Original Article

Comparison of the efficacy and safety of sacral root magnetic stimulation with transcutaneous posterior tibial nerve stimulation in the treatment of neurogenic detrusor overactivity: an exploratory randomized controlled trial

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Background: Both repetitive sacral root magnetic stimulation (rSMS) and transcutaneous posterior tibial nerve stimulation (TTNS) have demonstrated clinical benefits for lower urinary tract dysfunction. However it still remains unclear that which method is more effective and safer to treat neurogenic detrusor overactivity (NDO).

Methods: From December 2020 to December 2021, 50 patients (31 men and 19 women, aged 47.9±12.4 years) with NDO secondary to suprasacral spinal cord injury (SCI) were enrolled and randomly allocated to the rSMS or TTNS group based on a computer-generated random numbers table. The stimulation was applied continuously 5 times per week for 20 sessions. Urodynamic test was conducted at baseline and the day after the final 20th treatment session. The primary outcome was the individual change (Δ) in maximum cystometric capacity (MCC) from baseline to post-treatment. Secondary outcomes included changes (Δ) for the following parameters: volume at 1st involuntary detrusor contraction (1st IDCV), maximal detrusor pressure (Pdetmax), bladder compliance (BC), postvoid residual (PVR) volume, and bladder voiding efficiency (BVE). Additionally, adverse reactions including pain and skin irritation during stimulation were observed and recorded as safety outcomes.

Results: Finally 47 patients completed the study (23 in rSMS and 24 in TTNS group). A per-protocol (PP) analysis was performed, and Mann-Whitney U test and unpaired t-test were used for statistical analysis. Compared with the efficacy of TTNS, rSMS showed statistically greater ΔMCC [median +43 mL (IQR, 22–62 mL) *vs.* +20 mL (IQR, 15–25 mL), P=0.001, with a between-group difference of +22 mL (95% CI: +7 to +35 mL)] and ΔBVE [median +10.0% (IQR, 3.8–15.7%) *vs.* +3.5% (IQR, 0.0–7.8%), P=0.003, with a between-group difference of +5.9% (95% CI: +1.2% to +9.7%)]. No significant differences were found in Δ1st IDCV (P=0.40), ΔPdetmax (P=0.67), ΔBC (P=0.79) and ΔPVR (P=0.92) between the two groups. Meanwhile, patients exhibited high tolerance to both protocols, and no adverse reactions were observed.

Conclusions: RSMS may be more effective to improve urodynamics in the treatment for NDO than TTNS, cause it led to a statistical improvement in bladder capacity and voiding efficiency, without any side effects. RSMS is thus worthy of further clinical promotion.

Trial Registration: Chinese Clinical Trial Registry ChiCTR2100050663.

Keywords: Neurogenic detrusor overactivity (NDO); urodynamics; repetitive sacral root magnetic stimulation (rSMS); transcutaneous posterior tibial nerve stimulation (TTNS)

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Introduction

Spinal cord injury (SCI) frequently results in neurogenic bladder dysfunction. Neurogenic detrusor overactivity (NDO) is the most common consequence of suprasacral SCI, relevantly impairs patients' quality of life, and has an enormous socioeconomic impact (1). NDO can lead to spontaneous reflex bladder contractions at lower bladder volumes, causing urinary incontinence and serious damage to the upper urinary tract (2). The main aim of treating NDO is the preservation of a high-capacity reservoir at low intravesical pressures, and the protection for the upper urinary tract.

Currently, management strategies for NDO and upper urinary tract damage from NDO remain limited. Conventional therapies usually include anticholinergics, intravesical botulinum toxin-A injections, and surgical procedures (3). However, the common adverse effects of anticholinergics include dry mouth, blurred vision for near objects, constipation, and occasionally tachycardia, which may not be well accepted by a portion of patients (4). Intravesical botulinum toxin-A injections are invasive interventions, which required cystoscopy under local anesthesia in most neurological patients, and there is evidence of decreasing efficacy over time for patients who had repeated injections (5). Additionally, surgical procedures involving augmentation cystoplasty is traumatic and are generally applied only after the failure of conservative treatment (4).

