International Urogynecology Journal (2019) 30:1735–1745
https://doi.org/10.1007/s00192-018-3834-9

ORIGINAL ARTICLE

Predictors of successful percutaneous tibial nerve stimulation (PTNS) in the treatment of overactive bladder syndrome

Ghazaleh Rostaminia[1] · Cecilia Chang[1] · Joseph B. Pincus[2] · Peter K. Sand[2] · Roger P. Goldberg[2]

Received: 5 September 2018 / Accepted: 19 November 2018 / Published online: 29 November 2018

Abstract

Introduction and hypothesis Multiple publications have demonstrated the efficacy of percutaneous tibial nerve stimulation (PTNS) for overactive bladder syndrome (OAB). However, patient characteristics associated with successful treatment have not been well established.

The aim of this study was to identify prognostic factors for successful PTNS treatment.

Methods This was a retrospective chart review of women who underwent PTNS therapy for OAB between January 2011–Decemeber 2017. Treatment success was defined by subjective improvement according to patient self-report and objective bladder diary parameters including the intervoiding interval, nocturia episodes and urgency urinary incontinence (UUI) episodes per day, before and after PTNS treatment. Baseline symptoms were dichotomized for each symptom based on severity.

Results One hundred sixty-two women with a mean age of 72.7 ± 11.3 years and BMI of 28.5 ± 7.1 were included in the study. There was a statistically significant improvement in all three OAB symptoms after treatment. Multivariable analysis revealed that a history of depression and anxiety was associated with subjective improvement, whereas decreased subjective improvement was associated with a history of hypertension, prior intravesical onabotulinnumtoxinA injection and sacral neuromodulation. While dichotomizing subjects into two groups defined by < 50% versus ≥ 50% improvement, depression/anxiety, urodynamic volume at first sensation to void and more severe baseline urgency urinary incontinence severity were all significant predictors of subjective improvement.

Conclusions Among women treated with PTNS for refractory OAB, a history of depression/anxiety and severe baseline urgency urinary incontinence were positive predictors of a successful PTNS outcome.

Keywords Overactive bladder syndrome · Percutaneous tibial nerve stimulation · Lower urinary tract symptoms

Introduction

Overactive bladder syndrome (OAB) is a clinical diagnosis characterized by the presence of bothersome urinary symptoms. The International Urogynecological Association and the International Continence Society Joint Terminology Committee defines OAB as the presence of "urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of UTI or other obvious pathology" [1]. In population-based studies, OAB prevalence rates range from 7% to 27% in men and 9% to 43% in women [2–4]. The negative impact of OAB symptoms on psychosocial functioning and quality of life also has been well documented [4, 5]. Recent studies indicate that over 50% of individuals with OAB discontinue pharmacotherapy at 12 months (regardless of the agent) because of the lack of efficacy or intolerable side effects [6, 7]. In the patient who has failed behavioral and pharmacologic therapies or who is not a candidate for these therapies, onabotulinumtoxinA therapy, PTNS or neuromodulation may be offered.

Percutaneous tibial nerve stimulation (PTNS) is an alternative accepted neuromodulation therapy approved by the Food and Drug Administration for nonneurogenic lower urinary tract dysfunction (LUTD) [8, 9]. Effectiveness of PTNS in

✉ Ghazaleh Rostaminia
ghazalerostaminia@yahoo.com

[1] NorthShore University HealthSystem Research Institute, Evanston, IL, USA

[2] Division of Urogynecology, NorthShore University HealthSystem, University of Chicago Pritzker School of Medicine, 9650 Gross Point Road, Suite 3900, Skokie, IL 60076, USA

Table 1 Demographics comparing those who completed vs. those who did not complete 12 weekly sessions

	Completed (*N* = 162)		Not completed (*N* = 21)		*p value*
	N	%	*N*	%	
Age (years), mean ± SD	72.65 ± 11.30		73.81 ± 10.75		0.6583
Race					
African-American	3	1.85	0	0.00	0.8957
Caucasian	133	82.10	18	85.71	
Asian	4	2.47	0	0.00	
Other	21	12.96	3	14.29	
Declined/unknown	1	0.62	0	0.00	
Weight (kg), mean ± SD	71.10 ± 17.86		71.41 ± 19.35		0.9408
Height (inches), mean ± SD	5.21 ± 0.46		5.17 ± 0.42		0.7240
BMI (kg/m2), mean ± SD	28.47 ± 7.10		28.89 ± 7.26		0.8006
Gravidity, median (range)	2 (0–14)		3 (0–6)		0.3850
Parity, median (range)	2 (0–14)		2 (0–5)		0.6040
H/o breast cancer					
Yes	24	14.81	2	9.52	0.5135
No	138	85.19	19	90.48	
Diabetes					
Yes	17	10.49	5	23.81	0.0775
No	145	89.51	16	76.19	
Hypertension					
Yes	57	35.19	6	28.57	0.5484
No	105	64.81	15	71.43	
Spine disease					
Yes	60	37.04	8	38.10	0.9248
No	102	62.96	13	61.90	
Depression/anxiety					
Yes	49	30.25	3	14.29	0.1270
No	113	69.75	18	85.71	
Peripheral neuropathy					
Yes	1	0.62	0	0.00	0.7181
No	161	99.38	21	100.00	
CNS					
Yes	28	17.28	5	23.81	0.4643
No	134	82.72	16	76.19	
H/o Spine surgery					
Yes	27	16.67	1	4.76	0.1539
No	135	83.33	20	95.24	
H/o Urogynecology surgery					
Yes	83	51.55	12	57.14	0.6296
No	78	48.45	9	42.86	
H/o Gastric bypass					
Yes	3	1.85	0	0.00	0.5295
No	159	98.15	21	100.00	
H/o interstim					
Yes	10	6.17	2	9.52	0.5594
No	152	93.83	19	90.48	
H/o botox					
Yes	30	18.52	4	19.05	0.9532
No	132	81.48	17	80.95	
H/o Instillation					
Yes	3	1.85	3	14.29	**0.0026**
No	159	98.15	18	85.71	
Ucx + during treatment period, median (range)	0 (0–5)		0 (0–1)		0.2558
First sense volume (ml), mean ± SD (Urodynamics study)	128.64 ± 81.12		95.53 ± 55.82		0.1289
Strong desire volume (ml), mean ± SD (Urodynamics study)	268.83 ± 118.13		206.27 ± 62.91		**0.0036**
Capacity (ml), mean ± SD	428.03 ± 166.73		382.80 ± 158.63		0.3239
DO max pressure (cm H2O), mean ± SD (Urodynamics study)	26.45 ± 32.31		26.33 ± 18.29		0.9834
DO start volume (ml), mean ± SD (Urodynamics study)	334.10 ± 166.40		250.13 ± 174.54		0.0730
PVR (ml), mean ± SD	40.73 ± 43.85		40.94 ± 40.78		0.9848
OAB duration (years), mean ± SD	8.65 ± 14.59		10.57 ± 8.21		0.3736
Number of failed medications, mean ± SD	3.22 ± 1.69		3.24 ± 1.79		0.9555
Subjective improvement (%), mean ± SD	57.29 ± 24.96		22.86 ± 21.25		**<.0001**

