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Sacral neuromodulation for neurological disease-induced lower urinary tract symptoms in Saudi Arabia: a single-centre experience

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Abstract

Objective: To evaluate the effectiveness of sacral neuromodulation therapy (SNM) for lower urinary tract symptoms (LUTS) caused by neurological diseases.

Methods: This prospective cohort study enrolled patients that developed LUTS secondary to neurological disorders. All patients underwent staged SNM. A 5-day voiding diary was used to evaluate their response to the stage 1 procedure. Implantation of the full system during the stage 2 procedure was undertaken in patients that had $\geq$50% improvement on their voiding diary.

Results: Twenty-one patients were included in the study with the following neurological aetiologies: diabetes mellitus ($n = 2$), myelitis ($n = 3$), multiple sclerosis ($n = 5$), spinal cord injury ($n = 10$) and cerebrovascular accident ($n = 1$). Fifteen patients underwent the stage 1 procedure successfully; their mean age was 47.5 years and the mean follow-up was 29 months. SNM resulted in significantly increased voided volume/void/day, decreased leaking episodes/day, decreased post-voiding residual/day and decreased number of clean intermittent catheterization/day compared with baseline. Five patients were highly satisfied, nine were moderately satisfied and one patient was not satisfied with the therapy.

Conclusion: SNM was an effective therapy for LUTS caused by neurological disease and there was a high rate of patient satisfaction.

Keywords

Sacral neuromodulation, neurogenic bladder, neurogenic lower urinary tract symptoms, neurological disease

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Introduction

Normal bladder function is under full neurological control for both the filling and voiding phases.[1] When diseases affect the nervous system, neurogenic lower urinary tract symptoms (nLUTS) occur with a wide range of lower urinary tract symptoms, including overactive bladder, urinary incontinence and urine retention.[2,3] Neurogenic bladder is diagnosed in patients with neurologic disorders,[4] including diabetes mellitus (DM),[5–7] multiple sclerosis (MS)[8–10] and spinal cord injury, all through its neural involvement.[11,12]

The World Health Organization has reported that Saudi Arabia ranks as the second-highest in the Middle East and seventh in the world for the rate of DM.[13] It is estimated that around 7 million Saudis have DM and almost 3 million have prediabetes.[13] An increased prevalence of MS has been reported in Saudi Arabia, which is alarming and warrants immediate public health action.[14] The true incidence of global spinal trauma is unknown.[15] Annual international incidences vary between 16 and 64/100 000.[16,17] Saudi Arabia has one of the highest spinal cord injuries worldwide secondary to road traffic accidents.[18,19] According to the Global Burden of Disease report, traumatic injuries represent 22.6% of years of potential life lost in Saudi Arabia.[20]

With the reported high incidence of neurological diseases in Saudi Arabia, high numbers of patients with neurogenic bladders would be expected. Despite the available therapy for nLUTS, some patients do not respond.[12] The use of minimally-invasive procedures shows promising results.[21]Sacral neuromodulation (SNM) is a US Food and Drug Administration-approved therapy for lower urinary tract symptoms.[21,22] Although the mechanism of action has not been identified, SNM has shown successful results (off-label) in nLUTS.[22]

This current study aimed to determine whether SNM is a good option for treating nLUTS in Saudi Arabia. To the best of our knowledge this is the only study in Saudi Arabia and the Gulf Cooperation Council region.

Patients and methods

Study design and population

This prospective cohort study enrolled consecutive patients with an underlying neurological diagnosis undergoing sacral neuromodulation for LUTS in the Department of Urology, Faculty of Medicine, King Abdulaziz University Hospital, Jeddah, Saudi Arabia between March 2017 and August 2020. The inclusion criteria were as follows: (i) patients with LUTS secondary to neurological diseases, including DM, MS, cerebrovascular accident (CVA), spinal cord injury and myelitis, that did not respond well to conservative and medical therapy (e.g. intermittent catheterization +/– anticholinergic, beta agonist); (ii) patients with refractory overactive bladder (LUTS not relieved with more than one type of anticholinergic medications); (iii) both Saudi and non-Saudi patients living in Saudi Arabia; (iv) patients with DM that had nonobstructive urine retention with a urodynamic diagnosis of atonic bladder; (v) patients with MS were included if they had stable disease for the previous 2 years and were able to use the device, after obtaining their consent to use a non-magnetic resonance imaging (MRI) compatible device and the possibility that they would need to explain the device in the need of an MRI; (vi) spinal cord patients with incomplete injury were only included as early therapy in the first 2 years post injury. All patients with LUTS clinically caused by their neurological disease with objective evidence of atonic bladder, or an overactive bladder in their

