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Outcomes of Sacral Nerve Stimulation for Treatment of Refractory Overactive Bladder Among Octogenarians

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Objective: Sacral nerve stimulation (SNS) is an effective treatment for refractory overactive bladder (OAB). However, advanced age is often cited as a reason to avoid SNS in the elderly. This study evaluates the safety and efficacy of SNS for refractory OAB among our octogenarian population.

Methods: A retrospective review from a single institution was performed on all SNS lead placements from December 1998 to June 2017 for refractory OAB. Octogenarians were characterized as 80 years of age or older at the time of Stage I. Efficacy and safety were determined by the rate of progression to Stage II, subsequent need for multimodal therapy, and rate of surgical revision and explantation. All patients were followed for a minimum of 12 months.

Results: Of 374 patients in this study, 37 (9.9%) were octogenarians. There was no difference in gender, race, smoking history, or prior OAB treatment regimens between cohorts. The rate of progression to Stage II was 56.8% for octogenarians compared to 60.5% for nonoctogenarians ($p = 0.66$). The rate of surgical revision, explantation, and need for multimodal therapy did not differ between groups. Subgroup analysis of octogenarians did not reveal any significant differences between successful and nonsuccessful Stage I patients.

Conclusions: The safety and efficacy of SNS was similar between cohorts. This result suggests that SNS is a safe and effective therapy that should be considered among the treatment options for refractory OAB in octogenarian patients. Further studies are needed to determine predictive factors of Stage I success in elderly patients.

Keywords: Elderly, octogenarian, refractory overactive bladder, sacral nerve stimulation, sacral neuromodulation

Conflict of Interest: Craig Comiter, MD, is a consultant for Neuspera Medical Systems. The remaining authors have no conflicts of interest to report.

INTRODUCTION

Overactive bladder (OAB) is a common urologic condition that is characterized by urinary urgency with or without urgency incontinence, often associated with urinary frequency and nocturia (1). Previous studies have shown that the incidence of OAB increases with age, affecting between 15% and 26% of patients age 18–29 years of age, and over one-third of individuals more than 60 years of age (2–4). Advancing age can cause structural and physiologic changes in the lower urinary tract, which can result in decreased maximum bladder capacity and an increase in OAB symptoms (5,6).

The symptoms of OAB can lead to social isolation, expedite institutionalization, and negatively impact overall quality of life (7). The psychosocial impact of OAB has proven to be particularly devastating in the octogenarian population (8,9). First- and second-line treatments for OAB include lifestyle modifications, bladder retraining, and pharmacologic therapy with anticholinergic and/or beta-adrenergic medications. However, oral medications can be problematic in the elderly population. Barriers such as cognitive deficits, intolerance of side effects, and multiple comorbidities often lead to poor medication compliance and concern for polypharmacy (10–12). Patients whose OAB symptoms are refractory to initial treatments are offered advanced therapies, which include intradetrusor onabotulinumtoxinA injection, percutaneous tibial nerve stimulation (PTNS), and/or sacral nerve stimulation (SNS).

SNS has shown to be an effective therapy in approximately 70–90% of subjects with refractory OAB (13,14). SNS placement is usually performed as a two-stage outpatient procedure with a test stimulation prior to permanent placement. This is performed via peripheral nerve evaluation (PNE) or staged implantation. Despite its efficacy, advanced age is often cited as a reason to avoid this treatment modality due to the potential risk of anesthesia, concerns regarding treatment efficacy, and risk of complications. Consequently, this group is poorly represented in the published literature. Therefore, the primary objective of this study is to

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determine the safety and efficacy of SNS in our octogenarian population. The secondary aim is to analyze the role of multimodal therapy in octogenarian and nonoctogenarian patients with loss of SNS treatment efficacy over time, despite reprogramming and device revision, when applicable.

METHODS

Study Design and Patient Population

We performed a retrospective review of all patients with refractory OAB who underwent SNS lead placement (InterStim®, Medtronic, Minnesota, MN) between December 1998 and June 2017 at our institution. In this study, octogenarians were characterized as patients who were 80 years of age or older at time of Stage I SNS lead placement. Indications for SNS therapy included refractory urinary frequency, urinary urgency, and/or urge incontinence.