Significant values are shown in bold

Table 2 Summary of outcome values at baseline and after 12 weekly PTNS sessions

	Baseline				3 Months				Change				*p value*
	N	*Mean*	*Median*	*SD*	*N*	*Mean*	*Median*	*SD*	*N*	*Mean*	*Median*	*SD*	
Inter-void duration (h)/day	162	2.04	2.00	0.94	162	3.10	3.00	0.98	162	1.06	1.00	1.04	**< 0.0001**
Nocturia/day	162	2.35	2.00	2.22	161	1.29	1.00	1.15	161	−1.06	−0.5	1.86	**< 0.0001**
Urge urinary leakage/day	162	2.25	1.50	3.15	161	0.91	0.50	1.46	161	−1.33	−0.5	2.47	**< 0.0001**

Significant values are shown in bold

OAB, specifically in non-neurogenic OAB, has been proven in sham-controlled trials in both the number of positive responders and voiding diary parameters of the patients [10, 11]. While comparing its efficiency with anti-muscarinic medications, in the OrBIT trial after 12 weeks of therapy PTNS treatments demonstrated clinically significant objective reductions in OAB symptoms and compared favorably to extended-release tolterodine [9, 12].

Despite reassuring reports on the effectiveness of PTNS therapy for the treatment of OAB symptoms, there are still patients whose response to PTNS is unsatisfactory and currently there are scarce data regarding patient selection characteristics. Efficacy is often not seen during the first 6 weeks of therapy leading to many patients discontinuing therapy before they complete a full 12 weeks. Such data regarding patient selection and predictors of success would be of value to clinicians to efficiently utilize PTNS as a healthcare resource and to minimize the likelihood of patient non-response. The current study aimed to investigate patient characteristics that are predictive of successful PTNS treatment in a sample of women with refractory OAB treated in a single urogynecology center.

Methods

This was a retrospective chart review study of women who underwent PTNS therapy for OAB symptoms between January 2011–December 2017 in our tertiary center. The study was approved by the Institutional Review Board of NorthShore University HealthSystem. Patients who had completed 12 weekly sessions were recruited to the study. We excluded charts with incomplete data.

Table 3 Percent of changes of outcome values from the baseline and after 12 weekly PTNS sessions

	N	*Mean*	*Median*	*SD*
3 Months				
Subjective improvement (%)	161	57.29	60.00	24.96
Changes in frequency (%)	162	85.44	50.00	120.24
Changes in nocturia (%)	159	−39.90	−40.00	41.70
Changes in UUI (%)	159	−46.44	−60.00	53.24

PTNS treatment protocol

Patients presented to the urogynecology clinic for 30-min sessions with the nurse once a week for 12 consecutive weeks. The PTNS technique has been previously described and consists of stimulating the nerve by means of a 34-gauge needle electrode inserted 4–5 cm cephalad to the medial malleolus, delivering an electric current in a continuous square wave form with a duration of 200 μs and a frequency of 20 Hz. Consistent with described best practices, our protocol involved observing for appropriate toe movement to confirm correct positioning of the needle electrode. Current intensity was determined by the highest level tolerated by the patient (Urgent® PC, Cogentix, Minnetonka, MN, USA). Before each treatment session, the nurse performing the PTNS asked the patient to report a percentage estimate of their subjective improvement or worsening from baseline on a scale of −100% to +100% over the prior week. The nurse also asked the patient to quantify the inter-voiding interval, nocturia episodes and urgency urinary incontinence (UUI) episode frequency over the prior week.

Outcome measures

Subjective outcome was defined by the self-reported percentage symptom improvement or worsening compared with baseline, collected serially at each treatment visit. “Objective outcome” was defined by patient-reported values including the inter-voiding interval, nocturia episodes and urgency urinary incontinence episodes per day before and after treatment.

Table 4 Correlation between subjective and objective outcome improvement

	r	*p value*
Changes in frequency (%)	0.2355	**0.0026**
Changes in nocturia (%)	−0.2862	**0.0003**
Changes in UUI (%)	−0.4383	**< 0.0001**

Significant values are shown in bold

We did not use the written bladder diary. An "objective improvement" percentage was calculated for each of these values. Additionally, each baseline symptom was dichotomized based on severity, specifically: intervoiding interval ≥ 1 h vs. < 1 h, nocturia ≥ 3 vs. < 3 episodes and urinary urgency incontinence ≥ 2 vs. < 2 daily episodes. Each subject's age, BMI, parity, medical and surgical history, urodynamic study variables and duration of OAB symptoms were collected from the electronic medical record.

