Randomized Trial

Two-Year Outcome of Percutaneous Bipolar Radiofrequency Neurotomy of Sacral Nerves S2 and S3 in Spinal Cord Injured Patients with Neurogenic Detrusor Overactivity: A Randomized Controlled Feasibility Study

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Background: Little research has been expended on the use of bipolar radiofrequency (RF) lesioning of sacral nerves in spinal cord injured (SCI) patients with neurogenic detrusor overactivity (NDO), and no study has been undertaken to demonstrate its long-term effect.

Objective: To investigated the effect of bipolar RF ablation of the second and third sacral nerves over 2 years in SCI patients with NDO.

Study Design: A prospective, randomized controlled feasibility study.

Setting: The outpatient clinic of a single academic medical center in Korea.

Methods: Ten SCI patients with NDO were recruited. These patients were randomly assigned to 2 groups; the intervention group (n = 5) and the control group (n = 5). Control group members received optimized conventional treatment. International Consultation on Incontinence Questionnaire (ICIQ), 3-day voiding diary, and the urinary incontinence quality of life scale (I-QOL) data were obtained at baseline and at 6, 12, and 24 months after intervention. Urodynamic study (UDS) was performed at baseline and 24 months after intervention. In the intervention group, percutaneous bipolar RF neurotomy was performed on both S2 and S3 nerves in each patient.

Results: Frequency of urinary incontinence and ICIQ and IQOL scores showed significant effects for time and for the group x time interaction ($P < 0.05$). Daily mean volume of urinary incontinence showed only a significant group effect. In UDS parameters, comparisons of values at baseline and at 24 months revealed all variables showed significant intergroup differences ($P < 0.05$).

Limitation: A small number of patients was recruited.

Conclusion: Percutaneous bipolar RF ablation of sacral nerves S2 and S3 effectively reduces urinary incontinence and improves quality of life (QoL) in SCI patients with NDO and the effects lasted over 2 years.

Key words: Neurogenic detrusor overactivity, bipolar RF neurotomy, sacral nerves, urinary incontinence, maximal detrusor pressure, maximum cystometric capacity

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Neurogenic detrusor overactivity (NDO) is an urodynamic observation characterized by involuntary detrusor contractions during the filling phase following a relevant neurological condition (e.g., spinal cord injury (SCI) or multiple sclerosis) (1). Associated NDO symptoms, such as urgency with or without urge incontinence, frequency, and nocturia are common complications in patients with SCI (2,3).

In particular, NDO causes urinary tract infections, renal damage, sleep disturbance, depression, and reduces sexual and physical activity, and thus, lowers quality of life (QoL) (3-5). Therefore, proper management of NDO can prevent other complications in patients with SCI, and consequently, aggressive management of NDO is required to improve QoL in patients with SCI.

Various traditional managements have been used to relieve NDO in patients with SCI, such as anticholinergic drugs, behavior adjustments (timed voiding, bladder retraining, pelvic floor training), and clean intermittent catheterization (CIC) (5,6). However, these managements have significant limitations. Anticholinergics, the first-line medication, can have unwanted effects, such as dry mouth, memory impairment, constipation, blurred vision, and tachycardia (7). CIC can cause urinary tract infections and urethral injury (8). In addition to these conventional managements, surgical and interventional managements have been used to treat NDO, such as penile prosthesis implantation, external sphincterotomy, augmentation cystoplasty, intramuscular botulinum toxin A injection, and sacral rhizotomy (5-14). Selective sacral neurotomy by radiofrequency (RF) ablation has been developed recently to increase bladder capacity and preserve detrusor reflex and sphincter function in SCI patients with NDO (15,16). Little research has been expended on the use of bipolar RF lesioning of sacral nerves in SCI patients with NDO, and no study has been undertaken to demonstrate its long-term effect.

In this study, we investigated the long-term effect of bipolar RF ablation of sacral nerves S2 and S3 over 2 years in SCI patients with NDO.