All patients underwent two-stage SNS placement with either unilateral or bilateral Stage I test phase, depending on surgeon preference. In the unilateral Stage I cohort, transforaminal needles were initially placed bilaterally and tested independently during the intraoperative procedure. The lead was placed on the side that demonstrated a motor response (e.g., bellows and/or contraction of the ipsilateral great toe) at a lower voltage threshold, and the other transforaminal needle was removed. In the bilateral Stage I cohort, bilateral leads were placed, and stimulated independently for seven days each during the 14-day trial period. If Stage I was successful, a unilateral implantable pulse generator (IPG) was placed (Stage II). In the bilateral cohort, placement was on the side that resulted in a greater improvement in voiding diary parameters. During the study period, bilateral lead placement during Stage I was instituted with the goal of maximizing success and improving outcomes. Our group evaluated outcomes of unilateral vs. bilateral lead placement among our patients, and determined there was no difference in Stage I success rates. Given this finding, routine unilateral lead placement was performed during the latter end of the study period. Stage I was considered a "success" if the patient experienced greater than 50%

Table 1. Demographic Information, Pre-SNS Data, and Stage I Success Rate.

	Octogenarian, $N = 37$ (%)	Nonoctogenarian, $N = 337$ (%)	p Value ($p < 0.05$)
Age at Stage I	83.5 ± 0.5	58.9 ± 0.8	**<0.01**
Gender			0.44
Male	16 (43.2)	124 (36.8)	
Female	21 (56.8)	213 (63.2)	
BMI	26.4 ± 0.7	28.8 ± 0.4	0.05
Race			0.24
African American	2 (5.4)	12 (3.6)	
Asian	0 (0.0)	14 (4.2)	
Native American	0 (0.0)	2 (0.6)	
Other	2 (5.4)	34 (10.1)	
Unknown or not reported	0 (0.0)	26 (7.7)	
White	33 (89.2)	249 (73.9)	
Comorbidities			
Cardiovascular disease	21 (56.8)	61 (18.1)	**<0.01**
Diabetes mellitus	7 (18.9)	46 (13.6)	0.38
Neurologic disease/injury	12 (32.4)	129 (38.3)	0.49
Previous genitourinary surgery or procedure	20 (54.1)	157 (46.6)	0.39
Stroke	3 (8.1)	25 (7.4)	0.88
Smoking history			0.86
Current smoker	3 (8.1)	24 (7.1)	
Former smoker	13 (35.1)	106 (31.5)	
Pack-years	21.0 ± 5.5	19.2 ± 1.9	0.76
Never smoker	21 (56.8)	207 (61.4)	
Prior OAB therapy			
Oral medications	36 (97.3)	335 (99.4)	0.17
OnabotulinumtoxinA	5 (13.5)	39 (11.6)	0.73
PTNS	1 (2.7)	13 (3.9)	0.73
SNS	0 (0.0)	10 (3.0)	0.29
OAB classification			**0.02**
OAB-wet	31 (83.8)	217 (64.4)	
OAB-dry	6 (16.2)	120 (35.6)	
Stage I lead stimulation			**0.03**
Unilateral	5 (13.5)	105 (31.2)	
Bilateral	32 (86.5)	232 (68.8)	
Progression to Stage II	21 (56.8)	204 (60.5)	0.66

Measures of central tendency are reported as mean ± SEM. Continuous variables were analyzed using Student's t test, and categorical variables were analyzed using Chi square test. Bolded values represent statistically significant p values showing differences between the cohort of octogenarians and the cohort of nonoctogenarians.
BMI, body mass index; OAB, overactive bladder; PTNS, percutaneous tibial nerve stimulation; SNS, sacral nerve stimulation.

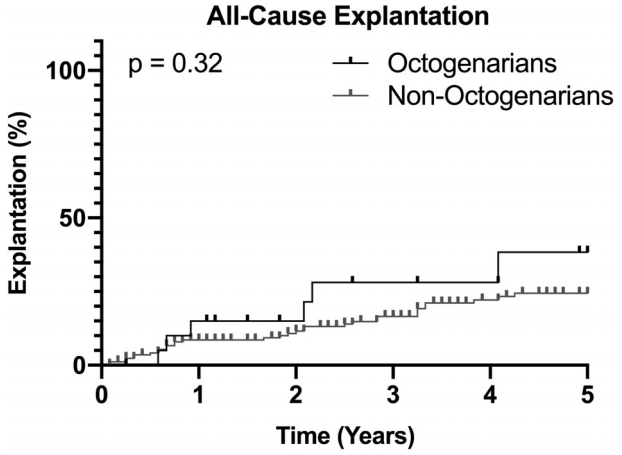

Figure 1. Analysis of five-year all-cause explantation of sacral nerve stimulation device among octogenarian and nonoctogenarian patients following Stage II permanent placement.