Statistical analysis

Demographic data were summarized as means with standard deviation for continuous variables and as frequencies and percentages for categorical variables. Paired *t*-tests were used to evaluate the change from baseline to the end of the study for each patient. *t*-tests and chi-squared tests were used to assess group differences from baseline to the end of the study. Multivariable regression models were utilized to identify significant predictors of subjective and objective outcomes. The final model was evaluated based on the area under the receiver-operating-characteristic curve (AUC) for good discrimination. All statistical analyses were conducted using SAS 9.3 (SAS Institute Inc., Cary, NC), and p values < 0.05 were considered statistically significant.

Results

One hundred sixty-two women with a mean age of 72.7 ± 11.3 years, BMI of 28.5 ± 7.1 and median parity of 2 (0–14) who completed the 12 weekly sessions entered the study. Additionally, 21 patients during same time period did not complete the treatment course. Demographic data are summarized in Table 1. There were no statistically significant differences in demographic values between patients who stopped the treatment and those who completed the course; however, their subjective improvement rate was significantly lower. There was statistically significant improvement ($p < 0.05$) in all three OAB symptoms after PTNS treatment (Tables 2 and 3). While overall subjective improvement was weakly correlated with improvement of objective variables, urgency urinary incontinence improvement showed a moderate association with self-reported subjective improvement (Table 4).

Multivariable analysis with continuous outcomes showed that a history of breast cancer was significantly associated with subjective improvement, and histories of hypertension, prior intravesical onabotulinnumtoxinA injection and prior sacral neuromodulation were significantly associated with less favorable subjective outcomes (Table 5). After dichotomizing the subjective and objective outcomes into two groups, < 50% versus ≥ 50% improvement, study variables were then compared between the two groups. This analysis revealed that a history of depression/anxiety was more prevalent among

Table 5 Multivariable analysis with continuous outcomes

	Subjective improvement			Frequency improvement			Nocturia improvement			UUI improvement		
	Estimate	SE	p value	Estimate	SE	p value	Estimate	SE	p value	Estimate	SE	p value
Intercept	73.6530	15.3169	< 0.0001	−4.1428	80.3601	0.9590	−0.6720	28.5013	0.9812	−93.5818	35.7234	0.0098
Age (years)	−0.1760	0.1794	0.3282	1.8484	0.9402	0.0512	−0.5063	0.3305	0.1278	0.5297	0.4163	0.2053
BM I (kg/m2)	0.1354	0.2768	0.6256	−0.3177	1.4585	0.8279	−0.6740	0.4971	0.1773	0.2840	0.6457	0.6608
H/o breast cancer	12.3057	5.3942	0.0240	26.3259	28.4259	0.3559	1.3013	9.6014	0.8924	−13.3255	12.5728	0.2910
Diabetes	3.6956	6.2281	0.5539	−3.5856	32.8219	0.9132	−10.3919	11.0906	0.3504	−5.1189	14.4957	0.7245
Hypertension	−8.3390	4.0712	0.0424	14.7830	21.3016	0.4888	−0.3693	7.2122	0.9592	7.6491	9.4713	0.4207
Spine disease	−1.8416	4.7579	0.6993	−24.2735	25.0346	0.3339	−4.9187	8.4977	0.5636	−1.7228	11.0991	0.8769
Depression/anxiety	7.1630	4.3616	0.1027	15.9493	22.9613	0.4884	3.9875	7.8470	0.6121	−10.8830	10.2384	0.2896
Peripheral neuropathy	−48.1527	23.8246	0.0451	−44.9675	125.5572	0.7208	3.6514	42.3735	0.9315	81.2741	55.4316	0.1448
CNS	−10.1397	5.1806	0.0523	−16.5074	27.2722	0.5460	19.3326	9.4184	0.0420	7.5956	12.1831	0.5340
Spine surgery	−1.3413	6.1359	0.8273	−30.0573	32.3307	0.3541	7.0793	10.8940	0.5169	−7.0351	14.2704	0.6228
H/o Urogynecology surgery	2.1206	3.9020	0.5877	−25.4044	20.4360	0.2159	13.4080	6.9893	0.0571	−6.8683	9.0692	0.4501
H/o Gastric bypass	−13.4013	14.7413	0.3648	−23.3699	77.6731	0.7639	20.9589	26.1919	0.4249	16.9018	34.3130	0.6231
H/o interstim	−16.2862	7.9783	0.0431	1.0619	42.0465	0.9799	17.3575	15.0301	0.2501	−4.3945	18.5760	0.8133
H/o botox	−9.9831	5.3943	0.0663	−31.0735	28.4295	0.2762	2.4551	9.9134	0.8048	12.4160	12.7099	0.3303
H/o instillation	−4.9678	14.1893	0.7268	−38.7516	74.7596	0.6050	15.0978	25.2227	0.5504	−13.9979	39.1060	0.7209
Number of failed medications	−1.0568	1.2241	0.3894	−3.6348	6.4512	0.5740	2.2125	2.1844	0.3129	1.4930	2.8588	0.6023

