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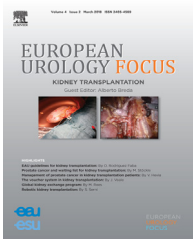

Review – Voiding Dysfunction

# Transcutaneous Electrical Nerve Stimulation and Percutaneous Tibial Nerve Stimulation to Treat Idiopathic Nonobstructive Urinary Retention: A Systematic Review

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**Abstract**

*Context:* Transcutaneous electrical nerve stimulation (TENS) and percutaneous tibial nerve stimulation (PTNS) provide minimally invasive ways to treat idiopathic nonobstructive urinary retention (NOUR).
*Objective:* To assess the efficacy of TENS and PTNS for treating idiopathic NOUR.
*Evidence acquisition:* A systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement. Embase, Medline, Web of Science Core Collection, and the Cochrane CENTRAL register of trials were searched for all relevant publications until April 2020.
*Evidence synthesis:* A total of 3307 records were screened based on the title and abstract. Eight studies met the inclusion criteria and none of the exclusion criteria. Five studies, all from the same group, reported the efficacy of PTNS and two that of TENS in adults with idiopathic NOUR. One study reported the efficacy of TENS in children with idiopathic NOUR. Objective success was defined as a $\geq$50% decrease in the number of catheterizations per 24 h or in the total catheterized volume in 24 h. The objective success rate of PTNS ranged from 25% to 41%. Subjective success was defined as the patient's request for continued chronic treatment with PTNS, and ranged from 46.7% to 59%. Eighty percent of women who underwent transvaginal stimulation reported an improvement such as a stronger stream when voiding. TENS in children reduced postvoid residual and urinary tract infections.
*Conclusions:* The efficacy of TENS and PTNS in the treatment of idiopathic NOUR is limited and should be verified in larger randomized studies before application in clinical practice.
*Patient summary:* The outcomes of transcutaneous electrical nerve stimulation and percutaneous tibial nerve stimulation for the treatment of urinary retention of unknown origin were reviewed. Whether these treatments are superior to other treatments could not be established.



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## 1. Introduction

Voiding disorders affect millions of people worldwide [1]. Symptoms related to difficulties emptying the urinary bladder are prevalent in 14.8–23% of the population [2]. These symptoms can be due to bladder outlet obstruction (BOO) or bladder dysfunction. Among elderly patients with lower urinary tract symptoms, detrusor underactivity (defined as a detrusor contraction of decreased strength and/or duration on urodynamics) has a prevalence of 25–48% in men and 12–24% in women [1,3]. This can be of unknown cause (idiopathic) or due to neurogenic diseases such as spinal cord injury and multiple sclerosis. The symptoms related to detrusor underactivity are often referred to as underactive bladder, which is defined by Chapple et al [4] as "a symptom complex suggestive of detrusor underactivity and is usually characterized by prolonged urination time with or without a sensation of incomplete bladder emptying, usually with hesitancy, reduced sensation on filling, and a slow stream" [2]. In our view, underactive bladder is clinically significant only in case of significant postvoid residual (PVR), which necessitates regular artificial drainage of the bladder. We prefer to use the term nonobstructive urinary retention (NOUR) since the term underactive bladder solely describes subjective parameters (symptoms) without incorporating objective parameters such as PVR. However, there is no consensus on the definition of significant PVR. In our view, a PVR of more than one-third of the patients' bladder capacity is the preferred definition of significant PVR as opposed to using an arbitrarily defined cutoff value, such as 200 ml [5,6].

Patients with idiopathic NOUR can present with symptoms such as slow urinary stream, hesitancy, and straining to void with the feeling of incomplete bladder emptying. Furthermore, patients can present with recurrent urinary tract infections (rUTIs) caused by incomplete bladder emptying. Urodynamics may reveal decreased contractility of the detrusor muscle during voiding. Most patients with idiopathic NOUR use clean intermittent catheterization (CIC), or indwelling catheters, to ensure timely drainage of the bladder and prevent complications. The possible long-term complications of catheterization include chronic inflammation, urethral strictures, increased risk of bacterial infection, stone formation, urosepsis, and renal failure [7,8]. The treatment of idiopathic NOUR consists of catheterization to ensure bladder emptying. Yet, catheterization merely prevents complications but does not improve voiding. In an attempt to decrease PVR, sacral neuromodulation (SNM) can be offered to selected cases, but it is an invasive procedure. Less invasive alternatives are transcutaneous electrical nerve stimulation (TENS) and percutaneous tibial nerve stimulation (PTNS). They are therefore possible treatment options worth trying before turning to SNM.