improvement in urinary frequency, incontinence episodes, and/or voided volume during the two-week Stage I trial period. Over the patients were retrospectively reviewed from Stage I lead placement until their last clinic follow-up visit by June 2018, to allow a minimum of one-year follow-up. During the follow-up period, patients were evaluated to determine whether they required multimodal OAB therapy, device revision, or explantation prior to their latest clinic follow-up. Multimodal OAB therapy refers to the subsequent addition of oral pharmacologic OAB medications (e.g., anticholinergic and beta3-agonists), onabotulinumtoxinA, PTNS, and/or pelvic floor physical therapy as a supplement to SNS therapy.

Statistical Analyses

The primary outcome for this study was efficacy of SNS, which was determined by the rate of progression to Stage II. Secondary analyses evaluated the need for subsequent multimodal therapy after permanent implantation, rate of surgical revision, and rate of explantation of the SNS device. Other variables analyzed include demographic data, comorbidities, smoking history, prior OAB therapy, classification of OAB symptoms (i.e., "wet" vs. "dry"), multimodal OAB therapies, and indications for revision and/or explantation.

Descriptive, chi-square, *t* test, multivariate logistic regression, and log-rank test analyses were performed using Stata v15.1 (StataCorp., 2017, College Station, TX) statistical software. Graphical analyses were performed using GraphPad Prism (Version 6.07, La Jolla, CA). A p value of <0.05 was deemed statistically significant. Measures of central tendency are reported as mean ± standard error. This study was approved by the Institutional Review Board at our institution.

RESULTS

In total, 374 patients underwent Stage I SNS at our institution during the study period. The average age of all patients was 61.3 ± 0.8 years of age, of which 37 (9.9%) were more than 80 years of age at the time of Stage I placement. There were 140 (37.4%) men and 234 (62.6%) women included in the study (Table 1). The majority of patients were White (75.4%), with 14 (3.7%) African Americans, 14 (3.7%) Asians, two (0.5%) Native Americans, 36 (9.6%) Other, and 26 (7.0%) Unknown. The average time from Stage I placement to latest clinic follow-up was 44.7 ± 2.7 months, which was similar between octogenarian and nonoctogenarian patients (41.5 ± 5.9 vs. 45.0 ± 2.9 months, $p = 0.71$).

There was no difference in gender, race, or smoking history between the octogenarian and nonoctogenarian cohorts. There was no statistical difference in body mass index (BMI), rate of diabetes, stroke and other neurologic disorders or diseases, including spinal surgery and Parkinson's disease. However, the octogenarian patient cohort had a higher prevalence of patients classified as "OAB-wet" compared to nonoctogenarians (83.8% vs. 64.4%, $p = 0.02$), and a higher incidence of cardiovascular disease (56.8% vs. 18.1%, $p < 0.01$). On multivariate analysis, neither of these

Table 2. Post Stage II SNS Information for Successful Stage I SNS Patients.

	Octogenarian, $N = 21$ (%)	Nonoctogenarian, $N = 204$ (%)	p Value ($p < 0.05$)
Time to latest follow-up (months)	41.5 ± 5.9	45.0 ± 2.9	0.71
Revision surgery	4 (19.0)	37 (18.1)	0.92
Indication for revision surgery			0.87
Battery exchange	3 (75.0)	16 (43.2)	
Poor function	1 (25.0)	12 (32.4)	
Pain	0 (0.0)	3 (8.1)	
Wire extrusion	0 (0.0)	3 (8.1)	
Lead migration	0 (0.0)	2 (5.4)	
Infection	0 (0.0)	1 (2.7)	
Explantation	6 (28.6)	42 (20.6)	0.40
Time to explantation (months)	19.7 ± 7.2	31.5 ± 4.7	0.36
Indication for explantation			0.67
Poor function	5 (83.3)	26 (61.9)	
Infection	0 (0.0)	5 (11.9)	
Magnetic resonance imaging	0 (0.0)	4 (9.5)	
Extrusion	1 (16.7)	4 (9.5)	
Pain	0 (0.0)	3 (7.1)	

Measures of central tendency are reported as mean ± SEM. Continuous variables were analyzed using Student's *t* test, and categorical variables were analyzed using Chi square test.