Table 6 Comparison of variables between outcome categories

(a) Subjective improvement

	Subjective improvement				
	< 50%		≥ 50%		*p value*
	N	%	*N*	%	
No. of patients	45	27.78	117	72.22	
Age (years), mean ± SD	74.13 ± 13.24		72.09 ± 10.47		0.3550
Race					
African-American	0	0.00	3	2.56	0.7584
Caucasian	37	82.22	96	82.05	
Asian	1	2.22	3	2.56	
Other	7	15.56	14	11.97	
Declined/unknown	0	0.00	1	0.85	
Weight (kg), mean ± SD	70.40 ± 18.87		71.37 ± 17.53		0.7571
Height (inches), mean ± SD	5.22 ± 0.49		5.21 ± 0.45		0.9277
BMI (kg/m2), mean ± SD	28.24 ± 7.27		28.56 ± 7.06		0.8004
Gravidity, median (range)	2 (0–14)		2 (0–11)		0.7434
Parity, median (range)	2 (0–14)		2 (0–8)		0.6715
H/o breast cancer					
Yes	6	13.33	18	15.38	0.7420
No	39	86.67	99	84.62	
Diabetes					
Yes	4	8.89	13	11.11	0.6793
No	41	91.11	104	88.89	
Hypertension					
Yes	21	46.67	36	30.77	0.0577
No	24	53.33	81	69.23	
Spine disease					
Yes	17	37.78	43	36.75	0.9036
No	28	62.22	74	63.25	
Depression/anxiety					
Yes	8	17.78	41	35.04	**0.0321**
No	37	82.22	76	64.96	
Peripheral neuropathy					
Yes	1	2.22	0	0.00	0.1058
No	44	97.78	117	100.00	
CNS					
Yes	11	24.44	17	14.53	0.1350
No	34	75.56	100	85.47	
H/o Spine surgery					
Yes	7	15.56	20	17.09	0.8139
No	38	84.44	97	82.91	
H/o Urogynecology surgery					
Yes	26	57.78	57	49.14	0.3249
No	19	42.22	59	50.86	
H/o Gastric bypass					
Yes	1	2.22	2	1.71	0.8283
No	44	97.78	115	98.29	
H/o interstim					
Yes	5	11.11	5	4.27	0.1053
No	40	88.89	112	95.73	
H/o botox					
Yes	11	24.44	19	16.24	0.2285
No	34	75.56	98	83.76	
H/o Instillation					
Yes	1	2.22	2	1.71	0.8283
No	44	97.78	115	98.29	
Ucx + during treatment period, median (range)	0 (0–2)		0 (0–5)		0.0841
First sense volume, mean ± SD (Urodynamics study)	123.93 ± 91.97		130.68 ± 76.51		0.6920
Strong desire volume, mean ± SD (Urodynamics study)	272.10 ± 108.55		267.52 ± 122.43		0.8564
Capacity volume, mean ± SD	440.34 ± 160.55		422.91 ± 170.00		0.6213
DO max pressure, mean ± SD (Urodynamics study)	31.62 ± 48.33		24.25 ± 22.43		0.4374
DO start volume, mean ± SD (Urodynamics study)	360.29 ± 158.03		322.16 ± 169.87		0.2927
PVR, mean ± SD	43.27 ± 53.57		39.69 ± 39.52		0.7146
OAB symptoms duration (years), mean ± SD	8.13 ± 5.72		8.86 ± 16.93		0.6918
Number of failed medications, mean ± SD	3.60 ± 1.89		3.07 ± 1.59		0.0727
Baseline frequency severity					
< 1 h	2	4.44	10	8.55	0.3718
≥ 1 h	43	95.56	107	91.45	
Baseline nocturia severity					
< 3 times	28	62.22	79	67.52	0.5235
≥ 3 times	17	37.78	38	32.48	
Baseline UUI severity					
< 2 times	29	64.44	63	53.85	0.2226
≥ 2 times	16	35.56	54	46.15	

(b) Frequency improvement

Table 6 (continued)

	Frequency improvement				
	< 50%		≥ 50%		*p value*
	N	%	*N*	%	
No. of patients	67	41.36	95	58.64	
Age (years), mean ± SD	70.78 ± 13.59		73.98 ± 9.22		0.0965
Race					
African-American	2	2.99	1	1.05	0.6016
Caucasian	55	82.09	78	82.11	
Asian	1	1.49	3	3.16	
Other	8	11.94	13	13.68	
Declined/unknown	1	1.49	0	0.00	
Weight (kg), mean ± SD	72.52 ± 19.93		70.11 ± 16.28		0.3994
Height (in), mean ± SD	5.23 ± 0.44		5.20 ± 0.47		0.7032
BMI (kg/m2), mean ± SD	28.92 ± 7.92		28.16 ± 6.49		0.5069
Gravidity, median (range)	2 (0–14)		2.5 (0–14)		0.5664
Parity, median (range)	2 (0–14)		2 (0–10)		0.9280
H/o breast cancer					
Yes	7	10.45	17	17.89	0.1889
No	60	89.55	78	82.11	
Diabetes					
Yes	7	10.45	10	10.53	0.9872
No	60	89.55	85	89.47	
Hypertension					
Yes	23	34.33	34	35.79	0.8479
No	44	65.67	61	64.21	
Spine disease					
Yes	30	44.78	30	31.58	0.0867
No	37	55.22	65	68.42	
Depression/anxiety					
Yes	19	28.36	30	31.58	0.6603
No	48	71.64	65	68.42	
Peripheral neuropathy					
Yes	1	1.49	0	0.00	0.2323
No	66	98.51	95	100.00	
CNS					
Yes	13	19.40	15	15.79	0.5491
No	54	80.60	80	84.21	
H/o Spine surgery					
Yes	15	22.39	12	12.63	0.1008
No	52	77.61	83	87.37	
H/o Urogynecology surgery					
Yes	36	53.73	47	50.00	0.6405
No	31	46.27	47	50.00	
H/o Gastric bypass					
Yes	2	2.99	1	1.05	0.3689
No	65	97.01	94	98.95	
H/o interstim					
Yes	6	8.96	4	4.21	0.2165
No	61	91.04	91	95.79	
H/o botox					
Yes	17	25.37	13	13.68	0.0593
No	50	74.63	82	86.32	
H/o Instillation					
Yes	2	2.99	1	1.05	0.3689
No	65	97.01	94	98.95	
Ucx + during treatment period, median (range)	0 (0–3)		0 (0–5)		0.6908
First sense volume, mean ± SD (Urodynamics study)	132.54 ± 83.47		125.79 ± 79.92		0.6999
Strong desire volume, mean ± SD (Urodynamics study)	260.61 ± 99.54		274.94 ± 130.69		0.5356
Capacity, mean ± SD	408.51 ± 157.22		442.82 ± 173.39		0.2894
DO max pressure, mean ± SD (Urodynamics study)	33.03 ± 43.80		21.84 ± 20.02		0.1378
DO start volume, mean ± SD (Urodynamics study)	318.90 ± 146.32		345.30 ± 180.23		0.4382
PVR, mean ± SD	46.54 ± 53.46		36.49 ± 35.03		0.2313
OAB symptoms duration (years), mean ± SD	6.81 ± 4.19		9.92 ± 18.61		0.1246
Number of failed medications, mean ± SD	3.37 ± 1.96		3.11 ± 1.47		0.3459
Baseline frequency severity					
< 1 h	0	0	12	12.63	**0.0025**
≥ 1 h	67	100	83	87.37	
Baseline nocturia severity					
< 3 times	45	67.16	62	65.26	0.8013
≥ 3 times	22	32.84	33	34.74	
Baseline UUI severity					
< 2 times	42	62.69	50	52.63	0.2033
≥ 2 times	25	37.31	45	47.37	
(c) Nocturia improvement					
	Nocturia improvement				
	> −50%		≤ −50%		*p value*