Fortunately, refinements in the technique and evidence that symptom improvements are durable have led to increasing interest in the area of neuromodulation. Neuromodulation incorporates electrical or magnetic stimulation to target specific nerves that control lower urinary tract dysfunction (LUTD), and includes sacral nerve stimulation (SNS), percutaneous or transcutaneous posterior tibial nerve stimulation (PTNS or TTNS), pudendal nerve electrical stimulation, and sacral root magnetic stimulation (SMS) (3,6). Among these, non-invasive TTNS is widely used to inhibit the detrusor activity of various neurogenic etiologies, which has been found to lead to significant improvements in patients with overactive bladder (7,8). Meanwhile, repetitive sacral root magnetic stimulation (rSMS), a non-invasive technique based on the principle of electric-field induction in the sacral root via exposure to a magnetic field, has also been shown to suppress unstable contractions of detrusors in patients with non-neurogenic bladder (9,10).

The posterior tibial nerve is a terminal branch of the sciatic nerve with origins in the lumbar and sacral roots (L4-S3). TTNS involves the S3 fibers, and it has been postulated that TTNS depolarizes somatic sacral and lumbar afferent fibers, inhibiting detrusor activity (11). However, TTNS usually achieved insufficient efficacy in clinical practice due to the attenuation of electrical signals in impedance tissue, or the inaccurate position of placed electrode (12). Similarly, direct stimulation of the S3 root has been shown to decrease overactive bladder in humans, and magnetic stimulation can penetrate human tissue to directly stimulate the target tissue with little impedance (13). But magnetic stimulation for S3 is not widely used in currently clinical treatment for NDO, and further research is mandatory to determine its clinical efficacy and safety.

We therefore aimed to compare the efficacy and safety of rSMS with TTNS for treating NDO and to prepare this randomized controlled clinical trial. We present the following article in accordance with the CONSORT reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-22-249/rc).

Methods

Patients involvement

This prospective randomized study was conducted at The First Affiliated Hospital, College of Medicine, Zhejiang University, from December 2020 to December 2021. Patients were selected if they met the following criteria: (I) were aged between 18 and 65 years old; (II) had been diagnosed by a urologist or rehabilitation physician with NDO dysfunction based on urological and neurological investigations, including a medical history, physical examination, urine analysis, and urodynamic testing; and (III) had been diagnosed within 1–12 months of suprasacral SCI onset. Patients were excluded from the study if they met any of the following exclusion criteria: (I) had other non-neurogenic causes of LUTD; (II) had a severe cognitive or communicative impairment; (III) had undergone a surgical procedure related to the bladder; (IV) had received an intravesical Botox injection within the last 6 months, pacemaker or implantable defibrillator, or had recently used other neuromodulation techniques in the pelvic region, back, or legs; and/or (V) had participated in any clinical investigations that could have affected their urinary or renal function within the last 6 months.

In this two-parallel RCT study, a total of 50 patients were enrolled according to the inclusion and exclusion

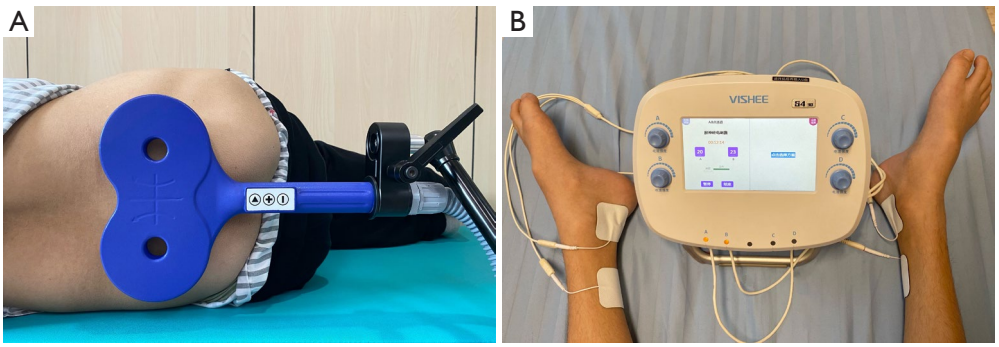

Figure 1 Examples of different treatment protocol. (A) rSMS; and (B) TTNS. rSMS, repetitive sacral root magnetic stimulation; TTNS, transcutaneous posterior tibial nerve stimulation.

criteria. Patients were randomly assigned into two groups using the random number table by a computer generated 1:1 randomization sequence. Assignments were sealed in opaque numbered envelopes. Group allocation and randomization procedures were performed by an off-site researcher who was not involved in any other aspect of the study. Blinding was not possible for patients and care providers because of obvious different interventions, but was feasible for study staff assessing the outcomes. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Ethics Committee Board of The First Affiliated Hospital, College of Medicine, Zhejiang University (2020, IIT No. 1031), and informed consent was taken from all the patients.