PTNS is an effective treatment in patients with overactive bladder (OAB) [9]. However, evidence regarding whether TENS is also an effective treatment option in patients with OAB is limited [10,11]. Furthermore, in patients with neurogenic causes of bladder dysfunction, TENS and PTNS might be effective and safe. The results in patients with neurogenic lower urinary tract dysfunction have been described previously in two systematic literature reviews [12,13]. For patients with idiopathic NOUR, the efficacy of these treatments has not been studied comprehensively. Thus, this systematic review focused on the efficacy of TENS and PTNS in patients with idiopathic NOUR.

## 2. Evidence acquisition

### 2.1. Study registration

This study was registered on PROSPERO (CRD42020165479; https://www.crd.york.ac.uk/PROSPERO) and was performed in accordance with the Cochrane handbook for systematic reviews of interventions [14]. The results are reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement [15].

### 2.2. Literature search

Embase, Medline, Web of Science Core Collection, and the Cochrane CENTRAL register of trials were searched for all relevant publications until April 2020. No date restrictions were applied. Duplicates were removed. The search string is presented in the Supplementary material. The study selection process is described using a PRISMA flow diagram.

### 2.3. Eligibility criteria

All publications on TENS or PTNS in patients of either sex with idiopathic NOUR were eligible for full-text retrieval. Publications were eligible only if the diagnosis of idiopathic NOUR was confirmed by urodynamics. Case reports or case series with fewer than 10 patients, publications with patients with neurogenic lower urinary tract dysfunction, non–English-text articles, editorials, reviews, conference abstracts, and systematic reviews were excluded. Furthermore, publications with mixed populations were excluded if the eligible population accounted for $<$90% of the study population (unless the data were reported separately).

### 2.4. Selection of studies

Two reviewers (R.C. and J.G.) independently screened the titles and abstracts in Endnote. The studies included for full-text retrieval were compared between the two reviewers and disagreements were discussed. The same reviewers independently screened the full text of the potentially eligible publications using a standardized screening form. A third reviewer (B.B.) resolved any disagreements between the two reviewers.

### 2.5. Data extraction

A list of predefined data were independently extracted from the included studies by two reviewers (R.C. and J.G.) using a standardized form. Any disagreements were resolved by a

third reviewer (B.B.). The data extracted included the type of study, recruitment period, intervention, duration of intervention, control, number of patients, sex, age, PVR at baseline, catheterized volume per 24 h at baseline, CIC frequency at baseline, rUTIs prior to study inclusion, and duration of follow-up.

### 2.6. Outcome measures

The primary outcomes of interest were CIC frequency, PVR, and rUTIs. The secondary outcome measures were symptoms and symptom severity, quality of life, and adverse effects.

### 2.7. Subgroup analysis

The predefined subgroups were type of intervention (TENS vs PTNS), sex (male vs female), and age (children vs adults).

### 2.8. Risk of bias assessment

The methodological quality of the studies was assessed independently by two reviewers (R.C. and J.G.), and disagreements were resolved by a third reviewer (B.B.). A risk of bias assessment was made for each included study using the Cochrane Risk of bias Assessment Tools for randomized interventions [16]. The following items that might account for a bias in the outcomes reported in the included studies were analyzed: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, other bias, a priori study protocol, and consecutive study participants. A list of confounders was made. The aspects of bias and the confounders were scored as "low," "unclear," or "high." The risk of bias was high if there was a high chance that the specific type of bias could have influenced the reported results. The confounding bias for a specific confounder was classified as high if the confounder was not adjusted for either in the study protocol or in the analysis of the results, or if it was imbalanced between the groups. The identified confounders were age, gender, neurourological pathology, BOO, previous treatment for NOUR, simultaneous other treatment for NOUR, and chronicity of symptoms. We used Review Manager version 5.3 (Cochrane Collaboration, London, UK) to construct the figure describing the risk of bias summary.

## 3. Evidence synthesis

### 3.1. Search results

The PRISMA flow diagram in Figure 1 shows the results of the literature search. The search resulted in 5297 articles. After duplicates were removed, 3307 articles remained. Forty-four publications were retrieved for full-text