Methods

Patients

Ten patients (mean age 41.2 ± 8.01 years [range 31 ~ 53]; 7 men) were recruited using the following inclusion criteria: (1) SCI (ASIA scale A & B) with NDO treated for > one year; (2) age 20 ~ 70 years; (3) no history of bladder or prostate surgery; and (4) no history of cardiovascular disease (e.g., refractory hypertension) or coagulopathy. Pregnant patients of ASIA scale C, D, or E were excluded. All patients provided written informed consent before enrollment, and institutional review board approval was obtained before commencing the study. The 10 patients were randomly assigned to either an intervention group (5 patients; 3 men; mean age 42.0 ± 8.46 years) or a control group (5 patients; 4 men; mean age 40.4 ± 8.4 years), members of which received conventional medical treatment.

The Bipolar Radiofrequency Procedure

The procedure was explained and discussed with the patients and informed consent was obtained. Patients were placed in the prone position and an appropriate antiseptic skin prep was performed. The fluoroscope was aligned to provide an optimal view of the S2 or S3 posterior foramen. Typically cephalad-caudad tilt was provided to square the adjacent sacral vertebral endplate. The 18 gauge cannulas used for the ablation procedure had a sharp tip with 10 mm exposed curved end and a total shaft length of 100 mm. Local anesthetic was injected into the skin around the insertion site. Utilizing antero-posterior (AP) fluoroscopic guidance, the cannulas were placed through the posterior foramen and the tips spaced to encompass the expected nerve locations. Electrode position was confirmed in a lateral fluoroscopic view to not pass beyond the sacral ventral surface. Sensory nerve stimulation was then performed using a RF generator (RFG4, Cosman Medical Inc., MA, USA). During sensory nerve stimulation, paresthesia and pain or muscle contraction around the sacrum should be observed at < 0.7V. After placing 2 cannulas through each foramen and assuring correct position, contrast media was injected to confirm the absence of inappropriate spread. The RF lesion was created using a temp of 80°C for 90 seconds. The procedure was performed in this manner bilaterally at both S2 and S3 nerve segments (Fig. 1).

Clinical Evaluations

Clinical assessments were conducted using a 3-day voiding diary, the International Consultation on Incontinence Questionnaire (ICIQ), the urinary incontinence quality of life scale (I-QOL), and urodynamic study (UDS). Three-day voiding diaries are commonly used to evaluate voiding frequency and volume of urinary incontinence during the day. ICIQ is a questionnaire that evaluates the symptoms of incontinence, and its reliability and validity have been well established (17). I-QOL is a questionnaire that evaluates urinary incontinence and QoL and is known to have excellent repeatability and validity for evaluating QoL in patients with urinary incontinence (18,19). In addition, UDS provides a useful means of assessing the physiological function and pathology of the lower urinary tract in patients with neurogenic bladder (20). UDS measures maximum cystometric capacity, maximum detrusor pressure dur-

