascular bundle.

^aTunneling: creating a space between the anterior prostate and the Denonvillier’s fascia at the mid-prostate level

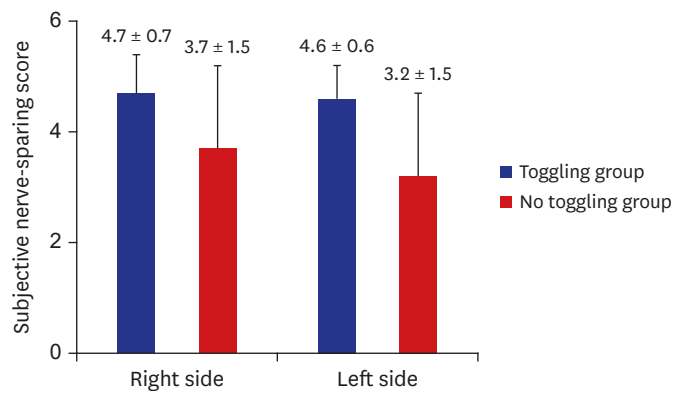


Fig. 2. Surgeon's subjective nerve-sparing score on right and left sides in both groups. Data are shown as mean ± SD.

Overall ED recovery rates in the groups with and without toggling were 82% (59/72) and 75% (54/72), respectively, during the 1-year follow-up. In Kaplan-Meier analysis, the curve showed ED reduction rate over time. In the log rank test, there was a significant difference between the two techniques ($P = 0.047$) at the 1-year follow-up, and the curve of the toggling group showed a faster potency recovery rate as depicted in the 3-month follow-up ($P = 0.013$, χ^2 test) (Fig. 3).

DISCUSSION

Although providing a high standard of oncological outcomes with radical prostatectomy is vital, preservation of the sexual function is important for majority of the prostate cancer

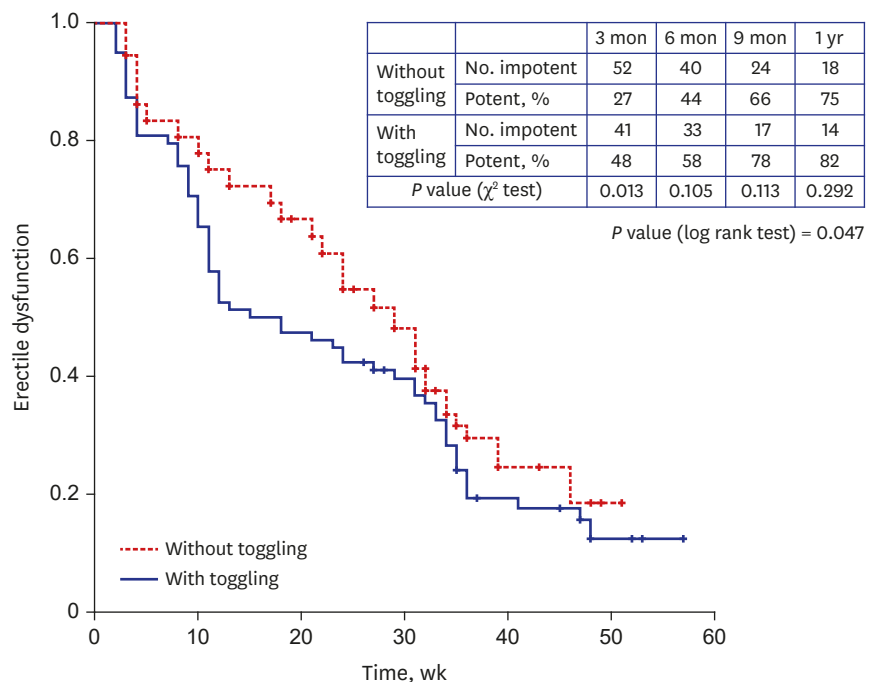


Fig. 3. Kaplan-Meier curve showing erectile dysfunction reduction rate over time. Numbers along the Y-axis represent rate of men at risk (those who were still impotent) at beginning of the corresponding timeline (weeks). Specific percentages depicted in the separate table represent proportion of those men who were potent by the end of the corresponding timeline.

patients. This poses a technical challenge to the surgeon with the competing goals of cancer control and nerve preservation.

There is a lot of evidence that nerve sparing grade is closely related to potency recovery.²⁰⁻²³ The specific points of NVB injury during radical prostatectomy is the use of thermal energy, excessive traction or direct damage to the bundle.²⁴ Mainly injured parts are prostatic pedicle, seminal vesicle area during apical dissection, and when NVB is unintentionally included during vesicourethral anastomosis.²⁵ If there is an appropriate surgical technique to overcome these problems, it will undoubtedly reduce NVB damage.^{25,26}

By combining the advantages of open radical prostatectomy and laparoscopic anterograde approach, we have suggested the athermal retrograde release of the NVB during RARP.¹⁷ The principle of this technique is to minimize traction during nerve sparing by attached the NVB both to the apex and base. They can be identified before pedicle control, thereby minimizing the risk of inadvertent injury. We believe that inadvertent/transient nerve injury can be minimized through a retrograde nerve sparing approach and this can lead to earlier potency recovery.