Treatment protocol

In the rSMS group (which comprised 25 patients, 16 males and 9 females), rSMS therapy was applied for 20 min, 5 times per week for 20 sessions. The patients were usually placed in a lateral decubitus position for the repetitive magnetic stimulation of the sacral roots, using a 70-mm outer diameter figure-of-8 air film cooling coil positioned in the midline over the sacrum to cover the bilateral third sacral neural foramen, which was connected to a magstim super rapid stimulator. The stimulation (20 Hz) was delivered at an intensity that produced a sense of contraction of the inner aspect of thigh or the perineum (usually 50% of the maximum stimulation intensity). Each daily stimulation consisted of 40 consecutive trains of 20 Hz pulses for 2 seconds on followed by 28 seconds off, with a total of 1,600 pulses (see *Figure 1A*).

In the TTNS group (which comprised 25 patients, 15 males and 10 females), the TTNS treatment was applied for 20 min, 5 times per week for 20 sessions. Bilateral TTNS was performed using two 50 mm × 50 mm self-adhesive electrodes on each side, with 1 electrode laid behind and the other laid approximately 10 cm above the medial malleolus. A current level of 1–5 mA at frequency 20 Hz with a fixed impulse width of 200 μs was selected based on each patient's foot and plantar motor and sensory responses. Positive motor responses included the flexion of the big toe or the fanning of all toes, and the motor response was usually accompanied by a response of radiating sensation spreading in the sole of the foot. The current was generally set at the highest tolerance to the patient (see *Figure 1B*).

Evaluation and procedures

Patients provided a 3-day voiding diary and underwent urodynamic testing at the baseline and the day after the final 20th treatment at the Urodynamic Center of our Rehabilitation Department. The definitions, methods and units conformed to the International Continence Society Standards. Filling cystometry was performed transurethrally using a 9-Fr. double lumen catheter and was recorded at the saline infusion rate of 20 mL/min. The following urodynamic evaluation parameters were noted or calculated: (I) the volume at the 1st involuntary detrusor contraction (1st IDCV); (II) the maximum cystometric capacity (MCC); (III) the maximal detrusor pressure ($Pdet_{max}$); and (IV) bladder compliance (BC).

The 1st IDCV was evaluated, and if NDO ceased after therapy, the 1st IDCV was noted as the MCC. The $Pdet_{max}$ was measured as the maximum contraction pressure of detrusor during the filling phase. If a patient had no bladder sensation, the perfusion of fluid was stopped when

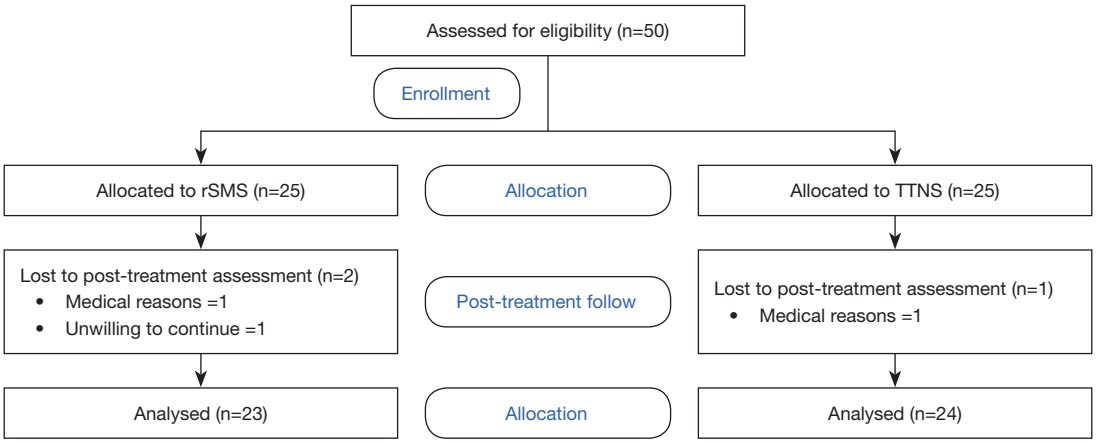

Figure 2 Participant randomization, follow-up, and analysis process. rSMS, repetitive sacral root magnetic stimulation; TTNS, transcutaneous posterior tibial nerve stimulation.

detrusor pressure exceeded 40 cmH_2O or urinary leakage occurred, and this volume was considered the MCC under these conditions. BC was calculated by dividing the volume change by the change in detrusor pressure during the transformation in bladder volume and was expressed in mL/cmH_2O. If patients could void, the postvoid residual volume (PVR) was collected by catheterization after the voiding phase, and bladder voiding efficiency (BVE, %) was calculated as follows: voided volume/(PVR + voided volume) ×100%.