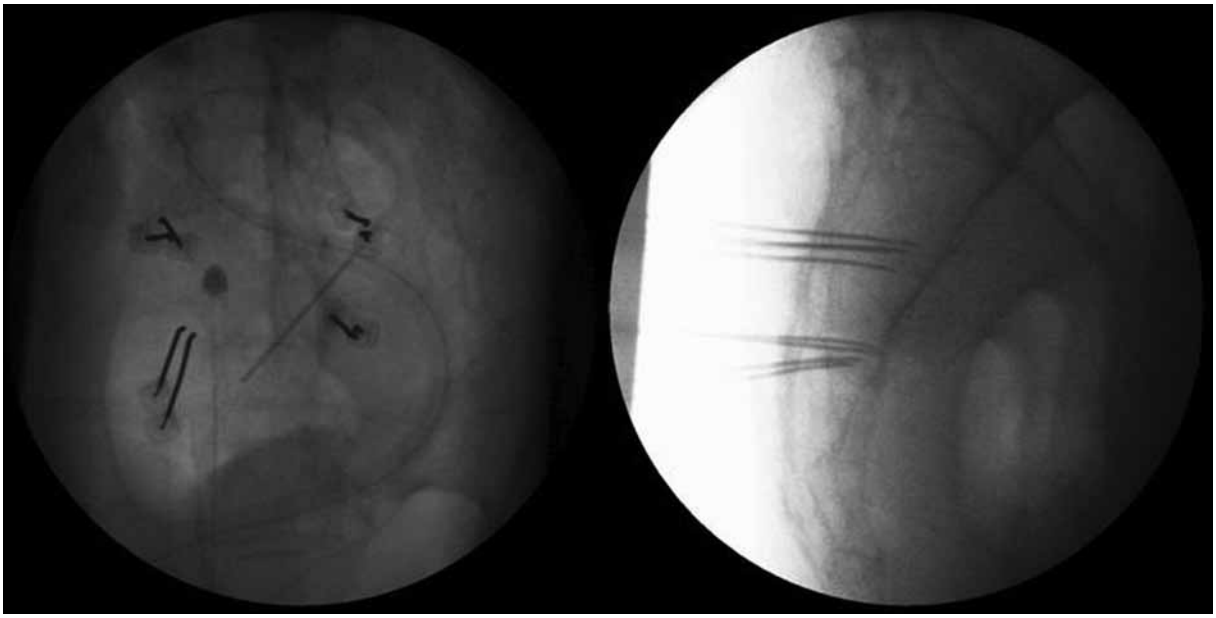

Fig. 1. *The image on the left side of the photograph shows an AP view of bipolar RF on both S2 and S3 nerve roots, and the image on the right shows lateral view of bipolar RF on both S2 and S3 nerve roots.*

ing filling, volume at maximal detrusor pressure during filling, and reflex detrusor volume at first contraction. For UDS, the bladder was filled with normal saline at 24 mL/min and detrusor pressure was defined as the difference between intravesical and abdominal pressure.

Patients in the intervention were assessed using the 3-day voiding diary, the ICOQ, and the I-QOL one month before the intervention (baseline) and at 6, 12, and 24 months after the intervention. Patients in the control group were also assessed using the same parameters; baseline and at 6, 12, and 24 after registration. UDS was performed one month before the intervention (baseline) and 24 months after the intervention only because of the associated risk of urinary tract infection and the risk of poor patient compliance in the intervention group. In the control group, UDS was also performed at baseline and 24 months after registration.

Statistical Analysis

SPSS software (v.19.0; SPSS, Chicago, IL, USA) was used for the analysis. Repeated measure 2 factor analysis was used to perform comparative effect analysis, as determined by clinical assessments (daily mean frequency, volume of urinary incontinence, and ICIQ and I-QOL scores) on the 2 groups. To analyze the difference between baseline and follow-up UDS parameters (maximum cystometric capacity, maximum detrusor pressure during filling, volume at maximal detrusor pressure during filling, and reflex detrusor volume at first contraction), pre/post intervention differences (baseline/24 months) were calculated. The Mann-Whitney U test was used to compare the 2 study groups with respect to the pre/post values of UDS parameters. Statistical significance was accepted for P values < 0.05.

Results

Table 1 summarizes the demographic and clinical data of the 10 patients, and includes baseline values for daily mean frequency and volume of urinary incontinence, ICIQ and I-QOL scores, and UDS parameters. Comparisons by time, group, and time x group with respect to daily mean frequency and volume of urinary incontinence, and ICIQ and I-QOL scores at baseline and at 6, 12 and 24 months after the intervention are provided in Table 2. Frequency of urinary incontinence and ICIQ and IQOL scores showed significant effects for time and for the group x time interaction (P < 0.05). Daily mean volume of urinary incontinence showed only a significant group effect. Values of UDS parameters at baseline and at 24-month follow-ups in both groups are shown in Table 3. Comparisons of values at baseline and at

Table 1. *Patient demographic and clinical data.*

Patient	Age /Gender	Level (ASIA scale)	Incontinence :Frequency	Incontinence :Volume	ICIQ	I-QOL	UDS parameters			
							RDV	MDP	V at MDP	MCC
Intervention group										
1	M/53	C4(A)	5	100	7	101	286	66	344	402
2	M/32	C5(B)	2	70	10	85	179	67	595	600
3	F/48	C4(B)	10	57	12	33	66	77	260	300
4	F/40	T6(A)	15	100	11	44	209	112	230	500
5	M/37	T12(A)	6	95	18	28	253	78	180	360
Control group										
1	M/46	C4(A)	7	221	7	100	162	153	189	315
2	M/36	C6(A)	2	125	10	37	215	48	298	400
3	F/31	T8(A)	5	150	12	71	232	41	277	320
4	M/52	T6(B)	2	120	12	91	49	50	101	275
5	M/37	T11(A)	6	90	17	30	250	31	171	345

ASIA: American Spinal Injury Association, ICIQ: International Consultation on Incontinence Questionnaire, I-QOL: urinary incontinence quality of life scale, UDS: urodynamic study, RDV: reflex detrusor volume at first contraction, MDP: maximum detrusor pressure during filling, V: volume, MCC: maximum cystometric capacity.

