Sacral neuromodulation for detrusor hyperactivity with impaired contractility

Derek B. Hennessey | Nathan Hoag | Johan Gani

1 Department of Urology, Austin Hospital, Heidelberg, Victoria, Australia
2 Department of Urology, Victoria General Hospital, Victoria, British Columbia, Canada

Correspondence
Derek B. Hennessey, Department of Urology, Austin Health, Heidelberg, Victoria, Australia.
Email: derek.hennessey@gmail.com

Introduction: Detrusor hyperactivity with impaired contractility (DHIC) is a challenging condition to manage. Sacral neuromodulation (SNM) is a proven treatment modality for both the individual aspects of DHIC. To date, data reporting the outcome of SNM for DHIC are lacking.

Materials and Methods: Consecutive patients undergoing SNM for DHIC were followed prospectively, from April 2013 to October 2016. Patient demographics, bladder diaries, subjective response rates, ICIQ-OAB, and PGI-I scores were recorded. Success was defined as greater than 50% improvement in storage symptoms and a 50% improvement in voided volume or reduction of post-void residual volumes.

Results: Twenty patients underwent stage 1 trial of SNM for DHIC. Median age was 68.5, IQR (54.25-76.25). Thirteen (65%) patients were female. A total of 14/20 (70%) of patients had a significant treatment response, 9/20 had a response to both elements of DHIC, 4/20 patients had a response to the detrusor overactivity (DO) alone, and 1/20 had a response to the voiding component alone. A total of 12/20 (60%) patients proceeded to insertion of an IPG. At mean follow-up of 17 months, IQR (1.5-35), 11/12 (91.7%) of patients are still using the SNM for DHIC. Median PGI score is 2, IQR (2-4). SNM for DHIC resulted in statistically significant improvements in voided volume ($P = 0.016$), PVR ($P = 0.0296$), ICIQ-OAB score ($P < 0.0001$), and ICIQ-OAB bother score ($P = 0.016$)

Conclusion: This is the first study we know of to report the results of SNM for DHIC. SNM is associated with satisfactory success rates, treating both the detrusor hyperactivity, and impaired contractility components of this condition.

KEYWORDS
- detrusor hyperactivity with impaired contractility
- detrusor overactivity
- DHIC
- sacral neuromodulation

INTRODUCTION

Detrusor hyperactivity with impaired contractility (DHIC) is a common clinical condition that is poorly understood, under-recognized, and difficult to effectively manage. It is a condition in which patients unexpectedly display detrusor overactivity (DO) during storage, yet are unable to mount a sufficient detrusor contraction during voiding to completely empty the bladder.1 It has been identified as the second most common cause of urinary incontinence in institutionalized elderly people.2 Since then, DHIC has been increasingly recognized as a cause of lower urinary tract symptoms (LUTS) in other elderly patients.3–5 DHIC has been identified...
as the principal dysfunction in up to 8-18% of elderly patients referred for urodynamic studies.\textsuperscript{5,6} There is no defined treatment algorithm for patients with DHIC, typically patients have been treated based on the severity of their particular symptoms.\textsuperscript{5,7} To date, pharmacotherapy in the form of alpha-blockers and anticholinergics, clean intermittent self-catheterization (CISC), and more recently intravesical onabotulinumtoxin A have been used. The disadvantage of these treatments are that they only treat one component of DHIC. Sacral neuromodulation (SNM) is currently approved as a treatment for both idiopathic DO, and non-obstructive urinary retention independently.\textsuperscript{8} It is theorized that SNM can potentially treat both aspects of DHIC, the DO and poorly contractile bladder, but there is no published data regarding this. In this study, we aim to be the first to evaluate the efficacy of SNM specifically for treating DHIC.

2 | METHODS

A review of prospectively collected data was carried out for consecutive patients who underwent SNM for DHIC by a single clinician from 2013 to 2016. Institutional ethics board approval was obtained and the trial was registered with Australian New Zealand Clinical Trials Registry (ANZCTR), trial number 126160015764. The diagnosis of DHIC in each case was made by the urologist performing multichannel videourodynamic studies (VUDS). VUDS were performed according to the International Continence Society (ICS) standards.\textsuperscript{9,10} Patients with evidence of bladder outlet obstruction (BOO), pelvic organ prolapse and stress urinary incontinence were excluded.