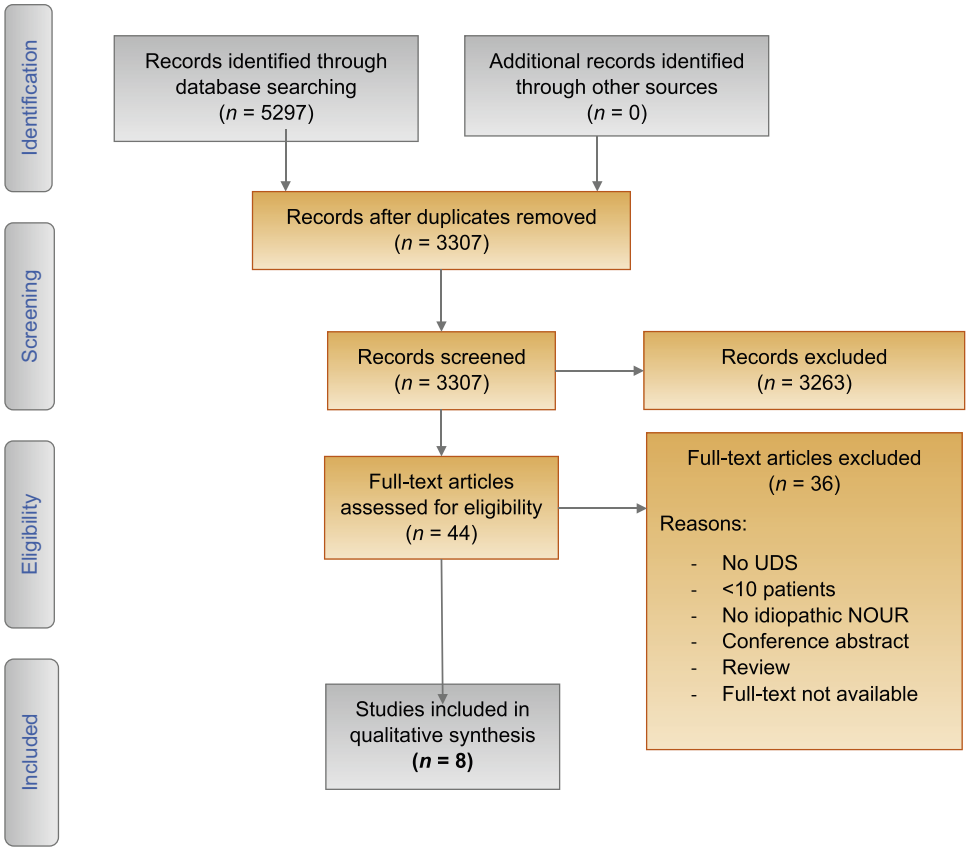


**Fig. 1 – Literature search and selection of studies.**
**NOUR = nonobstructive urinary retention; UDS = urodynamics.**

evaluation. Thirty-six articles were excluded and eight articles were included in a qualitative synthesis [17–24].

### 3.2. Characteristics of the included studies

Table 1 shows the characteristics of the included studies. The included studies are prospective studies, most of which included a single study arm. However, in two studies, two study arms were compared; one of these studies applied randomization to allocate the patients to one of the two study arms [23]. In the other comparative study, patients were allocated to a study arm based on the patients' treatment desire [19]. A total of 277 patients with idiopathic NOUR were included, of whom 36 were children. Some form of TENS or PTNS was applied in 211 of the included patients. It was unclear whether patients were included consecutively. All studies included patients without BOO. The urodynamic criteria to diagnose idiopathic NOUR were a detrusor contraction of reduced strength and/or duration. However, two studies did not report whether urodynamics was performed, and one study did not mention the exact urodynamic criteria that were used [22]. Most studies involved a mixed population of men and women. Seven studies assessed the efficacy of electrical stimulation in bladder function of adults, and one study was found to include children [23]. PTNS was performed in five studies [17,18,20,21,24]. The other three studies applied TENS at different locations: transvaginal, the symphysis pubis and the ischial tuberosity, and the second sacral foramina and the lower abdomen under the umbilicus [19,22,23]. There was no follow-up after treatment in the studies that performed PTNS. The three studies that applied TENS had a follow-up duration ranging from 4 wk to 1 yr [19,22,23].

PVR and CIC frequency at baseline were not reported in all studies. The mean/median PVR ranged from 154 to 336 ml, and the mean/median CIC frequency per day ranged from 2.5 to 5.3 in adults [17,18,20–22,24]. The mean PVR at baseline was 60–80 ml in children [23]. Artificial drainage of the urinary bladder was not applied in these children. Of the children, 38% in the intervention group and 61% in the control group suffered urinary tract infections (UTIs) prior to inclusion in the study.