Table 2. *Daily mean frequency and volume of urinary incontinence and ICIQ and IQOL scores at baseline (one month before intervention) and at 6, 12 and 24 months after intervention in the 2 study groups.*

	Incontinence : Frequency		Incontinence : Volume		ICIQ		I-QOL	
	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control
Mean (SD)								
Baseline	7.6 (5.030)	4.4 (2.302)	84.4 (19.731)	143.2 (47.657)	13.2 (3.271)	12.6 (7.765)	57.8 (26.167)	58.2 (32.783)
6 month	1.8 (2.168)	4.0 (2.000)	15.0 (17.321)	137.6 (105.796)	3.6 (4.099)	11.2 (5.541)	73.8 (25.203)	55.8 (24.783)
12 month	1.6 (2.608)	5.2 (1.483)	19.0 (26.077)	155.4 (84.293)	3.2 (5.215)	12.4 (6.465)	72.0 (23.948)	51.8 (22.466)
24 month	1.6 (2.302)	4.8 (1.304)	23.0 (31.937)	156.6 (86.555)	3.4 (5.273)	12.6 (6.804)	71.2 (23.973)	51.6 (22.963)
F (*P*-value)								
T	3.866 (0.003)*		1.673 (0.148)		8.540 (0.000)*		2.695 (0.025)*	
G	3.537 (0.097)		12.749 (0.007)*		5.375 (0.049)*		1.204 (0.304)	
T xG	4.747 (0.001)*		2.015 (0.082)		6.951 (0.000)*		4.690 (0.001)*	

*: Statistically significant with $P < 0.05$

T: Time, G: Group. SD: Standard Deviation, ICIQ: International Consultation on Incontinence Questionnaire, I-QOL: urinary incontinence quality of life scale.

Table 3. *Urodynamic study data at baseline (one month before intervention) and at 24 months after intervention and pre/post intervention differences between the 2 groups.*

Variable	Reflex detrusor volume at first contraction (mL)		Maximum detrusor pressure during filling (cmH2O)		Volume at maximal detrusor pressure during filling (mL)		Maximum cystometric capacity (mL)	
	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control
Baseline	198.6 (84.7)	181.6 (81.09)	80.0 (18.72)	64.6 (49.97)	321.8 (163.92)	207.2 (163.9)	432.4 (118.67)	331.0 (46.02)
24 M	281.6 (46.51)	211 (35.24)	63.2 (15.22)	78.6 (21.05)	341.4 (51.60)	241.2 (53.56)	467.8 (45.14)	347.8 (37.04)
Pre/post values (Baseline/24M)	82.4 (76.79)	-3.6 (5.86)	-16.4 (13.18)	7.4 (14.52)	81.6 (78.62)	7.2 (2.68)	70.4 (46.19)	-6.2 (14.04)
Z (*P*-value)								
Baseline/24M	-2.627 (**0.009**)*		-2.193 (**0.028**)*		-2.627 (**0.009**)*		-2.193 (**0.028**)*	

Values represent means (SDs); SD, standard deviation; M, months

24 months revealed all variables showed significant intergroup differences ($P < 0.05$).