urodynamic test, were defined as having neurogenic bladder. The exclusion criteria were as follows: (i) sacral neuromodulation was not undertaken in patients with poorly controlled DM; (ii) patients with DM with uncontrolled blood glucose levels (glycosylated haemoglobin >7%) were excluded to avoid postoperative wound complications (infection and erosions); (iii) patients that were comatose (could not communicate properly, could not fill the voiding diary); (iv) patients with bed ulcers that might develop infections; (v) patients with bladder cancer, a history of genitourinary malignancy within the previous 5 years (their LUTS might be caused by cancer rather than the neurological condition) and pregnant patients (contraindicated to do implantation during pregnancy and should be turned off during pregnancy). All included patients completed voiding diaries and underwent a urodynamic study for their functional diagnosis at a baseline.

Ethical approval was received from the Biomedical Ethics and Research Committee of King Abdulaziz University Hospital, Jeddah, Saudi Arabia (no. 398-20). All patients provided written informed consent. In error, this trial was not prospectively registered, but it was retrospectively registered at the Research Registry (https://www.researchregistry.com/: registration number 7936). The reporting of this study conforms to the CONSORT statements.[23]

Sacral neuromodulation procedure

All of the included patients underwent stage 1 sacral neuromodulation. The stage 1 procedure was the test phase in which the best responding nerve was identified and a single tined, 4-electrode lead (3889-28 tined lead kit; Medtronic, Minneapolis, MN, USA) was usually implanted into the S3 foramen. During the stage 1 procedure, S3 and S4 were tested bilaterally and the best responding nerve received the permanent electrode implant. The percutaneous nerve evaluation test was not used to avoid migration. As sensations in these patients are usually lost in the perineal area this study depended on the motor response of inward contractions of bellows. After the trial procedure, patients completed a voiding diary for 2 weeks that was compared with the baseline diary that was completed before the procedure. If the patient had ≥50% improvement subjectively and/or objectively recorded on their voiding diary (improved voided volume/void, decreased frequency, better control of urine leak and decreased postvoiding residual [PVR]), they underwent the stage 2 procedure and implantation of a permanent internal pulse generator (InterStim™ II System; Medtronic). Implant were usually situated at the higher buttock area after testing that there was no pressure in seated position. All patients received unilateral implantation of an MRI non-compatible device (3889-28 tined lead kit; Medtronic). This issue was explained to all patients and patients with MS and any that might need an MRI in future provided consent for the possibility of device removal if an MRI was required in the future. A 2-week interval between the stage 1 and 2 procedures was followed in all patients.

After the stage 2 procedure, patients had their device programmed and they were taught how to use their programmer. Patients with <50% improvement after the stage 1 procedure were not candidates for stage 2 and the electrode was removed. Postoperative clinical follow-up visits for wound healing and proper use of the device were undertaken 1 and 2 weeks. A follow-up visit at 6 months after the stage 2 procedure was undertaken to ensure that the patient was maintaining a good response and to assess the effect of SNM therapy on nLUTS. During the annual follow-up visit, the patient was asked to complete a voiding diary and a short satisfaction questionnaire in the

waiting area. These forms were collected by nurses. The last completed voiding diary was compared with the patient's baseline voiding diary.

Urodynamic test

A urodynamic test was undertaken for all patients before undergoing the stage 1 procedure as a baseline to confirm the functional diagnosis (i.e. which nLUTS type). The urodynamic test was completed using the International Continence Society standards.[24] The urodynamic result helped to establish a functional diagnosis of bladder function and counsel the patient according to the available published data. All patients underwent video-urodynamic testing. The diagnosis of overactive bladder was confirmed if there was evidence of uninhibited bladder contractions during the filling phase, while diagnosis of retention was confirmed by atonic bladder on the voiding phase of the urodynamic test. The result of the urodynamic test did not influence the indication for stimulation.

Outcome measures

Voiding diaries were used at baseline (before the stage 1 procedure) and on each annual visit. Voiding diaries were used to assess the following outcome variables: mean voided volume/void/24 h (the sum of total voided volume per void in a day divided by the number of voids/day); mean frequency of voiding/24 h (number of voiding times per day); mean leaking episodes/24 h (how many times documented leaking of urine happened/day); overall mean PVR (amount of PVR measured after a free void using clean intermittent catheterization [CIC] in 24 h/times of CIC); and number of CIC/24 h (number of CIC done per day).

Patient satisfaction was assessed by a self-developed short questionnaire for the level of therapy satisfaction and answers were categorized as follows: highly satisfied, moderately satisfied and not satisfied.