### 3.3. Electrical stimulation parameters

The methods used for electrical stimulation are presented in Table 2. The studies that applied PTNS used the method described by Cooperberg and Stoller [25]. This entails percutaneous placement of a 34 gauge needle 3–4 cm cephalad to the medial malleolus. Stimulation was carried out at 20 Hz with a pulse width of 200 μs for 30 min once a week for the duration of 12 wk. The three studies that applied TENS used different stimulation parameters [19,22,23]. Transvaginal electrical stimulation was carried out at 200 Hz with a pulse width of 300 μs for 15 min during one or two sessions per week [22]. Another study applied interferential electrical stimulation bilaterally over the skin of the symphysis pubis and the ischial tuberosity at a beat frequency of 5–55 Hz (with a carrier frequency of 4 kHz) with a pulse width of 250 μs for 20 min twice a week for 7.5 wk [23]. The third study applied TENS to the second sacral foramina and 3.0 cm under the umbilicus at 20 and 80 Hz, with a pulse width of 150 and 300 μs, respectively, for 70 min twice a day for 2 wk [19].

### 3.4. Treatment outcome

The primary and secondary outcome measures are summarized in Table 3. The predefined outcome measures of CIC frequency, PVR, rUTIs, symptom and symptom severity, quality of life, and adverse effects were not reported in every study. We added the outcome measures of change in catheterized volume per 24 h and success rate (objective and subjective) whenever success was defined clearly in the included studies.

#### 3.4.1. PTNS in adults with idiopathic NOUR

The five included studies on PTNS in patients with idiopathic NOUR reported an objective success rate ranging from 25% to 41% [17,18,20,21,24]. However, some defined success as a ≥50% reduction in the number of catheterizations, whereas others defined it as a ≥50% reduction in catheterized volume per 24 h. Subjective success was defined as the patient's request for continued chronic treatment with PTNS. The subjective success rates ranged from 46.7% to 59%. There was no follow-up of patients after the completion of the 12-wk PTNS treatment. The change in PVR was reported in three of the five studies [20,21,24]. In these studies, PVR was significantly lower after 12 wk than at baseline, with a mean/median decrease of 76–83.3 ml and a mean/median CIC frequency decrease of 0–0.8 [20,21,24].

None of the included studies reported the occurrence of UTIs prior to and during treatment. Three studies reported no serious side effects, and two studies did not state whether side effects were noted.

#### 3.4.2. TENS in adults with idiopathic NOUR

We included two studies that reported the efficacy of TENS in adults with idiopathic NOUR; in one of these studies transvaginal stimulation was performed, and in the other study stimulation was performed over the sacral foramina and the lower abdomen. The study in which transvaginal stimulation was applied did not report an objective success rate [22]. However, a mean PVR decrease of 107 ml (range not specified) was reported. A subjective success rate of 80% was reported in women who received transvaginal stimulation [22]. The subjective success rate was defined as the percentage of patients who reported a decrease in the feeling of bladder fullness and a stronger stream when voiding. The study in which electrical stimulation was applied over the sacral foramina and the lower abdomen combined with routine conservative treatment reported a 43% decrease in the number of patients relying on catheterization for bladder emptying, which was 12% in the control group that received routine conservative treatment only [19]. However, this was the case only in women with normal bladder compliance (intervention group: $n$ = 28,