Table 6 (continued)

	N	%	*N*	%	
No. of patients	84	51.85	78	48.15	
Age (years), mean ± SD	71.94 ± 12.58		73.42 ± 9.77		0.4016
Race					
African-American	2	2.38	1	1.28	0.6717
Caucasian	69	82.14	64	82.05	
Asian	3	3.57	1	1.28	
Other	10	11.90	11	14.10	
Declined/unknown	0	0.00	1	1.28	
Weight (kg), mean ± SD	69.60 ± 18.89		72.72 ± 16.66		0.2684
Height (inches), mean ± SD	5.23 ± 0.44		5.19 ± 0.48		0.6583
BMI (kg/m2), mean ± SD	27.66 ± 7.11		29.34 ± 7.02		0.1335
Gravidity, median (range)	2 (0–14)		3 (0–11)		0.6487
Parity, median (range)	2 (0–14)		2 (0–8)		0.7488
H/o breast cancer					
Yes	11	13.10	13	16.67	0.5226
No	73	86.90	65	83.33	
Diabetes					
Yes	6	7.14	11	14.10	0.1487
No	78	92.86	67	85.90	
Hypertension					
Yes	30	35.71	27	34.62	0.8837
No	54	64.29	51	65.38	
Spine disease					
Yes	30	35.71	30	38.46	0.7175
No	54	64.29	48	61.54	
Depression/anxiety					
Yes	31	36.90	18	23.08	0.0556
No	53	63.10	60	76.92	
Peripheral neuropathy					
Yes	1	1.19	0	0.00	0.3337
No	83	98.81	78	100.00	
CNS					
Yes	18	21.43	10	12.82	0.1477
No	66	78.57	68	87.18	
H/o Spine surgery					
Yes	14	16.67	13	16.67	1.000
No	70	83.33	65	83.33	
H/o Urogynecology surgery					
Yes	46	54.76	37	48.05	0.3948
No	38	45.24	40	51.95	
H/o Gastric bypass					
Yes	3	3.57	0	0.00	0.092
No	81	96.43	78	100.00	
H/o interstim					
Yes	7	8.33	3	3.85	0.2357
No	77	91.67	75	96.15	
H/o botox					
Yes	17	20.24	13	16.67	0.5587
No	67	79.76	65	83.33	
H/o Instillation					
Yes	3	3.57	0	0.00	0.0920
No	81	96.43	78	100.00	
Ucx + during treatment period, median (range)	0 (0–5)		0 (0–3)		0.4041
First sense volume , mean ± SD (Urodynamics study)	128.56 ± 84.43		128.72 ± 78.41		0.9919
Strong desire volume , mean ± SD (Urodynamics study)	264.29 ± 100.56		273.55 ± 134.79		0.6876
Capacity, mean ± SD	411.29 ± 158.88		445.07 ± 174.19		0.2923
DO max pressure, mean ± SD (Urodynamics study)	30.21 ± 40.05		22.78 ± 22.12		0.2629
DO start volume, mean ± SD (Urodynamics study)	324.37 ± 167.32		343.64 ± 166.63		0.5672
PVR, mean ± SD	41.36 ± 41.10		40.03 ± 47.02		0.8652
OAB symptoms duration (years), mean ± SD	9.48 ± 19.80		7.78 ± 5.02		0.4597
Number of failed medications, mean ± SD	3.31 ± 1.70		3.12 ± 1.68		0.4666
Baseline frequency severity					
< 1 h	6	7.14	6	7.69	0.8939
≥ 1 h	78	92.86	72	92.31	
Baseline nocturia severity					
< 3 times	59	70.24	48	61.54	0.2427
≥ 3 times	25	29.76	30	38.46	
Baseline UUI severity					
< 2 times	50	59.52	42	53.85	0.4661
≥ 2 times	34	40.48	36	46.15	
(d) UUI improvement					
	UUI improvement				
	> −50%		≤ −50%		*p value*
	N	%	*N*	%	
No. of patients	65	40.12	97	59.88	

Table 6 (continued)

