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The Presence of Fowler's Syndrome Predicts Successful Long-Term Outcome of Sacral Nerve Stimulation in Women with Urinary Retention

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Abstract

Objectives: Sacral nerve stimulation (SNS) is an effective treatment for women with urinary retention. Some women present specific electromyography abnormalities of the external urethral sphincter (Fowler's syndrome). The aim of this study was to evaluate whether Fowler's syndrome and psychologic preimplant screening could be predictive factors for long-term success of SNS in women with urinary retention.

Methods: All patients underwent electrophysiologic and urodynamic studies and voiding charts. A validated psychologic screening questionnaire was used. Women with successful temporary stimulation, received a definitive implant (Interstim Medtronic). They were followed prospectively every 6 months. Failure was defined as recurrent retention needing intermittent or permanent catheterisation.

Results: Sixty-two women were implanted, 30 with Fowler's syndrome, 32 with idiopathic retention. In those with Fowler's syndrome, 26.6% screened positive for somatisation, as did 43.8% in the idiopathic group (not significant [ns]). Screening for depression was positive in 30% and 18.8%, respectively (ns). There was no correlation with outcome. Twenty-eight patients failed: 9 with Fowler's syndromes, 19 without ($p = 0.04$). Kaplan-Meier analysis showed that patients with Fowler's syndrome benefitted significantly longer from SNS (log-rank test, $p = 0.005$).

Conclusions: The presence of Fowler's syndrome is a positive predictive factor for SNS in female urinary retention. Idiopathic urinary retention patients can benefit as well, but the success might be less predictable. Preimplant psychologic screening, using the Patient Health Questionnaire, does not correlate with long-term outcome of SNS in this population.

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1. Introduction

Sacral nerve stimulation (SNS) has proven to be an efficient treatment for chronic micturition disorders refractory to classic behavioural or pharmacologic treatment. In women with urinary retention a subset of patients can be defined by electrophysiologic studies of the external urethral sphincter. On concentric needle electromyography (EMG) of the external urethral sphincter, these patients show a specific pattern of decelerating bursts and complex repetitive discharges (CRDs) [1,2]. This finding is referred to as Fowler's syndrome. The underlying pathophysiology is unclear, although ephaptic spreading within the muscle bundles seems to be at the origin of the phenomenon and an association with polycystic ovaries has been suggested. An underlying channelopathy has also been suggested. Other authors question the value of CRD, since these can also be found in patients without obvious voiding problems [3]. Many treatments have been tried for women with urinary retention: urethral dilatation, intermittent catheterisation, botulinum toxin injection of the urethral sphincter, and alpha-blockers. Most of these treatments proved unsuccessful, and spontaneous recovery has not been described. SNS however has been shown to be the only efficient treatment, since it enables restoration of spontaneous voiding, which can be maintained for several years in many patients [4,5].

Female retention patients without this specific EMG abnormality are a diagnostic challenge. In most of those patients, no underlying neurologic, metabolic, or other causal disease can be identified [5]. These women are often thought to be at risk for somatisation and conversion disorders. Although many clinical urologists might have this impression, there are no objective reasons to deny these patients the possible benefit of SNS.

Since the specific EMG abnormality is present in only a subset of women with urinary retention, the question arose as to whether this finding could form a predictive factor for long-term success of SNS.

We present a retrospective analysis of prospective data on women with urinary retention undergoing a definitive SNS implant. The predictive value of Fowler's syndrome concerning the success rate and duration of success of SNS is assessed. The usefulness of a validated psychologic screening questionnaire in relation to long-term outcome is also evaluated.

2. Patients and methods

A consecutive series of women with nonobstructive urinary retention has been studied. Data were gathered prospectively

at regular time intervals in a database containing data on urodynamics, patient satisfaction, EMG, and micturition diaries, as well as technical data on implantation and revisions. Data collection was done in a specific automated registry to comply with Belgian reimbursement regulations. The database was organised by the Belgian Health Authorities (RIZIV), and the implanted systems were reimbursed by the same authorities. Data were analyzed by the authors. Only the data on women with retention are being analysed here.

All patients consented to this study. All patients had undergone maximal conservative therapy (intermittent catheterisation, permanent suprapubic catheter, pelvic floor rehabilitation, and/or alpha-blockers) before undergoing the percutaneous test stimulation.