Our primary endpoint was the individual change in MCC (ΔMCC) as determined by a urodynamic evaluation from the baseline to the end of treatment. The secondary outcomes included individual changes (Δ) in the following parameters from the baseline to the post-treatment: 1st IDCV, $Pdet_{max}$, BC, PVR, and BVE. Additionally, adverse reactions including pain and skin irritation during stimulation were observed and recorded as safety outcomes.

Statistical analysis

The data are presented as the mean ± standard deviation (SD) or median [interquartile range (IQR)] or number (%). The continuous variables were compared between groups using the unpaired *t*-test and Mann-Whitney U test for the normally and non-normally distributed variables, respectively. The Chi-squared test was applied to the qualitative data. Intragroup differences of normally distributed variables were analyzed by the paired-samples *t*-test, and the Wilcoxon signed-rank test was used for those with non-normally distributed data. The statistical analysis was performed using the Statistical Package for Social Sciences (version 26 for Windows), and a two-sided P value <0.05 was considered statistically significant.

Results

From December 2020 to December 2021, 50 patients participated in our study (25 in the rSMS group and 25 in the TTNS group). However, 1 patient dropped out from the course of therapy in each group for unrelated medical reasons (i.e., nosocomial respiratory infection and cardiac disease reoccurrence). Another patient in the rSMS group did not complete the treatment regimen for personal reasons. After excluding 3 cases with missing data, a total of 47 patients completed the study; 23 in the rSMS group and 24 in the TTNS group (see *Figure 2*). According to the PP analysis, all the patients completing the study displayed high tolerance for the protocol, and no adverse effects including pain and skin irritation were observed during treatment with either rSMS or TTNS therapy.

Baseline features of the patients

Patients' demographics and basic clinical evaluation results are set out in *Table 1*. On average, patients in the rSMS group were aged 47.8±12.8 years old, and 15 were male (65.2%) and 8 were female (34.8%). While on average, patients in the TTNS group were aged 48.0±12.1, and 15 were male (62.5%) and 9 were female (37.5%). In the rSMS group, 4 (17.4%) patients were diagnosed with complete and 19 (82.6%) with incomplete suprasacral SCI, while in

Table 1 Patients' demographics and basic clinical evaluation results

Variables	rSMS group (n=23)	TTNS group (n=24)	P value
Age (years), mean ± SD	47.8±12.8	48.0±12.1	0.68*
Gender, n (%)			
Male	15 (65.2)	15 (62.5)	0.85★
Female	8 (34.8)	9 (37.5)	
Course of disease (months), median (IQR)	2.1 (1.6–7.0)	2.9 (1.7–5.2)	0.48▲
Severity, n (%)			
Complete SCI (ASIA: A)	4 (17.4)	4 (16.7)	0.95★
Incomplete SCI	19 (82.6)	20 (83.3)	
Anticholinergics usage, n (%)	16 (69.6)	15 (62.5)	0.61★
Urine analysis, n (%)			
Free	18 (78.3)	19 (79.2)	0.94★
Urinary tract infection	5 (21.7)	5 (20.8)	
Hydronephrosis, n (%)	0	0	–

*, unpaired *t*-test; ★, Chi-squared test; ▲, Mann-Whitney U test. rSMS, repetitive sacral root magnetic stimulation; TTNS, transcutaneous posterior tibial nerve stimulation; SD, standard deviation; IQR, interquartile range; SCI, spinal cord injury; ASIA, American Spinal Injury Association.

the TTNS group, 4 (16.7%) patients were diagnosed with complete and 20 (83.3%) incomplete suprasacral SCI. No difference was observed between the two groups in terms of the demographics or the basic clinical evaluation results (see *Table 1*).