Age (years), mean ± SD	74.09 ± 19.48		71.69 ± 10.83		0.1858
Race					
African-American	2	3.08	1	1.03	0.1243
Caucasian	58	89.23	75	77.32	
Asian	0	0.00	4	4.12	
Other	5	7.69	16	16.49	
Declined/unknown	0	0.00	1	1.03	
Weight (kg), mean ± SD	72.58 ± 19.48		70.11 ± 16.72		0.3901
Height (inches), mean ± SD	5.28 ± 0.45		5.16 ± 0.46		0.1179
BMI (kg/m2), mean ± SD	28.36 ± 7.49		28.55 ± 6.87		0.8743
Gravidity, median (range)	2 (0–14)		3 (0–14)		0.5227
Parity, median (range)	2 (0–14)		2 (0–10)		0.6004
H/o breast cancer					
Yes	8	12.31	16	16.49	0.4621
No	57	87.69	81	83.51	
Diabetes					
Yes	5	7.69	12	12.37	0.3409
No	60	92.31	85	87.63	
Hypertension					
Yes	26	40.00	31	31.96	0.2935
No	39	60.00	66	68.04	
Spine disease					
Yes	24	36.92	36	37.11	0.9804
No	41	63.08	61	62.89	
Depression/anxiety					
Yes	17	26.15	32	32.99	0.3532
No	48	73.85	65	67.01	
Peripheral neuropathy					
Yes	1	1.54	0	0.00	0.2204
No	64	98.46	97	100.00	
CNS					
Yes	11	16.92	17	17.53	0.9208
No	54	83.08	80	82.47	
H/o Spine surgery					
Yes	10	15.38	17	17.53	0.7200
No	55	84.62	80	82.47	
H/o Urogynecology surgery					
Yes	33	50.77	50	52.08	0.8700
No	32	49.23	46	47.92	
Gastric bypass					
Yes	2	3.08	1	1.03	0.3438
No	63	96.92	96	98.97	
H/o interstim					
Yes	4	6.15	6	6.19	0.9934
No	61	93.85	91	93.81	
H/o botox					
Yes	15	23.08	15	15.46	0.2215
No	50	76.92	82	84.54	
Instillation					
Yes	1	1.54	2	2.06	0.8086
No	64	98.46	95	97.94	
Ucx + during treatment period, median (range)	0 (0–3)		0 (0–5)		0.7378
First sense volume, mean ± SD (Urodynamics study)	134.11 ± 89.23		124.80 ± 75.40		0.5575
Strong desire volume, mean ± SD (Urodynamics study)	271.72 ± 126.02		260.31 ± 112.80		0.3589
Capacity, mean ± SD	412.41 ± 159.28		438.60 ± 172.00		0.4236
DO max pressure, mean ± SD (Urodynamics study)	28.59 ± 42.34		25.02 ± 23.62		0.6337
DO start volume, mean ± SD (Urodynamics study)	331.63 ± 168.88		335.84 ± 166.09		0.9021
PVR, mean ± SD	53.48 ± 52.38		32.00 ± 34.65		**0.0112**
OAB symptoms duration (years), mean ± SD	7.18 ± 4.31		9.59 ± 18.35		0.2221
Number of failed medications, mean ± SD	3.35 ± 1.96		3.12 ± 1.48		0.4232
Baseline frequency severity					
< 1 h	4	6.15	8	8.25	0.6180
≥ 1 h	61	93.85	89	91.75	
Baseline nocturia severity					
< 3 times	45	69.23	62	63.92	0.4839
≥ 3 times	20	30.77	35	36.08	
Baseline UUI severity					
≤ 2 times	46	70.77	46	47.42	**0.0033**
≥ 2 times	19	29.23	51	52.58	

Significant values are shown in bold

women with ≥ 50% subjective improvement after PTNS treatment ($p = 0.0321$). Lower PVR and severe baseline urgency urinary incontinence (≥ 2 daily episodes) were independently predictive of ≥ 50% improvement in urge urinary leakage

Table 7 Multivariable analysis for patient characteristics with subjective and objective success (≥ 50%)

	Subjective improvement				Frequency improvement				Nocturia improvement				UUI improvement			
	OR	95% CI		p value	OR	95%CI		p value	OR	95% CI		p value	OR	95% CI		p value
Age (years)	1.007	0.928	1.092	0.8707	1.048	0.986	1.112	0.1301	1.001	0.950	1.055	0.9748	0.963	0.899	1.033	0.2917
BMI (kg/m2)	1.092	0.986	1.209	0.0906	0.945	0.871	1.025	0.1710	0.978	0.912	1.049	0.5410	0.965	0.873	1.067	0.4864
H/o breast cancer	2.499	0.372	16.794	0.3462	1.821	0.375	8.858	0.4575	1.349	0.299	6.085	0.6968	1.464	0.277	7.750	0.6539
Diabetes	5.789	0.227	147.750	0.2881	3.170	0.358	28.085	0.2999	1.404	0.206	9.581	0.7293	1.447	0.121	17.330	0.7705
Hypertension	0.990	0.190	5.147	0.9900	0.662	0.183	2.387	0.5280	1.093	0.331	3.612	0.8845	0.350	0.089	1.374	0.1324
Spine cisease	0.139	0.015	1.319	0.0856	0.405	0.077	2.136	0.2870	0.782	0.169	3.629	0.7538	0.560	0.093	3.376	0.5273
Depression/anxiety	29.473	1.926	451.059	**0.0151**	1.319	0.300	5.804	0.7144	0.977	0.265	3.606	0.9724	0.713	0.139	3.647	0.6844
CNS	0.265	0.036	1.923	0.1890	0.555	0.123	2.514	0.4453	0.296	0.065	1.347	0.1153	1.516	0.248	9.253	0.6520
H/o Spine surgery	13.167	1.028	168.627	**0.0476**	0.452	0.079	2.584	0.3720	0.988	0.187	5.225	0.9891	4.622	0.541	39.455	0.1618
H/o Urogynecology surgery	0.131	0.019	0.917	**0.0407**	0.297	0.080	1.112	0.0715	0.688	0.227	2.090	0.5098	2.367	0.593	9.455	0.2227
H/o interstim	0.854	0.028	26.128	0.9280	0.376	0.029	4.906	0.4552	0.503	0.048	5.238	0.5653	1.830	0.075	44.912	0.7113
H/o botox	1.341	0.165	10.900	0.7836	1.328	0.254	6.946	0.7365	1.157	0.241	5.552	0.8558	1.990	0.288	13.746	0.4854
H/o Instillation	0.433	0.005	34.891	0.7087	0.246	0.006	9.505	0.4520	0.076	<0.001 8.305		0.2820	0.436	0.011	17.130	0.6579
First sense volume (Urodynamics study)	1.010	0.997	1.023	0.1379	0.994	0.985	1.004	0.2264	0.996	0.987	1.005	0.3938	0.999	0.988	1.009	0.7968
Strong desire volume (Urodynamics study)	0.997	0.989	1.005	0.4552	0.999	0.993	1.006	0.8808	1.000	0.994	1.006	0.9626	0.996	0.988	1.004	0.3153
Capacity volume	1.003	0.993	1.014	0.5244	1.002	0.997	1.008	0.4070	1.003	0.998	1.008	0.1968	1.004	0.997	1.010	0.3032
DO max pressure (Urodynamics study)	0.970	0.943	0.997	**0.0276**	0.986	0.966	1.008	0.2073	0.985	0.966	1.005	0.1501	0.985	0.964	1.007	0.1765
DO start volume (Urodynamics study)	0.994	0.983	1.006	0.3141	1.000	0.994	1.005	0.9459	0.998	0.993	1.003	0.4951	1.000	0.993	1.007	0.9921
PVR	1.021	0.990	1.054	0.1854	0.996	0.978	1.015	0.7008	0.992	0.975	1.010	0.3871	0.969	0.948	0.991	**0.0063**
OAB symptoms durations (years)	1.110	0.955	1.289	0.1736	1.085	0.961	1.226	0.1880	1.040	0.930	1.164	0.4907	1.100	0.954	1.268	0.1891
Number of failed medications	0.473	0.226	0.991	**0.0472**	0.730	0.474	1.124	0.1531	0.982	0.663	1.455	0.9280	0.883	0.555	1.404	0.5981
baseline frequency severity	0.091	0.002	4.910	0.2386	0.253	0.026	2.493	0.2388	1.313	0.220	7.843	0.7650	0.295	0.039	2.216	0.2356
Baseline nocturia severity	0.103	0.013	0.846	**0.0344**	0.946	0.282	3.180	0.9287	2.336	0.758	7.202	0.1397	1.780	0.449	7.055	0.4118
baseline UUI severity	4.160	0.670	25.812	0.1259	1.055	0.267	4.171	0.9388	1.315	0.361	4.792	0.6780	3.749	0.870	16.155	0.0762