All patients underwent clinical examination, urodynamic examination, and cystoscopy. Urethral pressure profiles were not done. A frequency/volume chart was kept during at least 3 d. The duration of the urinary retention was calculated from when the patient started to use intermittent catheterisation or a permanent catheter. A concentric needle EMG of the external urethral and anal sphincter was performed together with the measurement of the ano-anal reflex. Somatosensory-evoked potentials of the pudendal nerve were also recorded. These measurements were always performed by the same electrophysiologist (F.B.). Patients were classified as having Fowler's syndrome if the EMG of the external urethral sphincter showed CRDs and decelerating bursts.

For assessment of psychologic comorbidity, all patients completed the Patient Health Questionnaire (PHQ). This self-administered version of the primary care evaluation of mental disorders is a validated screening tool for the presence of depression, somatisation, anxiety, eating disorders, or alcohol abuse [6,7]. The PHQ scores, however, were not used as an exclusion criterion for this study.

After fulfilling these preoperative procedures, patients underwent a peripheral nerve evaluation (PNE) with a subchronic stimulation phase of at least 4 d.

If the PNE showed restoration of spontaneous voiding with a residual volume of less than 100 cc, a definitive implant was proposed (InterStim Medtronic). After implantation patients were followed up at 1 and 3 mo and from then on every 6 mo.

Failure was defined as the recurrence of urinary retention, resistant to eventual technical revision of the Interstim device. Retention was defined as the need for intermittent catheterisation (postvoid residual > 150 cc) or for an indwelling catheter. This definition means that technical problems such as lead displacement or battery problems were not considered as clinical failures if surgical revision restored the bladder-emptying pathology. In this way the long-term effect of SNS on urinary retention in females could be studied. Statistical analysis was done with Graphpad Instat by using Kaplan-Meier survival analysis, the log-rank test, the Mann-Whitney U test, and the Fisher exact test according to the data characteristics.

3. Results

In total 62 consecutive women with urinary retention were implanted between March 1996 and

Fig. 1 – A Kaplan-Meier analysis showing the significant differences in the long-term efficacy between patients with idiopathic retention and those having Fowler's syndrome (log rank test $p = 0.005$).

November 2004. In the same period 82 women in retention underwent a PNE, leading to a 75.6% implant rate. In all patients the lead was positioned in the third sacral foramen at the right side. Thirty patients had Fowler's syndrome; 32 had idiopathic retention. The mean age of the Fowler's syndrome group was 49.8 ± 11.8 yr, and that of the idiopathic group was 54.1 ± 11.6 yr. The mean follow up was 43.4 ± 35.2 mo. The mean duration of the urinary retention was 31.3 ± 15.2 mo, with no significant difference between the two groups. Clinical or urodynamic examination revealed no specific items.

Somatosensory-evoked potential (SSEP) was delayed in three patients (two with Fowler's syndrome, one with idiopathic retention). All these patients had undergone back surgery for disc herniation. All of them had retention before the surgery, and the back surgery did not have an influence on their urinary problem. For that reason we did not expect a causal relationship between this finding and the retention.

The PHQ revealed no panic disorders or eating disorders. Thirty-five percent ($n = 22$) patients were at risk for somatisation, whereas 24% ($n = 15$) had symptoms of depression. Of the patients with Fowler's syndrome, 26.6% screened positive for somatisation, compared with 43.8% in the idiopathic group (NS). Screening for depression was positive in 30% of the patients with Fowler's syndrome and in 18.8% of the idiopathic group (NS).

Twenty-eight patients presented with a failure: 9 with Fowler's syndrome and 19 with idiopathic retentions ($p = 0.04$). A Kaplan-Meier curve shows the evolution over time of both groups (Fig. 1). The log-rank test shows a highly significant difference in favour of the patients with Fowler's syndrome

Table 1 – Number of revisions and explants in both groups

	Total	Fowler's syndrome	Idiopathic retention	
Revisions	13 (20.1%)	4 (13.3%)	9 (28.1%)	ns
Explants	9 (14.5%)	4 (13.3%)	5 (15.6%)	ns
There is no significant difference between the two groups (Fisher exact test, $p = 0.19$). ns: not significant.				