Statistical analyses

All demographic, voiding diary (the baseline and last visit data) and satisfaction level (last visit) data were collected into a Microsoft® Excel® spreadsheet (Microsoft, Redmond, WA, USA) and analysed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). A sample size calculation was not performed and it is acknowledged that a limited number of samples may affect the statistical significance of these results. Data were checked for normal distribution using an SPSS histogram. Descriptive statistics were reported as frequencies for categorical variables. Comparisons between the baseline and last visit voiding diary mean data were performed using Student's t-test. A P-value ≤ 0.05 were considered statistically significant.

Results

This prospective cohort study enrolled 21 patients (eight males and 13 females) (Figure 1). Their diagnoses were DM ($n = 2$), myelitis ($n = 3$), MS ($n = 5$), spinal cord injury ($n = 10$) and CVA ($n = 1$). All underwent a preoperative urodynamic test. Their functional diagnoses were neurogenic non-obstructive retention ($n = 10$), neurogenic overactive bladder ($n = 8$) and combined neurogenic retention plus neurogenic overactive bladder ($n = 3$). Detrusor-sphincter dyssynergia (DSD) was present in seven patients. All patients underwent the stage 1 procedure with success in 15 patients and failure in six patients (Table 1). The mean age was 47.5 years and the mean follow-up of 29 months in the 15 patients that progressed to stage 2 full device implantation.

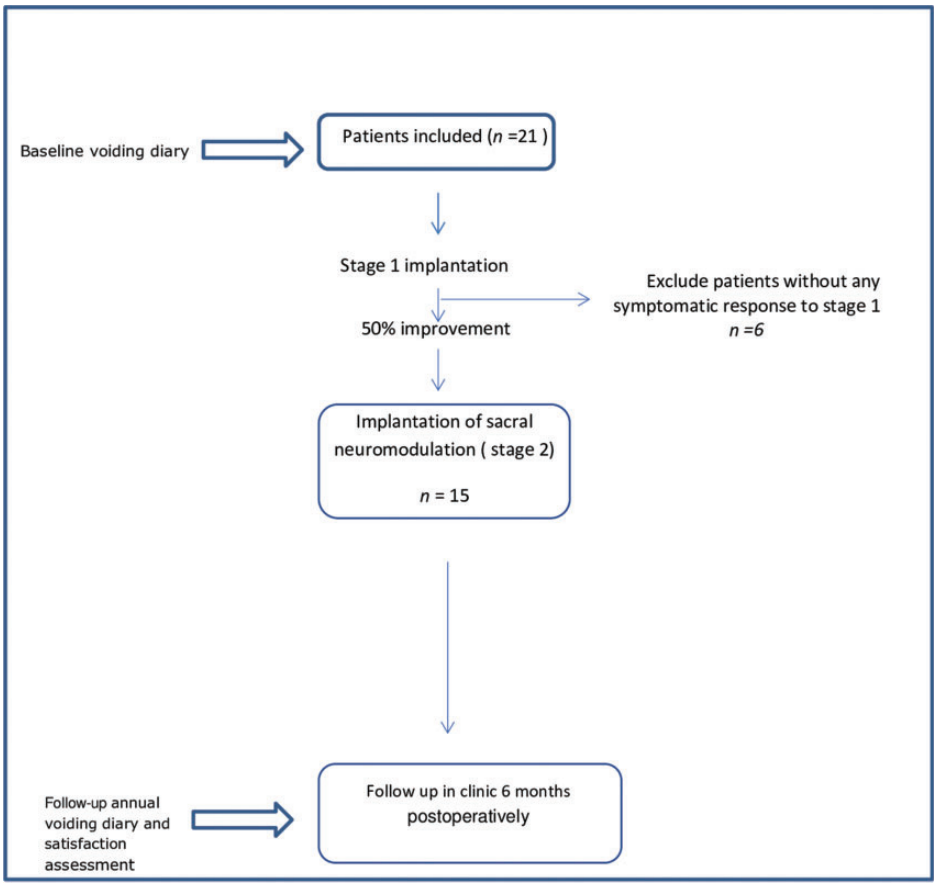

Figure 1. Flow diagram showing the number of patients implanted, excluded and included in the final analysis in a prospective cohort study designed to evaluate the effectiveness of sacral neuromodulation therapy for lower urinary tract symptoms caused by neurological diseases.

Table 1. Demographic and clinical characteristics of patients ($n = 21$) included in a prospective cohort study designed to evaluate the effectiveness of sacral neuromodulation therapy for the lower urinary tract symptoms caused by neurological diseases.

Variable	Study cohort $n = 21$
Sex	
Male	8 (38.1%)
Female	13 (61.9%)
Functional diagnosis	
Retention	10 (47.6%)
Overactive bladder	8 (38.1%)
Overactive bladder + retention	3 (14.3%)
Detrusor-sphincter dyssynergia	
Present	7 (33.3%)
Absent	13 (61.9%)
Neurological diagnosis	
Diabetes mellitus	2 (9.5%)
Myelitis	3 (14.3%)
Multiple sclerosis	5 (23.8%)
Spinal cord injury	10 (47.6%)
Cerebrovascular accident	1 (4.8%)
Stage 1 procedure result	
Success	15 (71.4%)
Failure	6 (28.6%)

(continued)

Table 1. Continued.

