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REVIEW

Non-pharmacologic options for the management of voiding dysfunction in multiple sclerosis

Lisa Parrillo, Eliza Lamin, Ariana Smith

Lisa Parrillo, Eliza Lamin, Ariana Smith, Perelman Center for Advanced Medicine, West Pavilion, Philadelphia, PA 19104, United States
Author contributions: Parrillo L, Lamin E and Smith A contributed to this paper.
Correspondence to: Ariana Smith, MD, Perelman Center for Advanced Medicine, West Pavilion, 3rd Floor, 3400 Civic Center Boulevard, Philadelphia, PA 19104, United States. ariana.smith@uphs.upenn.edu
Telephone: +1-215-6622891
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Abstract

Multiple sclerosis is a neuroinflammatory condition that can cause significant bladder dysfunction manifesting either as overactive bladder or impaired bladder emptying. Patients will often complain of urgency, frequency, nocturia, urgency incontinence, hesitancy, straining to void, and incomplete bladder emptying. While these symptoms can be treated with pharmacologic agents, often patients will require more significant treatments. Patients should first be evaluated with urodynamics in order to adequately diagnose the pathologic condition causing their symptoms. These interventions include catheter use, injection of botulinum toxin, neuromodulation, urethral stenting, sphincterotomy, suprapubic catheter with bladder neck closure, bladder augmentation and urinary diversion. The purpose of this review is to examine the evidence supporting each of these treatment options so urologic providers can better provide for this unique and complex patient population.

Key words: Multiple sclerosis; Neurogenic detrusor overactivity; Detrusor sphincter dyssynergia; Botulinum toxin; Sacral neuromodulation

Core tip: Patients with multiple sclerosis can present with a variety of different urologic symptoms. While they can be treated with multiple pharmacologic agents, at times they will require manipulation or surgical intervention. This article reviews the scientific evidence behind each treatment modality so providers may be more informed as they council patients.

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INTRODUCTION

Multiple sclerosis (MS) is the most common neuroinflammatory disease, affecting approximately 85 people in every 100000[1]. The disease causes demyelination plaques in central nervous system white matter. One of the most common manifestations of MS is bladder dysfunction. Bladder dysfunction results from interruption of neural pathways between the pontine micturition center and the sacral spinal cord by demyelinating plaques[2]. The clinical manifestations of neurogenic bladder dysfunction in MS include overactive bladder syndrome and impaired bladder emptying. Overactive bladder is defined by the International Continence Society as urinary urgency, with or without urgency incontinence, but usually with frequency and nocturia and can be neurogenic or idiopathic in origin[3]. Urodynamic findings of detrusor overactivity provide objective evidence of involuntary contractions of the bladder muscle, the presumed etiology of overactive bladder symptoms. Impaired bladder emptying in MS may range from symptoms of hesitancy and slow urinary stream to complete retention of urine requiring catheterization. Poor relaxation of the external urethral sphincter

is the culprit and can be demonstrated on urodynamic testing. During voiding, synergy of the bladder and urethra should occur allowing the bladder muscle to contract and the urethral muscle to relax, resulting in complete bladder emptying. In patients with MS, dyssynergy occurs such that the urethra does not relax during voiding resulting in high bladder pressure with poor or low flow through the urethra, this is termed detrusor sphincter dyssynergia (DSD).

Bladder dysfunction can be treated with pharmacologic agents and generally these are instituted prior to consideration of more invasive treatment options. Theoretically, pharmacologic agents for overactive bladder symptoms may worsen symptoms of emptying dysfunction in patients with MS and agents aimed at improving bladder emptying may worsen incontinence. In practice there are mixed results with these medications. Additional treatment options may be considered as the result of patient bother from bladder symptoms or poor bladder compliance with concern over upper urinary tract deterioration. Urodynamics can be useful in documenting the components of bladder dysfunction and monitoring bladder changes over time. For neurogenic detrusor overactivity non-pharmacologic treatment options range from simple measures such as condom catheters in men or incontinence pads in women to more invasive options such as Botulinum toxin injection or neuromodulation. For DSD with poor bladder emptying, treatment options range from urethral catheterization to sphincterotomy or intrasphincteric Botulinum toxin injection. Some patients may even require bladder augmentation or urinary diversion.

Patients with refractory bladder dysfunction as a result of MS have several therapeutic options that can be used as an adjunct to pharmacologic therapy or can be used as primary treatment when pharmacologic agents have failed. These therapies are described below.