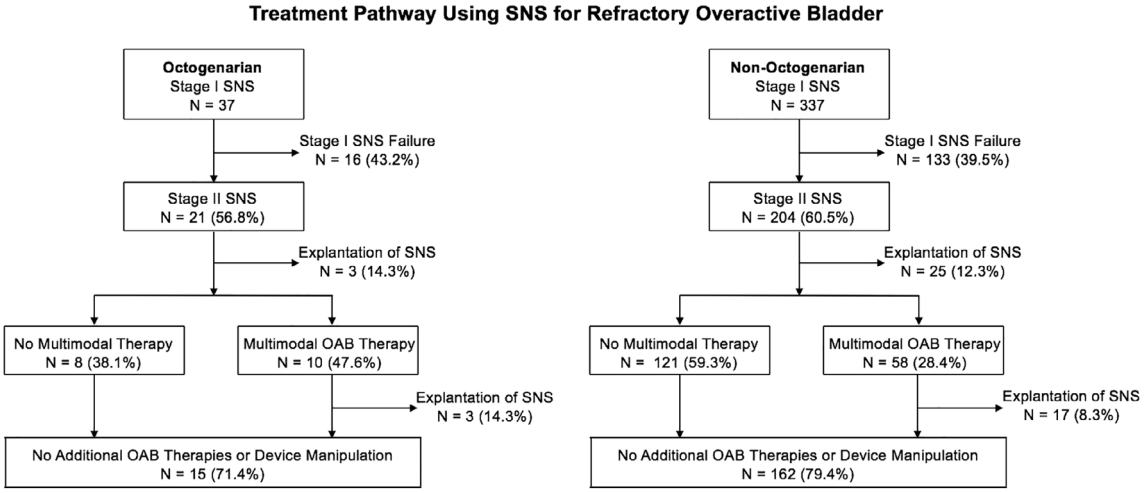

Figure 2. Flowchart showing the treatment pathway of all octogenarian (≥80 years of age, *N* = 37) and nonoctogenarian (<80 years of age, *N* = 337) patients with refractory overactive bladder (OAB). Sacral nerve stimulation outcomes evaluated whether the patient required device explantation or further treatment for OAB at their latest clinic follow-up.

Table 3. Summary of Multimodal OAB Therapy After Stage II SNS.

	Octogenarian, *N* = 10 (%)		Nonoctogenarian, *N* = 58 (%)		*p* Value ($p < 0.05$)
Time to therapy (months)	16.5 ± 5.0		24.9 ± 3.5		0.34
	No explantation	Explantation	No explantation	Explantation	
Type of therapy	7 (70.0)	3 (30.0)	41 (70.7)	17 (29.3)	0.97
Oral medications	4 (57.1)	3 (100.0)	33 (80.5)	10 (58.8)	0.27
OnabotulinumtoxinA	3 (42.9)	0 (0.0)	8 (19.5)	6 (35.3)	0.16
Physical therapy	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.9)	

Patients were evaluated for whether they underwent device explantation or required further treatment for OAB at their latest clinic follow-up visit. Measures of central tendency are reported as mean ± SEM. Continuous variables were analyzed using Student's *t* test, categorical variables were analyzed using Chi square test or Fisher's exact test.
OAB, overactive bladder.

variables showed a statistically significant impact with respect to progression to Stage II, explantation, or need for revision surgery ($p > 0.05$).

The two age cohorts also had similar OAB treatment regimens prior to Stage I SNS trial, with no difference shown between use of oral medications, onabotulinumtoxinA, or PTNS. A number of 110 (29.4%) patients underwent unilateral lead placement and 264 (70.6%) underwent bilateral lead placement. Although dependent on surgeon preference, octogenarians had a greater proportion of bilateral Stage I lead placement compared to nonoctogenarian patients ($p = 0.03$).