Discussion

Selective sacral neurotomy by RF ablation has been utilized to increase bladder capacity and preserve detrusor reflex and sphincter function in SCI patients with NDO (15,16). RF ablation is an effective interventional treatment that ablates nerves by generating a controlled region of heated tissue around a metal cannula's uninsulated tip which is positioned in close proximity to neural tissue. Several previous studies have reported selective sacral neurotomy using monopolar RF in patients with neurogenic bladder (13,21,22). Ferreira et al (16) demonstrated that sacral neurotomy using percutaneous monopolar RF effectively increased maximal cystometric capacity and reduced detrusor pressure at maximal cystometric capacity in patients with hyperactive neurogenic bladder. Subsequently, Cho and Lee (15) reported that percutaneous mono-polar RF sacral neurotomy improved bladder capacity and urinary incontinence in SCI patients with intolerable neurogenic bladder. In these studies the sacral nerve neurotomy was performed using a monopolar RF technique. Monopolar RF heat lesioning has been widely used in neurosurgery and for pain management. It has been proposed that bipolar RF may be more effective than monopolar RF. Monopolar RF generates a prolate spheroid lesion around the uninsulated cannula tip using a distant current return "grounding" electrode. Bipolar RF generates a lesion between and around 2 closely positioned uninsulated cannula tips. It is proposed that bipolar RF may produce denser electrical fields, faster tissue heating, and larger lesions (23-25).

In a preliminary study, we investigated the short-term effects (over 3 months) of bipolar RF neurotomy at 80°C for 90 seconds on sacral S2 and S3 nerves to treat NDO in SCI patients. We found that patients in the intervention group exhibited improvements in bladder capacity and had less urinary incontinence (26). This preliminary study raised questions regarding the longer term effects of bipolar RF neurotomy, and thus, in the present study, we investigated the effects of bipolar RF neurotomy on sacral nerves over a 2 year period. In our preliminary study, improvements of ICIQ and IQOL scores and daily mean frequency of urinary incontinence were found in the intervention group as compared with the control group with respect to time and time x group ($P < 0.05$). In the present study, these variables also showed significant improvements ($P < 0.05$), which indicates the effects of bipolar RF lesioning last for at least 2 years. In contrast, although daily mean volume of urinary incontinence in the intervention group also showed improvement in the present study, this lacked significance, which we attribute to the small number of patients enrolled. On the other hand, all UDS variables achieved significant intergroup differences at 24 months ($P < 0.05$). However, only volume at maximal detrusor pressure during filling and reflex detrusor volume at first contraction showed a significant intergroup difference between baseline and 3 months. We believe that while the beneficial effect of RF neurotomy continued over 2 years in the intervention group, urinary symptoms worsened in the control group. In fact, 4 of the 5 patients in the intervention group reduced anticholinergic usage after the intervention and continued to take anticholinergics at these reduced levels over the 2 year study period. On the other

hand, all 5 patients in the control group added another anticholinergic drug or increased medication intake. Furthermore, a significant intergroup difference was observed at 24 months. To the best of our knowledge, this is the first study to investigate the long-term effect of bipolar RF ablation on sacral nerves in SCI patients with NDO.

Bipolar RF neurotomy of the S2 and S3 nerves appears to be a safe treatment option. During and after the intervention, no serious complications, such as cannula insertion site infection, were encountered. Two men in the intervention group commented on a slight reduction of penial rigidity, and thus, sometimes used sildenafil citrate. In addition, some patients reported discomfort around the intervention site for a few days after the procedure. Furthermore, bipolar RF neurotomy of S2 and S3 nerves is more cost-effective than other treatment options, such as sacral neuromodulation and intravesical botulinum toxin A injection. Over the 2-year study period, the cost of sacral neuromodulation including sacral nerve stimulation was $15,743 and the cost of intravesical botulinum toxin A injection was $4,392, while the cost of bipolar RF neurotomy of S2 and S3 was $300 ~ 400 (27). It would seem that bipolar RF sacral neurotomy is likely the more cost-effective therapy for SCI patients with NDO.

In conclusion, we found percutaneous bipolar RF ablation of sacral nerves S2 and S3 effectively reduced urinary incontinence and improved QoL in SCI patients with NDO and that its effects lasted at least 2 years. Percutaneous bipolar RF neurotomy is also a relatively safe, cost-effective, repeatable, minimally invasive procedure, and thus we consider it one of the more favorable treatment options for SCI patients with NDO. The obvious limitation of the present study is the small number of patients recruited, and by the use of only 2 UDS evaluations per patient. Therefore, we suggest further study be undertaken on a larger number of patients with more frequent follow-up evaluations.

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