**Table 1 – Characteristics of the included studies.**

| Study | Study design | Recruitment period | Intervention | Duration of intervention | Control | Number of patients (intervention/control) | Sex (male/female) | Age (yr) | UDS (yes/no) | PVR at baseline (ml) | Catheterized volume per 24 h at baseline (ml) | CIC frequency per 24 h at baseline | Prior UTIs | Follow-up time |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bernier and Davila (2000) [22] | Prospective, single center | NR | Transvaginal electrical stimulation + voiding modifications or transvaginal electrical stimulation + voiding modifications + Urecholine | Once or twice a week 15 min (mean 6.5 visits) | None | 18/0 | 0/18 | Mean 61.8 (range 25–87) | Yes | Mean 154 (range 65–435) | NR | NR | *n* = 7 | 4 wk |
| van Balken et al (2001) [24] | Prospective, multicenter | 1999–2000 | PTNS | Once a week 30 min for 12 wk | None | 12/0 | 5/7 | Mean 50.8 (range 36–64) | Yes | Mean 336 (SD 171) | Mean 1552 (SD 776) | Mean 5.3 (SD 2.4) | NR | 0 |
| Vandoninck et al (2003) [21] | Prospective, multicenter | 1999–2000 | PTNS | Once a week 30 min for 12 wk | None | 39/0 | 12/27 | Median 53 (range 28–77) | Yes | Median 241 (range 74–675) | Median 800 (range 210–3000) | Median 2.5 (range 1–10) | NR | 0 |
| Vandoninck et al (2004) [20] | Prospective, multicenter | 1999–2000 | PTNS | Once a week 30 min for 12 wk | None | 39/0 | 12/27 | Median 53 (range 28–77) | Yes | Median 241 (range 74–675) | Median 800 (range 210–3000) | Median 2.5 (range 1–10) | NR | 0 |
| van Balken et al (2006) [17] | Prospective, multicenter | NR | PTNS | Once a week 30 min for 12 wk | None | 16/0 | 7/9 | Mean 51.3 (range 25–68) | NR | NR | NR | Mean 4.9 (range 2–10) | NR | 0 |
| van Balken et al (2006) [18] | Prospective, multicenter | 1999–2001 | PTNS | Once a week 30 min for 12 wk | None | 15/0 | 6/9 | Mean 50.9 (range 25–68) | NR | NR | NR | Mean 4.9 (range 2–10) | NR | 0 |
| Xu et al (2012) [19] | Prospective, comparative, single center | 2008–2011 | TENS + routine conservative treatment | 2 daily sessions of 70 min for 2 wk | Routine conservative treatment | 54/48 | 0/102 | I: mean 53.6 (SD 2.1) and 55.6 (SD 2.3) C: mean 56.2 (SD 4.1) and 54.5 (SD 4.0) | Yes | NR | NR | NR | NR | 4 wk |
| Kajbafzadeh et al (2016) [23] | Prospective, randomized, single center | 2011–2014 | IFES + standard urotherapy | Twice a week 20 min for 7.5 wk | Standard urotherapy | 18/18 | 15/21 | Mean 8.9 (SD 2.6, range 5–13) | Yes | I: mean 60 (SD 32) C: mean 80 (SD 48) | 0 | 0 | I: 7/18 (38%) C: 11/18 (61%) | 12 mo |

CIC = clean intermittent catheterization; IFES = interferential electrical stimulation; NR = not reported; PTNS = percutaneous tibial nerve stimulation; PVR = postvoid residual; SD = standard deviation; TENS = transcutaneous electrical nerve stimulation; UDS = urodynamics; UTIs = urinary tract infections.

**Table 2 – Stimulation parameters of the included studies.**

| Study | Intervention | Location of electrodes | Frequency (Hz) | Pulse width (μs) | Duration (min) | Sessions per week | Treatment duration (wk) |
|---|---|---|---|---|---|---|---|
| Bernier and Davila (2000) [22] | Transvaginal electrical stimulation + voiding modifications or transvaginal electrical stimulation + voiding modifications + Urecholine | Intravaginal | 200 | 300 | 15 | 1–2 | NR |
| ban Balken et al (2001) [24] | PTNS | Percutaneous inserted 34 gauge needle 3–4 cm cephalad to the medial malleolus, between the posterior margin of the tibia and soleus muscle | 20 | 200 | 30 | 1 | 12 |
| Vandoninck et al (2003) [21] | PTNS | Percutaneous inserted 34 gauge needle 3–4 cm cephalad to the medial malleolus, between the posterior margin of the tibia and soleus muscle | 20 | 200 | 30 | 1 | 12 |
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| van Balken et al (2006) [17] | PTNS | Percutaneous inserted 34 gauge needle 3–4 cm cephalad to the medial malleolus, between the posterior margin of the tibia and soleus muscle | 20 | 200 | 30 | 1 | 12 |
| van Balken et al (2006) [18] | PTNS | Percutaneous inserted 34 gauge needle 3–4 cm cephalad to the medial malleolus, between the posterior margin of the tibia and soleus muscle | 20 | 200 | 30 | 1 | 12 |
| Xu et al (2012) [19] | TENS + routine conservative treatment | The second sacral foramina and 3.0 cm under the umbilicus on the abdomen | 20/80 | 150/300 | 70 | 14 | 2 |
| Kajbafzadeh et al (2016) [23] | IFES + urotherapy | Bilaterally on the skin of the symphysis pubis and bilaterally under the ischial tuberosity | 5–55 (4 kHz carrier frequency) | 250 | 20 | 2 | 7.5 |

IFES = interferential electrical stimulation; NR = not reported; PTNS = percutaneous tibial nerve stimulation; TENS = transcutaneous electrical nerve stimulation.