Urodynamic changes from the baseline to post-treatment

The general statistical analysis showed a widespread distribution of urodynamic parameters, and urodynamic changes before and after treatment (see the summary in *Table 2*). In relation to the baseline urodynamic assessment, there were no significant differences in the 1st IDCV (P=0.14), MCC (P=0.30), $Pdet_{max}$ (P=0.97), BC (P=0.52), PVR (P=0.98), and BVE (P=0.36) between the rSMS and TTNS groups.

In relation to the primary outcome of change in the MCC (ΔMCC), the intragroup analysis showed a statistically significant improvement in the MCC from the baseline median of 346 mL to the post-treatment median of 390 mL in the rSMS group (P<0.01), and a median individual ΔMCC (post-treatment minus the baseline) of +43 mL (IQR, 22–62 mL). For those who were exposed to TTNS, the MCC increased from the baseline median of 372 mL to the post-treatment median of 390 mL (P<0.01), with a median individual ΔMCC increase of +20 mL (IQR, 15–25 mL). The intergroup analysis revealed a significant difference in the individual ΔMCC between the rSMS and TTNS groups after the treatment regimens (P=0.001, with a between-group difference of +22 mL (95% CI: +7 to +35 mL); see *Table 3* and *Figure 3*.

For the other cystometry evaluation, the 1st IDCV improved significantly compared to the pre-stimulation levels in both groups (P<0.01 in the rSMS group and P<0.01 in the TTNS group). During the filling phase, the $Pdet_{max}$ decreased significantly, and BC increased significantly compared to the pre-stimulation levels in both groups (P<0.01 in rSMS and P<0.01 in TTNS groups; see *Table 2*). However, no significant intergroup differences were found between the groups in terms of the individual Δ1st IDCV [+12 (IQR, 5–20) *vs.* +15 (IQR, 12–21) mL, P=0.40], $\Delta Pdet_{max}$ (–6.7±5.1 *vs.* –7.2±2.8 cmH_2O; P=0.67), and ΔBC [+3.3 (IQR, 1.8–6.9) *vs.* +3.5 (IQR, 2.9–4.2) mL/cmH_2O; P=0.79] at the post-treatment period (see *Table 3* and *Figure 3*).

The subjects who suffered from urinary retention decreased their PVR to some extent, but the reduction in PVR was not statistically significant before or after the different therapies (P=0.50 in the rSMS group and P=0.72

Table 2 Changes in the urodynamic parameters from the baseline to post-treatment

Variables	rSMS group (n=23)	TTNS group (n=24)	P value
1st IDCV (mL), median (IQR)			
Baseline	165 [115–192]	188 [148–236]	0.14▲
Post-treatment	170 [144–215]	199 [171–252]	
P value	<0.01◆	<0.01◆	
MCC (mL), median (IQR)			
Baseline	346 [256–395]	372 [335–383]	0.30▲
Post-treatment	390 [335–415]	390 [366–400]	
P value	<0.01◆	<0.01◆	
$Pdet_{max}$ (cmH_2O), median (IQR)			
Baseline	35 [25–40]	35 [27–39]	0.97▲
Post-treatment	23 [21–31]	27 [22–30]	
P value	<0.01◆	<0.01◆	
BC (mL/cmH_2O), median (IQR)			
Baseline	10.4 [6.4–16.3]	10.6 [9.0–14.5]	0.52▲
Post-treatment	15.2 [11.1–19.5]	14.5 [12.1–18.2]	
P value	<0.01◆	<0.01◆	
PVR (mL), median (IQR)			
Baseline	203 [152–320]	212 [151–358]	0.98▲
Post-treatment	183 [150–310]	203 [136–379]	
P value	0.50◆	0.72◆	
BVE (%), median (IQR)			
Baseline	20.2 [8.6–42.9]	39.1 [0.0–59.1]	0.36▲
Post-treatment	41.6 [19.2–55.4]	45.3 [0.0–64.4]	
P value	<0.01◆	<0.01◆	

▲, Mann-Whitney U test; ◆, Wilcoxon signed-rank test. rSMS, repetitive sacral root magnetic stimulation; TTNS, transcutaneous posterior tibial nerve stimulation; IQR, interquartile range; 1st IDCV, volume at the 1st involuntary detrusor contraction; MCC, maximum cystometric capacity; $Pdet_{max}$, maximal detrusor pressure during the filling phase; BC, bladder compliance; PVR, postvoid residual volume; BVE, bladder voiding efficiency.