Data presented as *n* of patients (%).

The success rate of the stage 1 procedure was 71.4% (15 of 21 patients). The success of the stage 1 procedure based on the aetiology of the nLUTS is shown in Figure 2. The success rate of the stage 1 procedure was higher in the neurogenic overactive bladder group (87.5%; seven of eight patients) than in the combined retention plus neurogenic overactive bladder group (66.7%; two of three patients) and the neurogenic non-obstructive retention group (60.0%; six of 10 patients) (Figure 3). The presence of DSD in patients with urodynamic tests decreased the success rate of the stage 1 procedure from 78.6% (11 of 14 patients) to 57.1% (four of seven patients) (Figure 4). All successful stage 1 patients proceeded to stage 2 implantation, while failed patients underwent electrode removal.

The main presentation of the 15 patients that had full device implantation (i.e. proceeded to stage 2) included urine retention in six and urine leak in nine (Table 2). These patients included six with atonic bladder, seven with neurogenic overactive bladders, four with DSD and two with combined overactive bladder and retention. The mean follow-up duration for the implanted patients was 29 months.

Sacral neuromodulation therapy resulted in a significantly increased voided volume/void/day ($P = 0.0001$), decreased leaking episodes/day ($P = 0.001$), decreased post-voiding residual/day ($P = 0.002$) and decreased number of CIC/day ($P = 0.002$) compared with baseline (Table 3).

Complications reported in the implanted cohort included skin erosion in one patient (Table 2). A conventional non-rechargeable

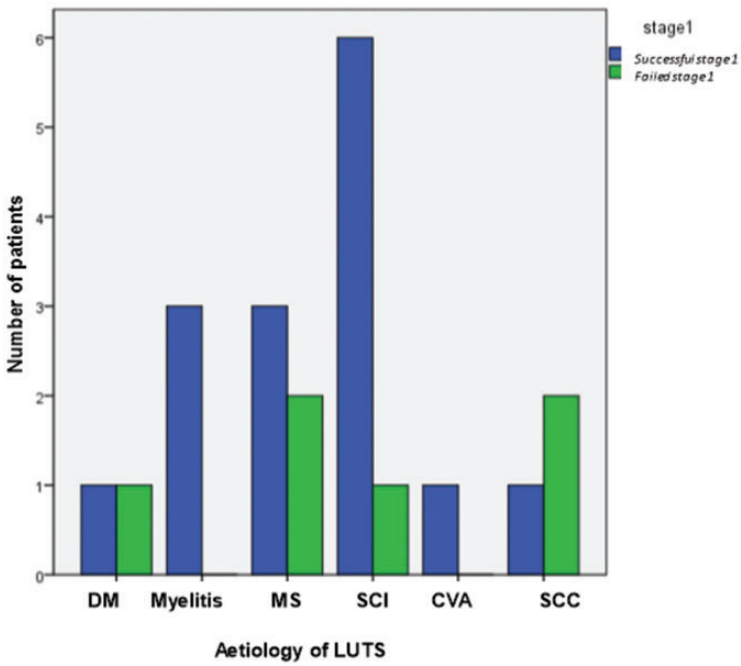

Figure 2. Results of the stage 1 procedure (success versus failure) according to the aetiology of the lower urinary tract symptoms (LUTS) in patients included in a prospective cohort study designed to evaluate the effectiveness of sacral neuromodulation therapy for LUTS caused by neurological diseases. DM, diabetes mellitus; MS, multiple sclerosis; SCI, spinal cord injury; CVA, cerebrovascular accident; SCC, spinal cord compression. The colour version of this figure is available at: http://imr.sagepub.com.