**Table 3 – Primary and secondary outcome measures.**

| Study | Objective success rate | Definition of objective success | Change in PVR (ml) | Change in catheterized volume per 24 h (ml) | Change in CIC frequency per 24 h | UTIs during follow-up | Subjective success rate (%) | Definition of subjective success | Change in QOL | Adverse effects |
|---|---|---|---|---|---|---|---|---|---|---|
| Bernier and Davila (2000) [22] | NR | NR | Mean change −107, range not specified | NR | NR | NR | 80 | % of patients who reported a decrease in the feeling of bladder fullness and a stronger stream when voiding | NR | NR |
| van Balken et al (2001) [24] | NR | NR | Mean change −83.3 (95% CI: +27.4, −194) | Mean change −537 (95% CI: +175, −1249) | Mean change −0.8 (95% CI: +0.6, −2.3) | NR | 58.3 | % of patients who requested continued chronic treatment | Only the SF-36 score for emotional well-being improved significantly in patients with subjective success of treatment | Complications were rarely noted |
| Vandoninck et al (2003) [21] | 41% | A reduction of ≥50% in total catheterized volume per 24 h | Mean change −76 (95% CI: −39, −113) | Mean change −228 (95% CI: −49, −528) | Mean change −0.5 (95% CI: −0.04, −0.9) | NR | 59 | % of patients who requested continued chronic treatment | Mean change (95% CI) iQOL: +14 (+5, +22); SF-36: +7 (+3, +11); QOL: +6 (+3, +10). | No serious side effects were reported. Transient pain at the stimulation site was noted |
| Vandoninck et al (2004) [20] | 41% | A reduction of ≥50% in total catheterized volume per 24 h | Median change −80 (range from −375 to 247; $p < 0.01$) based on frequency/volume chart. Median change −80 (range from −280 to 100; $p = 0.01$) based on UDS | Median change −200 (range from −2700 to 700; $p < 0.01$) | Median change 0 (range from −7 to 2; $p = 0.024$) | NR | 59 | % of patients who requested continued chronic treatment | Median change (range) iQOL: +11 (−2, 60; $p < 0.01$); SF-36: 3 (−18, 50; $p < 0.01$) | No serious side effects were reported. Transient pain at the stimulation site was noticed |
| van Balken et al (2006) [17] | 25% | A decrease of >50% in the number of catheterizations per 24 h | NR | NR | NR | NR | 50 | % of patients who requested continued chronic treatment | NR | NR |
| van Balken et al (2006) [18] | 26.7% | A decrease of >50% in the number of catheterizations per 24 h | NR | NR | NR | NR | 46.7 | % of patients who requested continued chronic treatment | No significant changes in sexual life satisfaction | NR |
| Xu et al (2012) [19] | I: 43% (normal compliance bladder, $p < 0.01$) and 4% (low compliance bladder, $p > 0.05$) C: 12% (normal compliance bladder, $p > 0.05$) and 0% (low compliance bladder, $p > 0.05$) | Decrease of the number of patients relying on catheterization for bladder emptying | NR | NR | NR | NR | NR | NR | NR | NR |
| Kajbafzadeh et al (2016) [23] | NR | NR | I: mean 60 (SD 32) −>mean 22.5 (SD 10.3), −37.5 C: mean 80 (SD 48) −> mean 44.1 (SD 39), −35.9 $p < 0.03$ | NR | NR | I: 2/18 (11%) C: 6/18 (33%) $p = 0.145$ | NR | NR | NR | Parents and children reported no side effects during and after IFES |

CI = confidence interval; CIC = clean intermittent catheterization; IFES = interferential electrical stimulation; iQOL = incontinence QOL; NR = not reported; PVR = postvoid residual; QOL = quality of life; SD = standard deviation; UDS = urodynamics; UTIs = urinary tract infections.

control group: $n$ = 25). In patients with low compliance bladders, one patient in the group that received electrical stimulation together with conservative treatment ($n$ = 26) stopped catheterization after treatment, and none of the patients in the control group stopped catheterization ($n$ = 23). Subjective success was not reported in this study. Whether adverse effects occurred was not reported in both studies.

#### 3.4.3. TENS in children with idiopathic NOUR

One study on TENS in children with idiopathic NOUR was included [23]. In this randomized study, 18 children received interferential electrical stimulation, with surface electrodes placed on the skin of the symphysis pubis and the ischial tuberosity bilaterally in combination with standard urotherapy. The control group of 18 children received standard urotherapy. Standard urotherapy consisted of education about bowel and urinary function, fluid intake, timed voiding, toilet training, and correction of voiding posture. The mean PVR decreased by 37.5 ml in the intervention group and 35.9 ml in the control group. At baseline, 38% of children in the intervention group and 61% in the control group had a history of recurrent UTIs. This decreased to 11% in the intervention group and 33% in the control group after 12 mo of follow-up. Both parents and children did not notice side effects.