in the TTNS group) (see *Table 2*). The BVE increased from a baseline median of 20.2% to a post-treatment median of 41.6% in the rSMS group (P<0.01), and from a baseline median of 39.1% to a post-treatment median of 45.3% in the TTNS group (P<0.01; see *Table 2*). There were no notable differences in the ΔPVR between the rSMS and TTNS groups (P=0.92). rSMS had a statistically better effect on the ΔBVE with a median of +10.0% (IQR, 3.8–15.7%), than TTNS, which had a median of +3.5% (IQR, 0.0–7.8%) after therapy [P=0.003, with between-group difference of +5.9% (95% CI: +1.2% to +9.7%); see *Table 3* and *Figure 3*].

Discussion

NDO is a urodynamic phenomenon characterized by spontaneous reflex detrusor contractions at lower bladder volumes (14). Bladder function depends on both central and peripheral nervous systems for the harmonization of the filling and voiding phases, and neurogenic bladder can

Table 3 Comparison of individual urodynamic changes

Variables	rSMS group (n=23)	TTNS group (n=24)	P value	Estimated difference [rSMS minus TTNS (95% CI)]
Δ1st IDCV (mL), median (IQR)	+12 [5–20]	+15 [12–21]	0.40▲	−2 (−9 to +4)
ΔMCC (mL), median (IQR)	+43 [22–62]	+20 [15–25]	0.001▲	+22 (+7 to +35)▪
$\Delta Pdet_{max}$ (cmH_2O), mean ± SD	−6.7±5.1	−7.2±2.8	0.67*	+0.5 (−1.9 to +3.0)
ΔBC (mL/cmH_2O), median (IQR)	+3.3 [1.8–6.9]	+3.5 [2.9–4.2]	0.79▲	−0.2 (−1.3 to +1.8)
ΔPVR (mL), mean ± SD	−2.4±20.6	−3.0±18.9	0.92*	+0.6 (−11.0 to +12.2)
ΔBVE (%), median (IQR)	+10.0 [3.8–15.7]	+3.5 [0.0–7.8]	0.003▲	+5.9 (+1.2 to +9.7)▪

*, unpaired *t*-test with or without Welch's correction; ▲, Mann-Whitney U test; ▪, the CI was calculated with a Hodges-Lehmann estimate based on the Mann-Whitney U test. rSMS, repetitive sacral root magnetic stimulation; TTNS, transcutaneous posterior tibial nerve stimulation; IQR, interquartile range; SD, standard deviation; CI, confidence interval; 1st IDCV, volume at the 1st involuntary detrusor contraction; MCC, maximum cystometric capacity; $Pdet_{max}$, maximal detrusor pressure during the filling phase; BC, bladder compliance; PVR, postvoid residual volume; BVE, bladder voiding efficiency.