The overall rate of progression to Stage II among all study participants was 60.2% (225/374), with similar rates between age cohorts (56.8% vs. 60.5%, $p = 0.66$). After permanent IPG placement, octogenarians and nonoctogenarians had similar rates of revision surgery (19.0% vs. 18.1%, $p = 0.92$) and rates of device explantation (28.6% vs. 20.6%, $p = 0.40$) from the time of Stage II implantation to most recent clinic follow-up visit date. Analysis of Kaplan–Meier curve of five-year all-cause explantation after permanent placement was also similar between cohorts (Fig. 1, $p = 0.32$). Indications for revision and explantation were similar between both groups ($p = 0.87$ and 0.67, respectively) (Table 2).

A greater proportion of octogenarians ultimately required multimodal therapy compared to nonoctogenarians. However, this difference was not statistically significant (47.6% vs. 28.4%, $p = 0.07$). Our results show that overall, with or without the implementation of multimodal therapy, 78.7% of patients who underwent Stage II permanent placement did not undergo device explantation nor require additional treatment at latest clinic follow-up (Fig. 2). Comparison between oral medications and onabotulinumtoxinA as first-line multimodal treatment with SNS did not reveal any statistically significant difference in OAB treatment outcomes (Table 3).

Lastly, subgroup analysis of the octogenarian population treated with SNS did not reveal any significant differences in age, BMI, comorbidities, smoking history, prior OAB treatment, or type of lead placement (unilateral vs. bilateral) between successful and nonsuccessful Stage I patients (Table 4).

DISCUSSION

The prevalence of OAB increases with age, and most commonly affects patients more than 60 years old (4). The primary aim of

Table 4. Subgroup Analysis of Octogenarian SNS Patients.

	Stage I success, $N = 21$ (%)	Stage I failure, $N = 16$ (%)	p Value ($p < 0.05$)
Age at Stage I	83.0 ± 0.5	84.3 ± 0.8	0.16
Gender			0.47
Male	8 (38.1)	8 (50.0)	
Female	13 (61.9)	8 (50.0)	
BMI	26.8 ± 1.0	25.9 ± 1.1	0.55
Race			0.96
African American	1 (4.8)	1 (6.3)	
Unknown or not reported	1 (4.8)	1 (6.3)	
White	19 (90.5)	14 (87.5)	
Comorbidities			
Cardiovascular disease	11 (52.4)	10 (62.5)	0.54
Diabetes mellitus	5 (23.8)	2 (12.5)	0.38
Neurologic disease or injury	7 (33.3)	5 (31.3)	0.89
Previous genitourinary surgery or procedure	13 (61.9)	7 (43.8)	0.27
Stroke	3 (14.3)	0 (0.0)	0.12
Smoking history			0.09
Current smoker	3 (14.3)	0 (0.0)	
Former smoker	9 (42.9)	4 (25.0)	
Pack-years	22.1 ± 6.9	17.7 ± 6.5	0.71
Never smoker	9 (42.9)	12 (75.0)	
Prior OAB therapy			
Oral medications	21 (100.0)	15 (93.8)	0.25
OnabotulinumtoxinA	4 (19.0)	1 (6.3)	0.26
PTNS	1 (4.8)	0 (0.0)	0.38
OAB classification			0.21
OAB-wet	19 (90.5)	12 (75.0)	
OAB-dry	2 (9.5)	4 (25.0)	
Stage I lead stimulation			0.26
Unilateral	4 (19.0)	1 (6.3)	
Bilateral	17 (81.0)	15 (93.8)	

Measures of central tendency are reported as mean ± SEM. Continuous variables were analyzed using Student's t test, and categorical variables were analyzed using Chi square test.
BMI, body mass index; OAB, overactive bladder; PTNS, percutaneous tibial nerve stimulation; SNS, sacral nerve stimulation.

our study was to report on the safety and efficacy of SNS in the largest cohort of octogenarian patients in the published literature. Our analysis finds that almost 60% of patients more than 80 years of age achieve Stage I success and proceed to permanent implantation. This rate was not statistically different between octogenarians and the general population at our institution. Our overall Stage I success rate (60.2%) is comparable to success rates previously published using large Medicare and commercial insurance-based cohorts, as well as the success rate (63%) reported by Schmidt et al. (16–20). In our study, all patients were followed for a minimum of one year, and had an average time to latest follow-up clinic visit of more than 40 months. During this period, the overall explantation rate was 21.3% (48/225) and rate of revision surgery was 18.2% (41/225). These results were also not significantly different between octogenarian and nonoctogenarian patients. Taken together, our findings provide evidence that SNS is equally safe and effective in elderly patients as it is in the general population.