### 3.5. Subgroup analysis

A subgroup analysis of TENS and PTNS was intended to determine which mode of electrical stimulation is superior in terms of efficacy and safety in the predefined subgroups. This comparison is unfeasible based on the included studies since the methods used for TENS are heterogeneous, whereas all studies on PTNS used the method described by Cooperberg and Stoller [25]. Furthermore, the definition of subjective success was different between the studies and the objective parameters indicating treatment effects were heterogeneous. A subgroup analysis of men and women was impossible since the results were not reported separately. Besides, a subgroup analysis of children and adults was unattainable as only one of the included studies involved children, whereas all other studies reported the efficacy of TENS or PTNS in adults.

### 3.6. Risk of bias assessment

The risk of bias in the included studies was assessed by using the Cochrane Risk of Bias Assessment Tool. Bias and

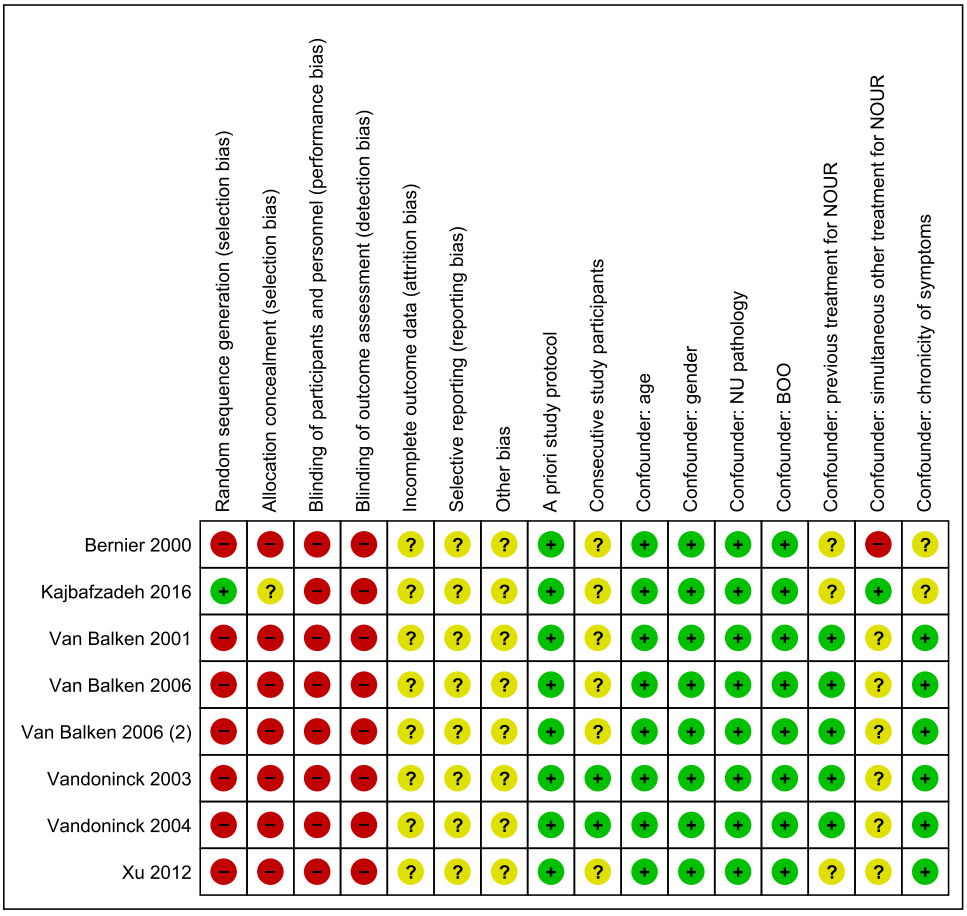


**Fig. 2 – – Risk of bias assessment.**
**+ = low risk of bias;? = unclear risk of bias; – = high risk of bias; BOO = bladder outlet obstruction; NOUR = nonobstructive urinary retention; NU = neurourological.**

possible confounding factors were classified as low, unclear, or high. Overall, a high or an unclear risk of bias is present in the included studies. The risk of confounding bias was mostly classified as low or unclear. The summary of the risk of bias assessment is presented in Figure 2.

### 3.7. Discussion

Patients with idiopathic NOUR with significant PVR, which necessitates artificial drainage of the urinary bladder, mostly rely on CIC for timely drainage of the bladder. Catheterization is performed to prevent complications of urinary retention. However, catheterization is merely a way to ensure drainage of the urinary bladder but does not restore voiding. Minimally invasive options to restore voiding include TENS and PTNS, which can be performed in the outpatient clinic and sometimes even at home. For the treatment of idiopathic NOUR as opposed to OAB, it is not yet well established whether TENS and PTNS are effective. Therefore, the aim of this study was to investigate the evidence supporting the hypothesis that TENS and PTNS can (partially) restore voiding and decrease the necessity for artificial drainage of the urinary bladder in adults and children with idiopathic NOUR.