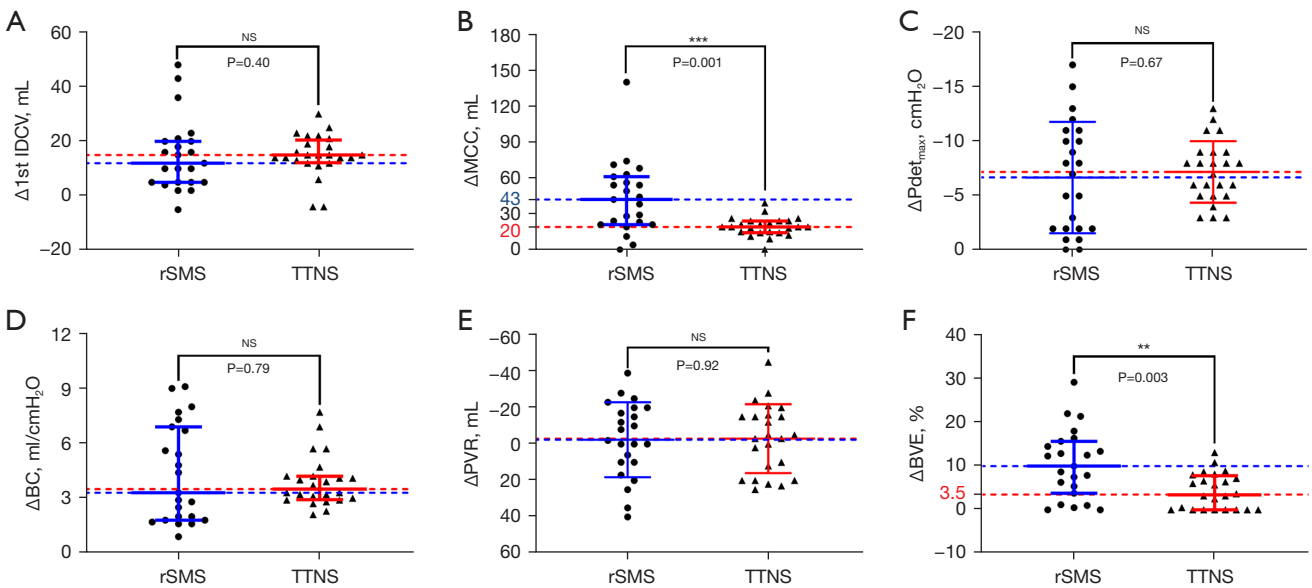

Figure 3 Comparison of individual urodynamic changes between rSMS and TTNS. The results are shown as the individual values and as the median ± IQR (A, B, D, and F) or the mean ± SD (C and E). The analyses were performed with Mann-Whitney U (A, B, D, and F), unpaired *t* (E), or Welch's *t* (C) tests. Differences in the Δ1st IDCV (A), $\Delta Pdet_{max}$ (C), ΔBC (D) and ΔPVR (E) were NS, while the ΔMCC (B) and ΔBVE (F) differed significantly between the two groups. **, P<0.01; ***, P≤0.001. rSMS, repetitive sacral root magnetic stimulation; TTNS, transcutaneous posterior tibial nerve stimulation; IQR, interquartile range; SD, standard deviation; 1st IDCV, volume at the 1st involuntary detrusor contraction; $Pdet_{max}$, maximal detrusor pressure; BC, bladder compliance; PVR, postvoid residual volume; NS, not significant; MCC, maximum cystometric capacity; BVE, bladder voiding efficiency.

be described as a pathological change in micturition reflex. It is speculated that a new spinal reflex circuit regulated by C fibers develops as response to the reorganization of synaptic connections in the spinal cord, which leads to the occurrence of NDO (2). Suprasacral SCI usually results in a voiding pattern consistent with NDO; thus, we selected these patients as our research objects, and urodynamic investigations are essential to assess treatment effects.

Anticholinergics are the mainstays of NDO treatment, but a certain number of patients do not respond to

anticholinergics or are unsatisfied with the side effects. Invasive procedures are used when conservative treatment fails, but adverse events may not be well accepted. During recent decades, TNS has developed into a conservative and cost-effective treatment option for LUTD (15). TNS propagates electrical currents to modulate the spinal detrusor reflex arc and inhibits detrusor muscle activity to decrease incontinence and is commonly used for patients with an overactive bladder who do not respond well to anticholinergic or behavioral therapy (16). TNS has also proven itself to be a valuable treatment option for NDO.

The percutaneous stimulation of the posterior tibial nerve, which is referred as PTNS for short, was originally developed as an electroacupuncture technique to stimulate the tibial nerve adjacent to the inner ankle. It is generally considered a peripheral and minimally-invasive type of sacral neuromodulation (17). Kabay *et al.* (18,19) successively investigated the acute and chronic effects of PTNS treatment on urodynamic parameters in Parkinson's disease patients, and found a statistically significant increase in the 1st IDCV and MCC in patients with NDO. TTNS uses adhesive skin surface electrodes to stimulate the posterior tibial nerve and has been demonstrated to be safer and easier to operate than needle-based PTNS, while also being similar in terms of its clinical efficacy (20). Chen *et al.* (21) compared the effectiveness of TTNS to with solifenacin succinate, and confirmed that TTNS was an effective method for treating NDO secondary to SCI, as it not only showed no difference compared to solifenacin succinate, but it was also non-invasive and easily managed by patients. Similarly, in our study, we found that 20 sessions of TTNS treatment led to a significant increase in bladder capacity, and to some extent, provided a compliant bladder with low filling pressure in patients with suprasacral SCI.

More recently, SMS has also been used by urologists or physiotherapists as a safe and non-invasive method for stimulating nervous tissue to improve lower urinary tract symptoms. It is believed to have the same mechanism as functional electrical stimulation, as it generates an electrical field similar to that produced by conventional electrical stimulators. Additionally, SMS effects on urinary incontinence and suppression of detrusor contraction have been reported (22).