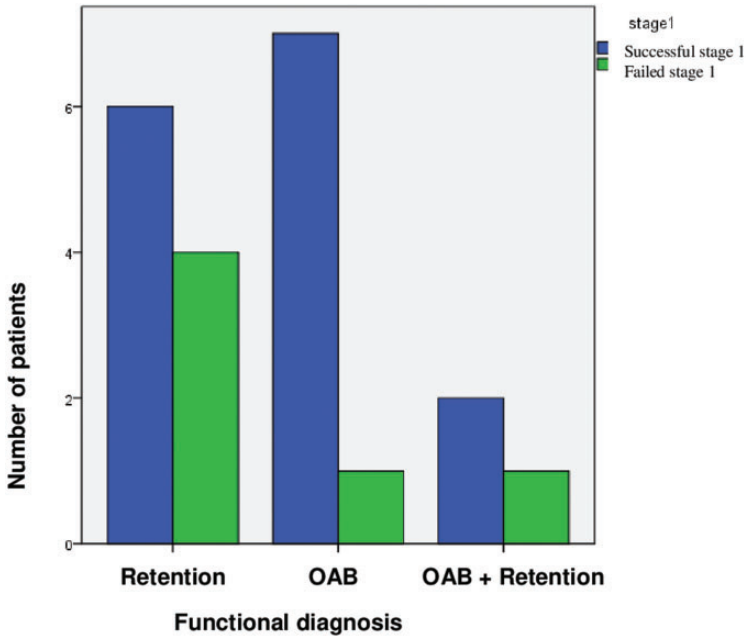

Figure 3. Results of the stage 1 procedure (success versus failure) according to the functional diagnosis of the lower urinary tract symptoms (LUTS) in patients included in a prospective cohort study designed to evaluate the effectiveness of sacral neuromodulation therapy for LUTS caused by neurological diseases. OAB, overactive bladder. The colour version of this figure is available at: http://imr.sagepub.com.

device was implanted in the current patients. When the battery becomes depleted, as detected by the physician programmer, and the patient loses device efficacy, the battery is exchanged. In this current study, only one patient needed a battery replaced. When patients were questioned regarding their satisfaction levels, five patients were highly satisfied, nine were moderately satisfied and one patient was not satisfied with the therapy.

Discussion

This current study showed evidence of efficacy of SNM in nLUTS with a level of patient satisfaction. Multiple studies worldwide have reported successful off-label use of SNM in nLUTS.[25–27] A previous study reported the use of SNM in a group of mixed nLUTS patients (including spinal cord injury, MS, cerebral palsy, peripheral nerve disorders, and stroke); with urinary incontinence in 62% of these patients.[28] A systemic review in 2010 reported a 68% success rate for stage 1.[29] The same meta-analysis reported that the success rate at stage 1 was lower in neurogenic non-obstructive urinary retention (nNOUR) compared with neurogenic overactive bladder (nOAB) (52% versus 61%, respectively), while combined nNOUR plus nOAB had a success rate of 69%.[29] This rate was the same as in another study that reported a 70% success rate in these groups combined.[30] A recent systemic review and meta-analysis published in 2021 confirmed these results and reported the success rate of stage 1 according to the type of neurogenic lower urinary tract dysfunction (nLUTD) as 61% in nOAB, 52% in nNOUR and 69% in the combination

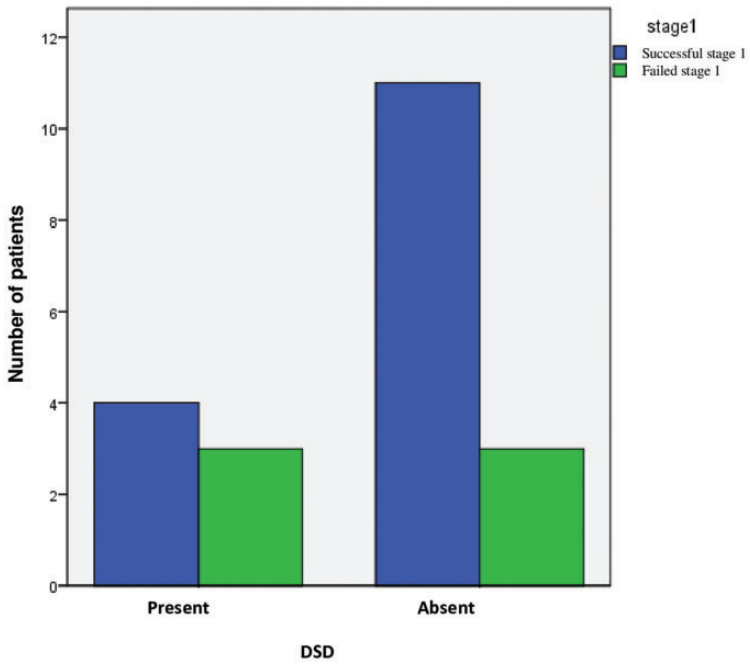

Figure 4. Results of the stage 1 procedure (success versus failure) according to presence versus absence of detrusor-sphincter dyssynergia (DSD) in patients included in a prospective cohort study designed to evaluate the effectiveness of sacral neuromodulation therapy for of the lower urinary tract symptoms caused by neurological diseases. The colour version of this figure is available at: http://imr.sagepub.com.

therapy group.[31] In contrast, another study concluded that the type of nLUTD had no impact on the test success rate.[32]