Of the patients receiving PTNS, 25–41% had a decrease of at least 50% in the frequency or volume of catheterization per 24 h. The efficacy of TENS in adults was reported heterogeneously. The subjective success rate of transvaginal TENS was 80% compared with 46.7–59% for PTNS [22]. The relatively high subjective success rate of transvaginal TENS must be interpreted with caution since the study on transvaginal TENS applied TENS in combination with voiding modifications, which might explain (part of) the results. TENS over the sacral foramina and the lower abdomen in combination with conservative treatment decreased the number of patients relying on catheterization for bladder emptying by 43%, which was 12% in the control group that received conservative treatment [19]. Electrical stimulation applied over the skin of the symphysis pubis and the ischial tuberosities combined with standard urotherapy decreased the number of rUTIs compared with that in children who received standard urotherapy. However, the group that received standard urotherapy had more rUTIs at baseline. In short, the included studies indicate improvement of multiple subjective and objective parameters during treatment with PTNS or TENS.

The mechanism by which TENS and PTNS modulate the lower urinary tract has been debated in the literature. It seems that these techniques modulate supraspinal brain areas. PTNS has been shown to modulate somatosensory pathways in patients with OAB [26]. Furthermore, chronic SNM modulates brain areas that are involved in alertness and awareness [27]. Most of the studies on the mechanism of action of electrical stimulation are studies on SNM in patients with OAB or animal studies. A functional magnetic resonance imaging study in women with urinary retention revealed changes in activation of supraspinal brain areas such as the periaqueductal gray during SNM [28]. We hypothesize that TENS and PTNS modulate the same brain networks as SNM, thereby improving voiding by modulating forebrain areas to increase awareness. This facilitates a more effective opening of the urethral sphincter during voiding and therefore decreases PVR [29]. However, TENS and PTNS are less robust than SNM, which is possibly due to the activation of fewer nerve fibers or due to the fact that stimulation is not continuous, as is the case for SNM.

This systematic review was conducted according to an a priori made protocol in accordance with the Cochrane handbook for systematic reviews of interventions, and gives an overview of the literature on TENS and PTNS for the treatment of idiopathic NOUR [14]. However, some limitations must be addressed. First, most of the included studies comprised relatively small samples of patients. Second, only two of the included studies were comparative and only one study applied randomization to determine study arm allocation. Third, a subgroup analysis was not possible due to the heterogeneity of the outcome measures that were reported and the omission of reporting outcomes for subgroups separately. Fourth, PTNS was applied using a similar method in all the included studies. In contrast, the locations and stimulation parameters used for applying TENS varied across the studies, making it unfeasible to compare these studies. Fifth, no fewer than five of the eight studies were from the same research group. Therefore, it is most likely that the described study groups partly contained the same patients. This introduces a bias, and therefore, the results must be interpreted with caution; ideally they should be replicated by other researchers in different study populations. Last, in most studies, success was defined as a $\geq$50% reduction of catheterization frequency or catheterized volume per day. This, however, does not indicate whether or not catheterization could be abolished. This is relevant since catheter use can give rise to complications such as rUTIs. In our view, abolishing the need for artificial drainage of the urinary bladder is the desired outcome of treatment, and therefore, this should be the primary outcome measure of studies that investigate the efficacy of TENS and PTNS in patients with idiopathic NOUR. Continuation of CIC at a lower frequency does not decrease the chance of symptomatic UTIs compared with baseline and, thus, should not be used as a primary endpoint [30]. Future, preferably randomized, studies must indicate absolute catheterization frequency before and after treatment in order to draw stronger conclusions on the efficacy of TENS and PTNS for the treatment of idiopathic NOUR. Furthermore, the included studies did not investigate long-term effects and whether lifelong maintenance therapy is required. Therefore, we speculate, based on studies investigating PTNS in patients with OAB, that maintenance therapy is required for a sustained response in the long term [31].

## 4. Conclusions

The eight included studies demonstrated beneficial effects of TENS and PTNS on several objective and subjective aspects of bladder function in patients with idiopathic NOUR. Both techniques seem to be safe; side effects of both

TENS and PTNS were negligible. However, the efficacy of these treatment options should be verified in larger randomized studies before application in clinical practice.

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*Study concept and design*: Coolen, Scheepe, Blok.
*Acquisition of data*: Coolen, Groen.
*Analysis and interpretation of data*: Coolen, Groen.
*Drafting of the manuscript*: Coolen, Groen.
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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.euf.2020.09.019.

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