($p = 0.005$). When these data were entered in a contingency table, the presence of Fowler's syndrome was shown to have a positive predictive value for success of 62% and a negative predictive value of 68% ($p = 0.02$). The relative risk was 1.92 (95% confidence interval, 1.05–3.5, $p = 0.024$). None of the other variables (somatisation, depression, duration of retention, age) reached any significant level.

The number of revisions for technical failures did not differ significantly in the two groups (Table 1). Revisions were done for pain at the implant site, battery change, or loss of the stimulation. Explants were done for the same reasons. Some patients with failures did not wish to undergo explant surgery and kept the stimulator in situ. The stimulator was inactivated in such cases.

4. Discussion

For the last decade SNS has been commercially available and has proven to be a very efficient treatment for refractory micturition disorders. Despite a large worldwide experience, no good predictive factors for success have been identified.

Psychiatric comorbidity, although poorly defined, has been proposed as a negative predictive factor by some authors [8], on the basis of retrospective data. Weil et al. [8] identified 11 patients with a history of psychiatric disorders and failed SNS out of a group of 36 implanted patients. Everaert et al. [9] stated that test stimulation was less reliable in patients with a psychiatric history. These studies were retrospective, and a definition of psychiatric disorder was not provided. Spinelli et al. [10] performed a prospective study on 15 women with idiopathic urinary retention, using the MMPI 2 (Minnesota Multiphasic Personality Inventory) and a psychological interview. Sixty percent of their patients had a somatoform disorder. In a second part of their study, 22 patients who had undergone a definitive implant were evaluated. Of eight failed patients, seven had psychotic signs. Because of the small sample and the design of the study, no recommendations can be given.

In our study the PHQ was used in a prospective way. However the screening results were not taken into consideration when deciding on a definitive implant, which was based only on the clinical result of restored spontaneous micturition without the need for intermittent catheterisation. The PHQ is a validated instrument based on the PRIME-MD (Primary Care Evaluation of Mental Disorders) [7,11]. In a study on obstetric-gynecologic and primary care patients, the prevalence of any psychiatric disorder ranged from 20% to 27%, diagnoses like somatisation from 10% to 12%, and depression from 6% to 10%. Despite these numbers, the result of the PHQ seemed to have little impact on clinical decision-making. Compared with these data the urinary retention patients in our study have a higher prevalence of somatisation (35%) and depressive disorders (24%), without a clear difference between patients with or without Fowler's syndrome. Moreover there was no correlation with the functional outcome of the SNS. Thus the clinical problem remains how to identify those patients who will probably fail SNS because of psychiatric conditions. Probably other conditions such as borderline personality disorders (impulsive, self-destructive, and unstable patients) and antisocial disorders (manipulative patients) could have an impact on the outcome of SNS, as on any other treatment. The early recognition of these disorders by nonpsychiatrists is however unlikely. The clinical appreciation of the patient's psychology and motivation for SNS by the implanting urologist seems to be the only realistic option at this point in time.

Malaguti et al. [12] showed that SNS can induce changes in the evoked potential characteristics. They hypothesised that these changes could have a potential predictive role. However their study involved only 24 patients in which two types of definitive sacral leads were used in a two-stage approach. The SSEP measurements were performed in the success group as well as in the failed group after the clinical decision had been made to implant or not implant the pulse generator. This post hoc evaluation of neurophysiologic changes cannot be considered a prognostic test, as long as this has not been confirmed in a prospective study in which the neurophysiologic findings would actually influence the clinical decision. Moreover the use of different electrode types might have interfered with the success rate as well. In our study the presence of CRD proved to be the only parameter reaching statistical significance that was predictive for long-term success. EMG of the external urethral sphincter is of course not available to every urologist, since the interpretation of the EMG signals necessitates