As early as 2004, Bycroft *et al.* (23) investigated the application of magnetic stimulation to sacral nerve roots in complete SCI patients with NDO and confirmed the ability of SMS to suppress detrusor contractions. Tsai *et al.* (9) conducted a sham-controlled SMS trial on patients with refractory stress urinary incontinence (SUI), and the patients who underwent the 12-session SMS protocol showed a significantly greater improvement than those from sham group in urodynamic changes and symptom scales. Tsai *et al.* also found that more severe SUI symptoms were predictive of a more favorable response to SMS modulation. Animal experiments also indicated that SMS ameliorates bladder hyperreflexia by desensitizing C-afferent fibers and reducing c-fos gene expression, and this might be the underlying mechanism of SMS (24). Recently, rSMS, with energy targeted by figure-8 coils to some specific parts of the body to ensure long-time stimulation, has been widely used in the treatment of post-prostatectomy urinary incontinence, monosymptomatic nocturnal enuresis, and so on, and has achieved very promising clinical results (25,26).

Further, numerous comparative studies have investigated whether magnetic or electrical stimulation is better for LUTD. For example, Fergany *et al.* (27) compared the effectiveness of electromagnetic therapy and transcutaneous electrical nerve stimulation (TENS) on NDO in patients with SCI and found that a significant greater increase in the MCC and 1st IDCV was obtained by 15 Hz rSMS than TENS. However, no efficacy comparison has been conducted of rSMS and TTNS in the treatment of detrusor overactivity, regardless of neurogenic or non-neurogenic etiologies.

In the present study, taking large individual differences and the widespread distribution of urodynamic parameters into account, we selected individual urodynamic changes as our outcome indicators. Both rSMS and TTNS were found to be effective in urodynamic assessments associated with NDO in suprasacral SCI; however, rSMS exhibited greater efficacy than TTNS in the detrusor suppression of the filling phase and bladder capacity augmentation. Additionally, rSMS also showed a potential for improving bladder voiding function, and to a certain extent, enhanced voiding efficiency, but it failed to significantly reduce the residual urine volume. This is analogous to the findings of Niu *et al.* (28), who found that low-frequency transcutaneous magnetic stimulation of the lumbar spine allowed 5 patients with SCI to achieve voluntary micturition or eliminate the need for bladder self-catheterization. However, it should be noted that in our study, we applied a high-frequency of 20 Hz magnetic stimulation to the sacral root rather than a low frequency, as there is ample research that high-frequency magnetic stimulation may be a more favorable option for LUTD (29).

Unlike electrical stimulation on the posterior tibial nerve that decreases as a function of tissue impedance, rSMS penetrates tissues with little impedance and falls off in magnitude as the inverse square of the distance (30). As a result, greater efficacy may be achieved on the nervous tissue at greater depths with less discomfort at the surface of the application. Thus, rSMS is an attractive therapy of neuromodulation, and it is more effective to improve urodynamic parameters in the treatment for NDO than TTNS. Simultaneously, rSMS is non-invasive and painless, and is thus worthy of clinical promotion in the treatment for NDO in suprasacral SCI.

Our research also had several limitations. The exploratory study was only conducted to compare an overall urodynamic difference between the two different types of stimulation and not to identify the improvement of NDO clinical symptoms. Furthermore, the sample size was relatively small, and a larger sample size is required to determine the true clinical improvement of rSMS and TTNS for NDO.

Conclusions

RSMS may be more effective to improve urodynamic parameters in the treatment for NDO than TTNS, cause it led to a statistically significant improvement in bladder capacity and voiding efficiency, without any side effects. Therefore, rSMS is worthy of clinical promotion, and these results could serve as the basis for further research into the improvement of NDO clinical symptoms.

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Footnote

Reporting Checklist: The authors have completed the CONSORT reporting checklist. Available at https://tau.amegroups.com/article/view/10.21037/tau-22-249/rc

Trial Protocol: Available at https://tau.amegroups.com/article/view/10.21037/tau-22-249/tp

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-22-249/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work, including ensuring that any questions related to the accuracy or integrity of any part of the work have been appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Ethics Committee Board of The First Affiliated Hospital, College of Medicine, Zhejiang University (2020, IIT No. 1031), and informed consent was taken from all the patients.

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