Regarding the background of this technique, Patel et al. devised a method to make NVB sparing easier in 2014 when the Da Vinci Xi system was introduced. The advantage of using the Xi system is greater than that when using the Si system because there is no need to change the camera direction by removing and inserting the camera. The operator can change the direction by simply pushing a button on the console. The key is to secure the interfascial plane through toggling by retrograde early release. The operator can then spare NVB directly from the anterior part of the prostate with minimal dissection. However, despite the ease and superiority of this procedure, there has been no report regarding the difference in ED recovery rates according to the usage of toggling.

The major advantage is the precise delineation of the course of the NVB prior to controlling the pedicle. This allows the vascular pedicle to be ligated while avoiding inadvertent injury to the bundle. The three-dimensional vision, relatively bloodless field, and wristed instrumentation of robotic technology allow us to enter the interfascial plane between the NVB and prostatic fascia and release the NVB in a retrograde fashion. The NVB is at risk of damage at this location with the traditional laparoscopic antegrade nerve-sparing approach. **Table 2** presents the results comparing the NVB tunneling success rates. When we performed toggling, 125 out of 144 trials were successful, showing a success rate of 87%. When dissection between the prostate and bundle was performed after retrograde dissection, the tunneling was already present, except in some cases where the adhesion was severe (**Fig. 1C**).

In this study, we found a positive correlation between the tunneling success rate and SNS score, leading to better ED recovery quality. The clinical significance of successful tunneling has not been previously reported, but it is a crucial part in retrograde early release. If bleeding occurs in the process of separating bundles from the prostate anterior surface and tunneling is not well done, the surgical process and nerve sparing in an accurate retrograde manner become difficult. However, if tunneling is done well, retrograde nerve sparing is easy and quick. Therefore, the tunneling rates were investigated separately, which showed a statistically significant success rate in the toggling group compared to the group without toggling (87% vs. 74%, $P = 0.001$). Additionally, we confirmed that such a high tunneling rate leads to improvement of SNS scores bilaterally, and this was statistically confirmed between the groups with and without toggling (right side: 4.7 ± 0.7 vs. 3.7 ± 1.5 , $P = 0.011$; left side: 4.6 ± 0.6 vs. 3.2 ± 1.5 , $P < 0.001$).

Table 3. Potency outcomes of representative studies after robot-assisted radical prostatectomy (≥ 1 year follow-up)

References	No. of patients	Age, yr	Follow-up, mon	Preoperative potency value	NVB sparing approach method	Potency, ^h % at number months			
						3	6	9	12
Zorn et al. ^{8,a}	60	60	12	SHIM score ≥ 22	Bilateral	47	65	-	80
Finley et al. ^{3,b}	58	57	24	SHIM score ≥ 22	Bilateral cautery free	30	-	63	80
Hakimi et al. ^{4,c}	60	60	12	-	Bilateral	31	67	-	77
Patel et al. ^{6,d}	1,100	56–65	18	SHIM score ≥ 22	Interfascial bilateral	67	82	-	95
Sooriakumaran et al. ^{7,e}	115	63	24	- ^e	Inter + interfascial	40	-	-	53
Coughlin et al. ^{1,f}	157	35–70	24	IIEF average score, 29.78	Interfascial bilateral	-	39	-	51
Kang et al. ⁸	150	63	12	SHIM score ≥ 17	With toggling	48	58	78	82
					Without toggling	27	44	66	75

SHIM = Sexual Health Inventory for Men, IIEF = The International Index of Erectile Function Questionnaire, NVB = neurovascular bundle.

^aAbility to achieve an erection sufficient for penetration with or without phosphodiesterase-inhibitor medication; ^bPatient-reported questionnaire (SHIM score, EPIC-26): “erection adequate for penetration?,” “satisfactory?”; ^cSHIM question 2, 3: achieve and maintain erection satisfactorily for intercourse $>$ half the time; ^dSHIM question 2, 3: achieve and maintain erection satisfactorily for intercourse $>$ half the time, with or without the use of oral phosphodiesterase-5 inhibitors; ^e“Stiff enough less than half of the time,” “stiff enough more than half of the time,” or “stiff enough every time” in ≥ 1 domains; ^fMore than half the time or almost always + Less than half the time or about half the time; ^gSHIM question 2, 3: achieve and maintain erection satisfactorily for intercourse $>$ half the time, with or without the use of oral phosphodiesterase-5 inhibitor; ^hDefinition of potency in each study.

Moreover, statistically significant results were obtained in the result analysis of whether such high SNS score or high tunneling success rate ultimately leads to patient’s ED recovery. The overall potency rate of this study was comparable to that of previous studies (Table 3). Remarkably, unlike other studies, in this study, the preoperative SHIM score was ≥ 17 points, and not 22 points. In addition, this study is the first to prove that there are differences in the ED recovery rate (at 3 months after surgery, the toggling group had superior results) and the ED recovery proportion after 1 year according to the usage of toggling. We believe that this technique should be widely applied so that many urologists can achieve NVB sparing with surgical facilitation.

The limitation of this study was that the proposed SNS score was subjective. Hence, the authors investigated an objective successful tunneling rate and confirmed that the toggling group indeed achieved a higher SNS score. However, since there was no verification process of the tunneling rate affecting the nerve-sparing quality, a further verification process will be needed.

In conclusion, the majority of men presenting with prostate cancer today are candidates for nerve-sparing operations. NVB preservation is a key technical requirement to maintain innervation of a corpus cavernosum. With retrograde early release using the toggling technique, we were able to clearly delineate the path of the NVB and eliminate potential inadvertent injury to it when ligating the vascular pedicle of the prostate. Thus, according to our study, this technique improves the feasibility and quality of NVB tunneling.

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