No formal ICS definitions for DHIC currently exists.\textsuperscript{5} For the purpose of this study, DO was defined as the presence of phasic detrusor contraction during filling. Impaired detrusor contractility was defined by using the bladder contractility index (BCI): BCI = detrusor pressure at maximal flow rate (PdetQmax) + 5 maximal flow rate (Qmax). Impaired contractility was represented by a value <100.\textsuperscript{5,11} Patient information recorded included age, gender, symptoms, bladder diaries, and medical history. International Consultation on Incontinence Modular Questionnaire on overactive bladder (ICIQ-OAB), median voided volumes, median post-void residual volumes (PVR) by clean intermittent self-catheterization (CISC), and patient Global Impression of Improvement (PGI-I) were recorded at baseline, and at 2 weeks post-first stage SNM, to assess treatment response. Success was defined as greater than 50% symptom improvement in urgency, urge incontinence, and frequency for the DO component. For the impaired contractility (IC) component, success was defined as greater than 50% improvement in voided volume or reduction of post-void residual volumes, or an improvement in voiding efficiency (voided volume divided by total bladder capacity) on urodynamic studies in those who could not do CISC.

Unless otherwise stated, data are represented as median (interquartile range) and $N$ represents the number of patients included in the analysis. Statistical analysis was performed using the SPSS ver. 17.0 (SPSS Inc., Chicago, IL). Clinical characteristics, urodynamic parameters, and clinical outcomes were compared using the Student’s $t$-test where appropriate. A significant difference was defined as $P < 0.05$. Post hoc power calculation revealed that with 12 patients, we have about 88% power to detect a halving or doubling in the outcome measure assuming the standard deviation of the difference is equal to the value of the difference.

3 | RESULTS

3.1 | Patient selection and trial response

Twenty patients with DHIC underwent a trial of stage 1 SNM timed lead insertion for 2 weeks. Patient demographics are shown in Table 1. A total of 14/20 (70%) patients had a successful stage 1 trial, and were offered insertion of an implantable pulse generator (IPG). A total of 6/20 (30%) patients had inadequate response. A total of 9/20 had a response to both the DO component and the voiding component of DHIC. A total of 4/20 patients had a response to the DO component only, and 1/20 patient had a response to the voiding component only. Response to SNM is shown in Table 2. One patient who had a response to the DO component only, declined to have insertion of an IPG due to anxiety. One patient who had a response to the IC component only, also declined IPG implantation.

<table>
<thead>
<tr>
<th>TABLE 1 patient characteristics</th>
<th>Total, N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td>20</td>
</tr>
<tr>
<td>Age, median (IQR)</td>
<td>68.50 (54.25-76.25)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male, (%)</td>
<td>7 (35)</td>
</tr>
<tr>
<td>Female, (%)</td>
<td>13 (65)</td>
</tr>
<tr>
<td>Baseline assessment</td>
<td></td>
</tr>
<tr>
<td>BCI</td>
<td>63 (48-70.2)</td>
</tr>
<tr>
<td>Voided vol (mL), median (IQR)</td>
<td>151 (134-176.3)</td>
</tr>
<tr>
<td>PVR (mL), median (IQR)</td>
<td>175 (100-300)</td>
</tr>
<tr>
<td>ICIQ OAB, median (IQR)</td>
<td>9 (7-10)</td>
</tr>
<tr>
<td>ICIQ OAB Bother, median (IQR)</td>
<td>28 (21-32)</td>
</tr>
</tbody>
</table>

Vol, volume; PVR, post-void residual; ICIQ OAB, International Consultation on Incontinence Modular Questionnaire on overactive bladder.
3.2 Pre-trial and post-trial variables of IPG implanted patients

A total of 12/20 (60%) had an IPG inserted, treatment schematic is shown in Fig. 1. A total of 9/12 of these patients had responses to both components of DHIC. A total of 3/12 had a response to the DO component only. Two of these three patients had their PVRs monitored and one patient continued to do CISC. The median age of this cohort is 67.5 years, IQR (54.25-74). A total of 11/12 patients were female, the median BCI was 57.5, IQR (10.5-65). The median pre-trial voided volumes were 152 mL, IQR (138-180) and PVR was 209 mL, IQR (150.8-302.5). Baseline, ICIQ OAB score was 9, IQR (8-10) and ICIQ OAB bother score was 29 (25-33).