Significant values are shown in bold

episodes ($p < 0.05$), as illustrated in Table 6 a,b,c,d. Multivariable analysis with decategorized outcomes identified a baseline history of depression/anxiety; a higher first sensation to void during cystometry and severe baseline urgency urinary incontinence had higher odds of having a ≥ 50% subjective improvement (Table 7, Fig. 1). On the other hand, patients with higher maximum detrusor pressure on multichannel urodynamics and severe baseline nocturia demonstrated a significantly lower likelihood of ≥ 50% subjective improvement (Table 7).

Discussion

The majority of refractory OAB patients in our study experienced subjective and objective improvement after 12 weekly sessions of PTNS treatment although interestingly self-reported subjective improvement was weakly associated with objective voiding diary improvement. A history of depression/anxiety and more severe baseline urinary urgency leakage (≥ 2 episodes) were positive predictors of successful PTNS treatment (OR 11.7, $p = 0.02$ and OR 8.2, $p = 0.01$, respectively). On the other hand, a baseline history of > 2 nocturia episodes was a negative predictor of successful PTNS treatment (OR 0.15, $p = 0.03$). Higher detrusor pressures during urge urinary leakage were associated with a greater chance of failure with PTNS. We have shown this to be true with other therapies for detrusor overactivity [13].

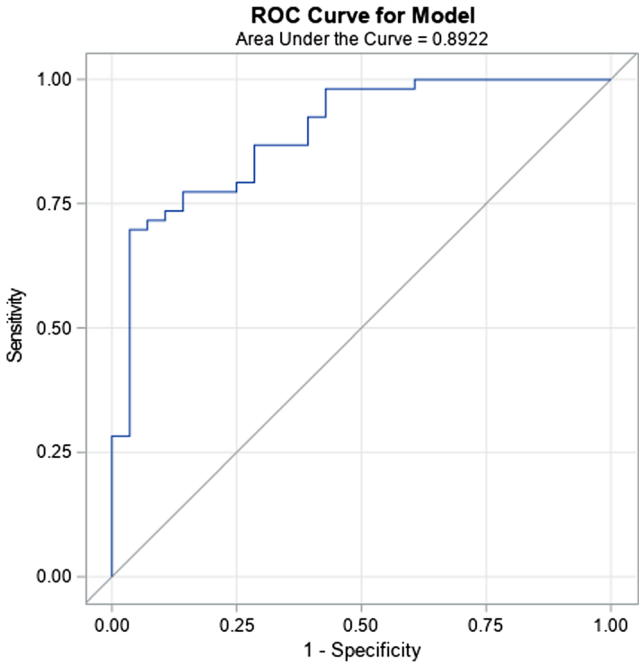

Fig. 1 Receiver-operating characteristic (ROC) curve for the final multivariable subjective improvement model adjusting for age, BMI, history of (breast cancer, diabetes, hypertension, spine disease, depression/anxiety, CNS, spine surgery, urogynecology surgery, gastric bypass, interstim, botox, instillation), first sensation volume, strong desire volume, capacity, DO max pressure, DO start volume, PVR, OAB duration, number of failed medications and baseline symptom severity

Vandoninck et al. studied the effect of PTNS for UUI. In a prospective multicenter study, 35 patients with complaints of urge incontinence underwent 12 weekly PTNS sessions. Twenty-two patients (63%) reported a subjective success in that study, with 24 (70%) showing ≥ 50% reduction in total number of leakage episodes. Sixteen (46%) of these patients were completely cured (i.e., no leakage episodes) after 12 sessions. None of the baseline characteristics proved to be a significant predictor for subjective success [14]. Van Balken et al. investigated patient prognostic characteristics for successful PTNS therapy in 83 patients treated for OAB, 16 for non-obstructive urinary retention and 33 for chronic pelvic pain. All patients had to complete voiding or pain diaries as well as quality of life questionnaires before and after treatment. Objective success was seen in 32.6% of patients, subjective success in 51.5%. Most evaluated clinical parameters proved not to be of prognostic value. However, a low total score at baseline in the Short Form-36 health survey questionnaire proved to be predictive for not obtaining objective [OR 0.444 (95% CI: 0.198–0.996), $p = 0.04$] or subjective success [OR 0.424 (CI: 0.203–0.887), $p = 0.02$] [10]. Especially patients with a low SF-36 Mental Component Summary were prone to fail neuromodulation therapy: OR 0.123 (95% CI: 0.273–0.552), $p = 0.006$ for objective success. An additional analysis of 90 patients evaluated urodynamic changes after PTNS for the treatment of OAB to identify urodynamic-based predictive factors; logistic regression showed that none of the baseline characteristics (cystometric capacity, volume at detrusor instability, detrusor pressure at detrusor instability) were significant predictors of subjective success [15].