This current study showed a success rate of the stage 1 procedure of 71.4% (15 of 21 patients). The rate of success of the stage 1 procedure was higher in the overactive bladder group (87.5%; seven of eight patients) than in the combined retention plus neurogenic overactive bladder group (66.7%; two of three patients) and the neurogenic non-obstructive retention group (60.0%; six of 10 patients), which was comparable with international reports.[31] The presence of DSD in the current patients decreased the success rate of the stage 1 procedure from 78.6% to 57.1%. Previous studies have reported clinical improvement in patients with DSD treated with SNM.[31–34]

Complications reported in the current implanted cohort included skin erosion in one patient and the need for battery replacement in one patient. A previous study reported complications in 25% of 494 nLUTD patients that developed complications after SNM.[31] This previous finding was similar to a pooled complication rate of 24% reported previously.[29] The patient satisfaction rate was high in this current study and similar to that previously reported for 32 patients treated with SNM for nLUTS.[35] At the last follow-up, 21 patients were very satisfied, nine were satisfied, one was unchanged and one was unsatisfied.[35]

This current study showed different success rates for the stage 1 procedure according to the aetiology of the neurological

Table 2. Demographic and clinical characteristics of patients ($n = 15$) that underwent sacral neuromodulation therapy stratified according to the neurological disease causing the lower urinary tract symptoms.

Neurological disease	DM $n = 1$	Myelitis $n = 3$	MS $n = 3$	SCI $n = 7$	CVA $n = 1$	Total $n = 15$
Age, years	62	44	46	47	52	47.5
Follow-up period, months	33	27	29	22	35	29
Sex						
Male	0	0	0	6	0	6
Female	1	3	3	1	1	9
Voiding dysfunction						
Urine retention	1	2	1	2	0	6
Urine leakage	0	1	2	5	1	9
Urodynamic diagnosis						
Atonic bladder	1	2	1	2	0	6
Overactive bladder	0	0	2	4	1	7
Overactive bladder + retention	0	1	0	1	0	2
Detrusor-sphincter dyssynergia	0	1	2	1	0	4
Complications						
Erosion	0	1	0	0	0	1
Battery depletion	0	0	1	0	0	1
Revision	0	0	0	0	0	0
None	1	2	2	7	1	13
Satisfaction level						
Highly satisfied	0	1	0	3	1	5
Moderately satisfied	1	2	2	4	0	9
Not satisfied	0	0	1	0	0	1

Data presented as mean or *n* of patients.
DM, diabetes mellitus; MS, multiple sclerosis; SCI, spinal cord injury; CVA, cerebrovascular accident.

Table 3. Baseline and last visit voiding diary data from patients ($n = 15$) that underwent sacral neuromodulation therapy for the lower urinary tract symptoms caused by neurological diseases.

	Mean voided volume/void/24 h	Mean frequency of voiding/24 h	Mean leaking episodes/24 h	Mean PVR	Mean number of CIC/24h
Base line	38.67 ± 35.12	8.87 ± 7.74	2.80 ± 2.30	178.67 ± 186.73	2.60 ± 2.61
Last visit	313.0 ± 100.6	5.1 ± 1.0	0.3 ± 0.5	17.7 ± 24.4	0.2 ± 0.4
Statistical analyses[a]	$P = 0.0001$	NS	$P = 0.001$	$P = 0.002$	$P = 0.002$

Data presented as mean ± SD.
[a]Student's *t*-test; NS, no significant between time-point difference ($P > 0.05$).
PVR, postvoiding residual; CIC, clean intermittent catheterization.

disorder leading to nLUTS. All three patients with myelitis had a successful stage 1 procedure compared with six of seven of the patients with spinal cord injury. This might be explained by the possible injury to the spinal cord tracts that are involved in the SNM therapy pathway in patients with spinal cord injury.

This theory is supported by the fact that only three of five patients with MS had successful stage 1 procedures, which might have been due to damaged spinal tracts.

This current study had several limitations. First, the sample size was small, but this was not unexpected for the type and nature of the study, especially as SNM has only been recently introduced in Saudi Arabia. Secondly, the study only included patients with DM that had stable blood glucose levels in order to avoid postoperative wound complications. Thirdly, the stage 2 procedure was only undertaken in those patients with $\geq$50% symptomatic improvement at stage 1, so SNM is unlikely to benefit all patients with nLUTS. Finally, it should be noted that the study included heterogeneous patients and did not include all types of neurological disease that can cause nLUTS. However, this study had the advantage of being a prospective cohort design addressing the impact of therapy on nLUTS in Saudi Arabia.