Previous reports on SNS outcomes in elderly patients with refractory OAB are primarily limited to small observational studies, and have shown conflicting outcomes and results. Some suggest that SNS is less effective in older patients, with lower rates of symptom resolution and progression to permanent device implantation (16–18). For example, a report by Amundsen et al. (21) identified that SNS success was significantly lower in patients more than 55 years of age. In direct contrast to this finding, Anger et al. (20) utilized Medicare claims data and found no difference in rate of progression to Stage II between patients younger than, and older than, 55 years of age. Other investigations also support our finding that increasing age does not correlate with SNS Stage I failure (22,23). Emerging evidence focused on patients of extreme elderly age, including octogenarians, has shown that age does not negatively impact the effectiveness of SNS (15,24). Faris et al. (15) examined SNS progression rates across all ages for any indication of SNS placement, and found that patients older than 80 years of age had similar rates of progression to Stage II as patients in younger decades of life. The discrepancy in SNS success makes it difficult to reach a consensus decision regarding the use of SNS in older patients. However, it is possible that differences in method of lead placement, definition of treatment success, duration of follow-up, definitions of "elderly", and improvement in technique over time have made it difficult to directly compare and aggregate results. This variation may account for the inconsistencies reported in previously published reports.

When compared to other studies, our explantation rate (21.3%) was slightly higher than the previously published literature (10–15%). However, our follow-up time was more than 40 months

and our revision rate was lower than previous reports (15,25). Among patients that progressed to Stage II, a total of five (2.2%) devices were explanted due to infection. This rate is lower than many published rates of SNS-related infections, which have been reported between 4% and 9% (26–28).

There are no established treatment guidelines to direct clinical practice in patients who report loss of adequate SNS efficacy over time, despite reprogramming and device revision. In our practice, if a patient presents with recurrence of OAB symptoms after SNS Stage II permanent placement, their behavioral practices are queried and modifications are suggested. The SNS device is also interrogated, including an evaluation of the battery, impedance check, and fluoroscopic evaluation of the lead position. The decision to undergo revision, explantation, or multimodal therapy is based upon symptom severity and patient preference. However, our group advises the use of salvage multimodal therapy (e.g., SNS with oral therapy, SNS with onabotulinumtoxinA injection, etc.) rather than immediate device explantation in these patients. Approximately, 30% of our patient population required subsequent multimodal therapy at a mean time of 23.9 ± 3.1 months after IPG placement. There was no statistical difference in mean time from Stage II to implementation of multimodal therapy between age cohorts ($p = 0.34$) (Table 3). SNS, with or without the implementation of multimodal therapy with oral medications or onabotuliumtoxinA, resulted in 78.7% of patients not requiring SNS explantation after Stage II permanent placement at latest clinic follow-up. This long-term outcome is comparable to previously published results. In a study of 104 patients with OAB treated with SNS followed for a mean of 28.6 months after IPG placement, overall SNS success rate determined by >50% improvement in one clinical parameter of OAB symptoms, was found to be 70% for urgency urinary incontinence and 68% for urgency frequency syndrome (29). Our results support the use of multimodal treatment as salvage therapy for patients who experience reduced efficacy with SNS over time.

Our study is not without limitations. Due to the retrospective nature of the study, we may not capture patients who were lost to follow up and began subsequent treatment with another provider. While bladder diaries were collected perioperatively, standardized questionnaires and voiding diaries were not collected postoperatively, and therefore objective outcomes were not available for review. We relied on patient-reported outcomes as documented in the clinical notes. Strengths of the study include the relatively large number of octogenarians included in the study, the length of follow-up, and the characterization and description of responses to subsequent multimodal therapies by cohort.

CONCLUSIONS

The efficacy and safety of SNS did not differ between octogenarian and nonoctogenarian patients. As the largest study focused on this age cohort, our results indicate that SNS should be considered in the treatment algorithm for octogenarian patients with refractory overactive bladder.

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Authorship Statement

All authors of this research paper have directly participated in the study's conception and design, the drafting and revision of this paper, and final approval of the version to be published.

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