Our study is limited by the inclusion criteria that limited the study sample to subjects who completed 12 weekly PTNS treatment sessions. While this allows for a valuable retrospective assessment of success among a sample of women who committed time and resources to PTNS induction, these criteria represent a limitation as they exclude women who discontinued treatment before the end of their 12-week induction. As a result, our study may be impacted by self-selection and thus may underestimate the percentage of women with refractory OAB who experience unsuccessful PTNS treatment. However, it is worth noting that PTNS treatment should involve a standard protocol of patients and clinicians committing to the full 12-week induction period before drawing conclusions, so in this respect our study design represents a realistic clinical setting and analysis. Strengths of our study include a relatively large study population, and PTNS treatments delivered by nurses highly experienced with PTNS practicing in a single tertiary setting. Additionally, our urodynamics protocol, serial measurement of patient self-reported outcome at each treatment visit and robust EMR allowed us to analyze a wide range of variables and assess their role in treatment success.

In summary, the majority of women with refractory OAB in our study experienced substantial symptom improvement after 12-week PTNS induction. More severe baseline UUI and depression and anxiety were independently predictive of treatment success, while more severe nocturia (≥ 3) and high pressure detrusor over-activity predicted less successful outcomes. These findings may help to refine patient selection for this treatment modality as clinicians continue to understand the most efficient and clinically beneficial ways in which to target this promising therapy.

Compliance with ethical standards

Conflicts of interest None.

References

1. Haylen BT, Freeman RM, Lee J, Swift SE, Cosson M, Deprest J, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint terminology and classification of the complications related to native tissue female pelvic floor surgery. Int Urogynecol J. 2012;23(5):515–26. https://doi.org/10.1007/s00192-011-1659-x.
2. Choo M-S, Ku JH, Lee JB, Lee DH, Kim JC, Kim H-J, et al. Cross-cultural differences for adapting overactive bladder symptoms: results of an epidemiologic survey in Korea. World J Urol. 2007;25(5):505–11.
3. Corcos J, Schick E. Prevalence of overactive bladder and incontinence in Canada. Can J Urol. 2004;11(3):2278–84.
4. Coyne KS, Sexton CC, Vats V, Thompson C, Kopp ZS, Milsom I. National community prevalence of overactive bladder in the United States stratified by sex and age. Urology. 2011;77(5):1081–7.
5. Donaldson M, Thompson JR, Matthews RJ, Dallosso H, McGrother C. The natural history of overactive bladder and stress urinary incontinence in older women in the community: a 3-year prospective cohort study. Neurourol Urodyn. 2006;25(7):709–16.
6. Siegel S, Noblett K, Mangel J, Griebling TL, Sutherland SE, Bird ET, et al. Results of a prospective, randomized, multicenter study evaluating sacral neuromodulation with InterStim therapy compared to standard medical therapy at 6-months in subjects with mild symptoms of overactive bladder. Neurourol Urodyn. 2015;34(3):224–30.
7. Siegel S, Paszkiewicz E, Kirkpatrick C, Hinkel B, Oleson K. Sacral nerve stimulation in patients with chronic intractable pelvic pain. J Urol. 2001;166(5):1742–5.
8. Levin PJ, Wu JM, Kawasaki A, Weidner AC, Amundsen CL. The efficacy of posterior tibial nerve stimulation for the treatment of overactive bladder in women: a systematic review. Int Urogynecol J. 2012;23(11):1591–7.
9. Peters KM, MacDiarmid SA, Wooldridge LS, Leong FC, Shobeiri SA, Rovner ES, et al. Randomized trial of percutaneous tibial nerve stimulation versus extended-release tolterodine: results from the overactive bladder innovative therapy trial. J Urol. 2009;182(3):1055–61.
10. Van Balken M, Vergunst H, Bemelmans B. Prognostic factors for successful percutaneous tibial nerve stimulation. Eur Urol. 2006;49(2):360–5.
11. Finazzi Agrò E, Petta F, Bove P, D'Amico A, Germani S, Campagna A, et al. Percutaneous tibial nerve stimulation (PTNS) in the treatment of urge incontinence: a double blind, placebo controlled study. Urodinamica. 2005;15(3):171–2.
12. Peters K, MacDiarmid S, Wooldridge L, Leong F, Shobeiri S, Rovner E, et al. Neurourol Urodyn. 2009;7:881–2.
13. Gamble TL, Botros SM, Beaumont JL, Goldberg RP, Miller J-JR, Adeyanju O, et al. Predictors of persistent detrusor overactivity after transvaginal sling procedures. Am J Obstet Gynecol. 2008;199(6):696.e691–7.
14. Vandoninck V, van Balken MR, Agró EF, Petta F, Caltagirone C, Heesakkers JP, et al. Posterior tibial nerve stimulation in the treatment of urge incontinence. Neurourol Urodyn. 2003;22(1):17–23.
15. Vandoninck V, van Balken MR, Finazzi Agrò E, Petta F, Micali F, Heesakkers JP, et al. Percutaneous tibial nerve stimulation in the treatment of overactive bladder: urodynamic data. Neurourol Urodyn. 2003;22(3):227–32.