In conclusion, SNM was an effective therapy for LUTS caused by neurological disease, with a high satisfaction rate in the current cohort of patients. Studies with larger sample sizes are recommended.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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References

1. Nyberg-Hansen R. Innervation and nervous control of the urinary bladder. Anatomical aspects. *Acta Neurol Scand* 1966; 42: 7–24. doi: 10.1111/j.1600-0404.1966.tb02015.x. PMID: 5328649.
2. de Groat WC, Griffiths D and Yoshimura N. Neural control of the lower urinary tract. *Compr Physiol* 2015; 5: 327–396. doi: 10.1002/cphy.c130056. PMID: 25589273; PMCID: PMC4480926.
3. Sugaya K, Nishijima S, Miyazato M, et al. Central nervous control of micturition and urine storage. *J Smooth Muscle Res* 2005; 41: 117–132. doi: 10.1540/jsmr.41.117. PMID: 16006745.
4. Ginsberg D. The epidemiology and pathophysiology of neurogenic bladder. *Am J Manag Care* 2013; 19: s191–s196. PMID: 24495240.
5. Frimodt-Møller C. Diabetic cystopathy. A review of the urodynamic and clinical features of neurogenic bladder dysfunction in diabetes mellitus. *Dan Med Bull* 1978; 25: 49–60. PMID: 344005.
6. Gandhi J, Dagur G, Warren K, et al. Genitourinary complications of diabetes mellitus: an overview of pathogenesis, evaluation, and management. *Curr Diabetes Rev* 2017; 13: 498–518. doi: 10.2174/1573399812666161019162747. PMID: 27774877.
7. Koubaa S, Ben Salah FZ, Miri I, et al. Neurogenic bladder in diabetes mellitus. *La Tunisie Medicale* 2009; 87: 279–282 [Article in French]. PMID: 19835286.
8. Rashid TM and Hollander JB. Multiple sclerosis and the neurogenic bladder. *Phys Med Rehabil Clin N Am* 1998; 9: 615–629. PMID: 9894113.
9. Phé V, Chartier-Kastler E and Panicker JN. Management of neurogenic bladder in patients with multiple sclerosis. *Nat Rev Urol* 2016; 13: 275–288. doi: 10.1038/nrurol.2016.53. Epub 2016 Mar 31. PMID: 27030526.
10. de Sèze M, Ruffion A, Denys P, et al. The neurogenic bladder in multiple sclerosis: review of the literature and proposal of management guidelines. *Mult Scler* 2007; 13: 915–928. doi: 10.1177/1352458506075651. Epub 2007 Mar 15. PMID: 17881401.
11. Myers JB, Lenherr SM, Stoffel JT, et al. Patient reported bladder related symptoms and quality of life after spinal cord injury