The median post-trial voided volume was 227 mL, IQR (188-250), the median post-trial PVR was 60 mL, IQR (20-138). Median post-trial, ICIQ OAB, and bother scores were 4, IQR (3-5) and 14, IQR (6-21), respectively. SNM for DHIC resulted in a statistically significant improvement in voided volume \( P=0.0016 \), decrease in PVR \( P=0.0296 \), ICIQ OAB score \( P<0.0001 \), and decrease in ICIQ OAB bother \( P=0.0016 \). Trial response compared to baseline variables is tabulated in Table 3 and demonstrated in Fig. 2.

3.3 Medium term results

At a median follow-up of 17 months, IQR (1.5-35), 11/12 (91.7%) were still using the SNM device. One patient reported deterioration in symptoms and underwent tined lead and IPG removal 14 months after initial implantation. This patient had only responded to the DO component. One patient required revision surgery and had a contralateral tined lead inserted and the original lead removed 12 months post-initial implantation. She continued to do well after revision surgery.

4 DISCUSSION

DHIC is a condition, as its name implies, in which DO is associated with compromised detrusor contractile function. DHIC was initially described by Resnick et al in 1987. It was reported to be the second most common cause of urinary incontinence in elderly people. More recently, Ameda et al demonstrated in a study of 193 men with LUTS and without outlet obstruction on urodynamics, that 11% had DHIC overall. But it was present in 37% in those age greater than 70 years of age and 2% in those less than 70. In a community-dwelling population of women over age 80 who underwent urodynamic evaluation for the evaluation of LUTS, 16% were found to have DHIC. Despite increasing awareness and study of DHIC, there is no standardized definition, nor have specific diagnostic criteria for DHIC been endorsed by the ICS.

To date, there is no clear explanation as to why the detrusor muscle may become overactive during storage, yet poorly contractile while emptying in patients with DHIC. Furthermore, it is unclear if the pattern of symptoms found in DHIC are due to one common cause or due to the concurrence of two unrelated anomalies. There are several theories on causes of DHIC, these include micro-cellular variations such as bladder smooth muscle protrusion of junctions and abutments, widespread degeneration of muscle cells, and widening of interstitial spaces. Hormonal deviations and deficiency of ovarian hormones have been theorized to cause impaired detrusor contractility in women late in life. Reduced bladder blood flow can result in DO, and if prolonged, severe ischemia can eventually cause functional changes by replacement of bladder smooth muscle with fibrosis and collagen. Thus, ischemia could potentially produce a situation in which the bladder may be both overactive and poorly contractile as seen in patients with DHIC. Despite the findings of these studies, until more research elucidates the issue, the aetiology and pathophysiology of and DHIC remains poorly understood.

Conceptually, urologists are treating two problems concurrently, namely the storage symptoms of frequency, urgency, urge incontinence, and the voiding symptoms of weak stream, incomplete emptying. Patients have been
treated based on the severity of the predominant symptom. Treatment options for the storage component include, conservative measures such as Kegel exercises with or without pelvic floor physical therapy, and pharmacotherapy in the form of anticholinergics, beta 3 agonist and alpha blockers. Liu et al retrospectively determined that anticholinergics and alpha-blockers appear to be safe in patients with DHIC. More recently the effect of intravesical onabotulinumtoxinA in patients with DHIC was described. Wang et al reported that intravesical onabotulinumtoxinA was safe with minimal adverse events and had short term efficacy for DHIC patients comparable to patients with DO only. While intravesical onabotulinumtoxinA can ameliorate the storage symptoms of DHIC, there is the increased potential for urinary retention in these patients due to impaired detrusor contractility. Indeed, the above treatments can make bladder emptying worse and patients may then go into partial urinary retention and feel worse off even if their DO component has been treated. Thus when anticholinergics, beta-3-agonists or intravesical onabotulinumtoxinA is being considered as a treatment for DHIC, patients should be able and willing to perform CISC. However, it must be noted that DHIC patients are generally older and may be unable to do CISC. Thus, these treatments should potentially be avoided in DHIC patient with high PVRs (>250 mL).