specific training. However urethral pressure profiles could have a role in the selection of retention patients for SNS. Wiseman et al. [13] reported a significantly higher maximal urethral closure pressure (103 ± 26.4 vs 76.7 ± 18.4 cm H₂O; $p < 0.001$) and a significantly higher external urethral sphincter volume (2.29 ± 0.64 vs 1.62 ± 0.32 cm³; $p < 0.001$) in patients with Fowler's syndrome than in patients without it. The same authors also reported a retrospective study on 26 women, of whom 75% were still benefitting from SNS up to 5 yr after implant. These findings are in agreement with our data in which 72% of patients with Fowler's syndrome are still enjoying normal micturition, compared with 46% of idiopathic retention patients at 5 yr. In both groups, however, there seems to be a gradual decrease in the success rate, although the slope of the curve is much steeper in the idiopathic group. The mechanisms for this phenomenon are unknown but might include progression of the underlying pathology (channelopathy?) or a central adaptation phenomenon or even nerve damage. This decrease in efficacy over time has also been described by other authors. In a mixed population of urgency and retention patients, 59.7% of patients were still satisfied at a mean follow-up of 70 mo [14]. Of course this study offers no absolute proof for the long-term benefit of SNS, since some of the patients might have improved spontaneously over time. This is difficult to study since all patients had already benefitted from the PNE. Randomizing them afterwards in an active and control group might be possible but would be ethically difficult at this stage, since SNS had now been used for nearly a decade. Moreover the data on the natural history of the disease do not suggest that spontaneous recovery is likely to occur [5]. The number of explants is not a very relevant parameter, since some failed patients preferred not to undergo explant surgery and kept the stimulator, which was of course turned off in situ. Our general revision rate of 20.1% is low, compared with other studies in which revision rates up to 33% were reported [15,16]. The number of revisions did not differ significantly between the two groups. In this series no two-stage implants were done. This might have improved the initial implantation rate and could have been useful in some of the revisions [17,18].

5. Conclusions

This study shows that the presence of CRDs and decelerating bursts on concentric needle EMG of the external urethral sphincter of women with

nonobstructive urinary retention (Fowler's syndrome) is a predictive factor for the success of sacral nerve stimulation. Idiopathic retention patients can benefit from SNS as well, but they have to be informed that the success rate and the duration of success might be lower than those in the Fowler's patients. Presence of somatisation disorders or depression was not predictive for failure.

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Editorial Comment

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The aim of this study was to discover if either a diagnosis of Fowler's Syndrome (F'sS) or a patient's psychological profile were predictive factors for long-term success of sacral nerve stimulation (SNS) in the treatment of women in urinary retention. What De Ridder et al. have clearly demonstrated is that the presence of F'sS is, whereas the result of pre-implant psychological screening is not.

Urinary retention in young women has long presented a challenge to urologists. Prior to 1988 the prevailing view was that the disorder was primarily of psychogenic origin and the hypothesis proposed by Fowler et al. [1], on the basis of sphincter EMG, that retention was due to a primary failure of sphincter relaxation, attracted little attention until an effective treatment became available in the form of SNS [2]. That urinary retention, as well as urinary urgency and urgency incontinence responded to SNS initially seemed inexplicable but whereas other treatments are now challenging SNS as the

optimal treatment for severe detrusor overactivity, SNS remains the only effective treatment to restore voiding in some women. Furthermore as far as SNS goes, it works “better” for retention than in any other urinary indication.

The funding for implantable sacral nerve stimulators in Belgium meant that it was possible for a large prospective study of women with urinary retention to undergo sphincter EMG and psychological testing prior to SNS. Although F'sS has been shown to be the commonest cause of urinary retention in young women [3], it only explains a little over half of all cases; the underlying pathophysiology in women who do not have abnormal EMG remains unknown. In them it is clearly impossible to suggest any mechanism of action for SNS whereas current thinking is that in F'sS, tonic activity emanating from the striated sphincter which has an inhibitory effect on the detrusor is somehow cancelled out by SNS: “normalization of the brainstem” was demonstrated by functional imaging PET studies [4] and it is certainly striking how bladder sensation is promptly restored by switching on the sacral stimulator.

Psychological factors in women with retention remain a contentious issue: some patients with urinary retention have a cluster of symptoms,

some of which are thought of as classical somatisation disorders and although both groups had a significant incidence of such symptoms it was higher in the non-F's S group. However De Ridder et al.'s important findings show that although these may make the medical management of patients difficult their presence does not appear to be a determinant of the outcome of the duration of efficacy of SNS.

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