with different bladder management strategies. *J Urol* 2019; 202: 574–584. doi: 10.1097/JU.0000000000000270. Epub 2019 Aug 8. PMID: 30958741.
12. Hu HZ, Granger N and Jeffery ND. Pathophysiology, clinical importance, and management of neurogenic lower urinary tract dysfunction caused by suprasacral spinal cord injury. *J Vet Intern Med* 2016; 30: 1575–1588. doi: 10.1111/jvim.14557. Epub 2016 Aug 16. PMID: 27527382; PMCID: PMC5032886.
13. Abdulaziz Al Dawish M, Alwin Robert A, Braham R, et al. Diabetes mellitus in Saudi Arabia: a review of the recent literature. *Curr Diabetes Rev* 2016; 12: 359–368.
14. Al-Jumah M, Bunyan R, Al Otaibi H, et al. The Saudi Arabian National Multiple Sclerosis Registry (NMSR): Initial Results Saudi MS Registry Study Group. *Neurology* 2018; 90(15 Supplement): P2.390.
15. Kumar R, Lim J, Mekary RA, et al. Traumatic Spinal Injury: Global Epidemiology and Worldwide Volume. *World Neurosurg* 2018; 113: e345–e363. doi: 10.1016/j.wneu.2018.02.033. Epub 2018 Feb 14. PMID: 29454115.
16. Niemi-Nikkola V, Saijets N, Ylipoussu H, et al. Long-term Posttraumatic Survival of Spinal Fracture Patients in Northern Finland. *Spine (Phila Pa 1976)* 2018; 43: 1657–1663. doi: 10.1097/BRS.0000000000002687. PMID: 29664815.
17. Choi JH, Park PJ, Din V, et al. Epidemiology and clinical management of traumatic spine injuries at a major government hospital in Cambodia. *Asian Spine J* 2017; 11: 908–916. doi: 10.4184/asj.2017.11.6.908. Epub 2017 Dec 7. PMID: 29279746
18. Memish ZA, Jaber S, Mokdad AH, et al. Burden of disease, injuries, and risk factors in the Kingdom of Saudi Arabia, 1990-2010. *Prev Chronic Dis* 2014; 11: E169. doi: 10.5888/pcd11.140176. PMID: 25275806; PMCID: PMC4184091.
19. Robert AA and Zamzami MM. Traumatic spinal cord injury in Saudi Arabia: a review of the literature. *Pan Afr Med J* 2013; 16: 104. doi: 10.11604/pamj.2013.16.104.2902.
20. Gosselin RA, Spiegel DA, Coughlin R, et al. Injuries: the neglected burden in developing countries. *Bull World Health Organ* 2009; 87: 246–246a. doi: 10.2471/blt.08.052290. PMID: 19551225.
21. Hassouna MM, Siegel SW, Nyeholt AA, et al. Sacral neuromodulation in the treatment of urgency- frequency symptoms: a multicenter study on efficacy and safety. *J Urol* 2000; 163: 1849–1854. PMID: 10799197.
22. Banakhar M, Al-Shaiji T and Hassouna M. Sacral neuromodulation and refractory overactive bladder: an emerging tool for an old problem. *Ther Adv Urol* 2012; 4: 179–185. doi: 10.1177/1756287212445179.
23. Schulz KF, Altman DG and Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010; 340: c332. doi: 10.1136/bmj.c332. PMID: 20332509; PMCID: PMC2844940.
24. Drake MJ, Doumouchtsis SK, Hashim H, et al. Fundamentals of urodynamic practice, based on international continence society good urodynamic practices recommendations. *Neurourol Urodyn* 2018; 37: S50–S60. doi: 10.1002/nau.23773. PMID: 30614058.
25. Kessler TM, Wöllner J, Kozomara M, et al. Sacral neuromodulation for neurogenic bladder dysfunction. *Urologe A* 2012; 51: 179–183 [Article in German, English abstract]. doi: 10.1007/s00120-011-2779-0. PMID: 22269992.
26. Lo CW, Wu MY, Yang SS, et al. Comparing the Efficacy of OnabotulinumtoxinA, Sacral Neuromodulation, and Peripheral Tibial Nerve Stimulation as Third Line Treatment for the Management of Overactive Bladder Symptoms in Adults: Systematic Review and Network Meta-Analysis. *Toxins (Basel)* 2020; 12: 128. doi: 10.3390/toxins12020128. PMID: 32085542; PMCID: PMC7077313.
27. Redshaw JD, Lenherr SM, Elliott SP, et al. Protocol for a randomized clinical trial investigating early sacral nerve stimulation as an adjunct to standard neurogenic bladder management following acute spinal cord injury. *BMC Urol* 2018; 18: 72. doi: 10.1186/s12894-018-0383-y. PMID: 30157824; PMCID: PMC6116487.
28. Okafor H, Gill B, Pizarro-Berdichevsky J, et al. Sacral neuromodulation therapy in

patients with neurologic lower urinary tract dysfunction – Should it remain an off-label indication? analysis of 80 consecutive cases. *J Urol* 2016; 195: e188.
29. Kessler TM, La Framboise D, Trelle S, et al. Sacral neuromodulation for neurogenic lower urinary tract dysfunction: systematic review and meta-analysis. *Eur Urol* 2010; 58: 865–874. doi: 10.1016/j.eururo.2010.09.024.
30. Hennessey DB, Hoag N and Gani J. Sacral neuromodulation for detrusor hyperactivity with impaired contractility. *Neurourol Urodyn* 2017; 36: 2117–2122. doi: 10.1002/nau.23255.
31. van Ophoven A, Engelberg S, Lilley H, et al. Systematic literature review and meta-analysis of sacral neuromodulation (SNM) in patients with neurogenic lower urinary tract dysfunction (nLUTD): over 20 years' experience and future directions. *Adv Ther* 2021; 38: 1987–2006. doi: 10.1007/s12325-021-01650-9.
32. Chaabane W, Guillotreau J, Castel-Lacanal E, et al. Sacral neuromodulation for treating neurogenic bladder dysfunction: clinical and urodynamic study. *Neurourol Urodyn* 2011; 30: 547–550. doi: 10.1002/nau.21009.
33. Sievert KD, Amend B, Gakis G, et al. Early sacral neuromodulation prevents urinary incontinence after complete spinal cord injury. *Ann Neurol* 2010; 67: 74–84. doi: 10.1002/ana.21814. PMID: 20186953.
34. Minardi D and Muzzonigro G. Sacral neuromodulation in patients with multiple sclerosis. *World J Urol* 2012; 30: 123–128. doi: 10.1007/s00345-011-0669-0.
35. Wöllner J, Krebs J, and Pannek J. Sacral neuromodulation in patients with neurogenic lower urinary tract dysfunction. *Spinal Cord* 2016; 54: 137–140. doi: 10.1038/sc.2015.124.