Treatment options for the voiding component include observation, timed voiding, valsalva voiding, and CISC. Bladder outlet surgery such as TURP in men may help improve the voiding parameters in patients with DHIC. In men with DU only, TURP significantly improved IPSS, QOL index, Qmax, and PVR and reduced the risk of future retention, catheterization, or surgery, presumably by lowering outlet resistance and allowing more efficient straining when voiding. However, TURP does not treat the DO component of the disease directly. Thus for patients with DHIC, treatments often have to be instituted in combination, to treat both components of DHIC.

SNM is a proven treatment for both individual pathologies of DHIC and thus appears to be a logical choice of treatment for the disorder. It works by altering afferent pudendal signaling to inhibit voiding reflexes by suppressing the urethral and somatic sphincter complex of the guarding reflex. For DO, SNM affects pudendal afferent input to the sacral spinal cord turning off supra-spinally mediated hyperactive voiding by blocking ascending sensory pathway inputs. In addition to this, SNM affects the guarding reflex, so that there is outlet relaxation to enhance voiding and improve impaired bladder contractility.

### TABLE 3

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Pre-trial</th>
<th>Post-trial</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td>Voided Vol</td>
<td>151 (134-176.3) mL</td>
<td>227 (188-250) mL</td>
<td>0.0016</td>
</tr>
<tr>
<td>PVR</td>
<td>175 (100-300) mL</td>
<td>60 (20-138) mL</td>
<td>0.0296</td>
</tr>
<tr>
<td>ICIQ OAB</td>
<td>9 (7-10) mL</td>
<td>4 (3-5) mL</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ICIQ OAB</td>
<td>28 (21-32) mL</td>
<td>14 (6-21) mL</td>
<td>0.0016</td>
</tr>
</tbody>
</table>

SNM, sacral neuromodulation; Vol, volume; PVR, post-void residual; ICIQ OAB, International Consultation on Incontinence Modular Questionnaire on overactive bladder.

### FIGURE 2

A: Shows voided volume response of DHIC patients to SNM. Median voided volumes increased significantly, $P = 0.0016$. B: Shows change in PVR with SNM. Median PVR volumes decreased and was statistically significant, $P = 0.0296$. C: Shows the change in ICIQ OAB score with SNM. This was significant, $P < 0.0001$. D: Shows change in ICIQ OAB bother score, again this was statistically significant, $P = 0.0016$. SNM, sacral neuromodulation; mL, milliliter. *Assessed with the paired t-test.
demonstrated an efficacy of 70% in 152 patients with refractory idiopathic DO Ref.25 Overall, the success rate of SNM for the management of refractory DO ranges from 53% to 80%.26–28 For non-obstructive urinary retention, Al-Zahrani et al demonstrated a success rate of 87.4% in 16 patients, while Saber-Khalaf et al reported a response rate in 14 patients of 66.7%.29,30

Our results show increased response to the DO component than IC. This matches what the literature states about the higher response rate of SNM in DO patients compared to urinary retention patients. Three patients only had a response to the DO element of DHIC, but still opted to have the IPG implanted. Importantly, SNM did not increase the frequency of CISC. Other treatment options like anticholinergic or onabotulinumtoxinA bladder injection would likely have resulted in the need to do more CISC. Therefore SNM might be a more appealing option for these patients.

Six patients with DHIC failed to respond to the stage 1 SNM trial. We examined this group to identify any factors that would be helpful to identify patients who would not benefit from SNM. There is a non-statistically significant trend for this group to be older and male. BCI and baseline voided volumes, PVR, and ICIQ OAB scores did not predict a non-response.

A limitation of this study is the use of bladder contractility index (BCI) to define detrusor underactivity for all the patients. BCI has only been validated in men, it could be debated whether this formula could be extrapolated to the female cohort. The study also has relatively small patient numbers.

5 | CONCLUSION

This is the first report describing the efficacy of SNM for DHIC. SNM is a promising potential treatment option for patients with DHIC, and after medium-term follow-up, it continues to treat both the DO and IC components of this condition.

POTENTIAL CONFLICTS OF INTEREST

None to declare.

REFERENCES


**How to cite this article:** Hennessey DB, Hoag N, Gani J. Sacral neuromodulation for detrusor hyperactivity with impaired contractility. *Neurourology and Urodynamics*. 2017;9999:1–6. https://doi.org/10.1002/nau.23255