URODYNAMICS

Many patients with MS will present with specific urinary complaints; however, it is important to evaluate these patients objectively prior to treatment, as some neurogenic bladder dysfunction may be present and may progress to renal decompensation in the absence of symptoms. Typical complaints are include urgency, frequency, nocturia, urgency incontinence, hesitancy, straining to void, and incomplete bladder emptying[4]. The best way to assess the pathologic condition causing these symptoms is to perform urodynamics. Urodynamics is a broad term that includes studies that assess bladder function including uroflometry, post void residual measures, voiding cystometry, urethral pressure profilometry, and electromyography. Having a patient maintain a bladder diary prior to urodynamics will provide further information when the urodynamic study is being interpreted. These studies may include concomitant fluoroscopic imaging to assess anatomy during voiding; this is called video-urodynamics. Common urodynamic findings in MS patients include bladder hypersensitivity, detrusor overactivity, low urinary flow rate, elevated post void residual urine volume, and DSD. Patients may also have evidence of impaired compliance and high pressure voiding suggesting obstruction. In a study by Gallien *et al*[4] in 1998, 149 patients with MS who underwent standardized urodynamic studies DSD was found in nearly 60% of the population. Approximately half of these patients also had detrusor overactivity. They did not, however, find any significant correlation between the urodynamic findings and symptom presentation. A higher post void residual was the main risk factor for developing upper tract urinary infections in this population.

Having urodynamic data can be helpful in the treatment of neurogenic bladder dysfunction as treatment options vary widely and depend primarily on the underlying dysfunction found and patient bother. While it is not a common occurrence, prevention of upper urinary tract deterioration as a result of impaired bladder compliance is critical and must be address in affected patients.

TREATMENT OF NEUROGENIC DETRUSOR OVERACTIVITY

Neurogenic detrusor overactivity (NDO) secondary to the demyelination of the dorsal columns is the most prevalent urodynamic finding in patients with MS, with anywhere from 34%-99% of patients displaying this abnormality[2]. In a prospective study comparing the urodynamic tracings of women with MS to those with idiopathic detrusor overactivity, Lemack *et al*[5] found that the initial detrusor contractions in the MS subset were of higher amplitude and suggested that neurogenic detrusor overactivity may be harder to control[5]. In fact, it has been noted that patients with NDO require higher doses of anticholinergics for effective treatment[6]. Given the not insignificant side effect profile for these drugs, in addition to the potential lack of efficacy, it is logical that patients would seek out alternative forms of treatment such as condom catheters, sacral nerve stimulation, dorsal penile or clitoral nerve stimulation, percutaneous tibial nerve stimulation and injection of Botulinum A neurotoxin.

Catheters

In patients with neurogenic injuries to the bladder causing detrusor overactivity one of the least invasive non-pharmacologic treatments is either an indwelling or condom catheter. The biggest concerns for these patients are the increased risk of urinary tract infections and local irritation and infection of the genital tissues. Additionally, with indwelling catheters there is a risk of urethral erosion that may result in urinary leakage around the catheter, urethral tissue loss, and splitting of the glans and shaft of the penis in men. With condom catheters, approximately 40% of patients will develop urinary tract

infections (UTIs) with long-term use. An additional 15% of users are at risk of ulceration, necrosis and gangrene[7]. Suprapubic catheters are also an option to avoid genital ulceration, but the patient is still at increased risk for urinary tract infection and may continue to leak per urethra from involuntary bladder contractions. In general, catheters are used as a treatment of last resort.

Neuromodulation

Stimulation of the bladder nerves has been shown to inhibit detrusor overactivity in patients with NDO. Neuromodulation is felt to work *via* somatic inhibition of hyperstimulation and overactivity of the sympathetic and sacral motor neurons however, the exact mechanism of action remains unknown[8]. Bladder neuromodulation can be accomplished by stimulating the S3 sacral roots, the tibial nerve, the pudendal nerve, or one of the pudendal nerve branches which include the dorsal nerve of the penis or clitoris. It has also been shown that the posterior tibial nerve, which contains fibers originating from L4 to S3 can have similar effects when stimulated by depolarizing somatic lumbar and sacral nerves to the bladder[2].

In 2005, sacral neuromodulation was recommended by the International Consultation on Incontinence as a second-line therapy for NDO. In the United States, the Food and Drug Administration (FDA) has approved the InterStim Device® (Medtronic, Inc., Minneapolis, MN), a subcutaneous implantable pulse generator attached to a lead that stimulates the S3 nerve root, for the treatment of idiopathic frequency, urgency, urgency incontinence and non-obstructive urinary retention. It has been studied in patients with neurologic disease and found that 66% of patient with NDO can experience significant improvements in their lower urinary tract symptoms after placement and 75% of these patients will have continued success at mean follow-up of four years[9]. In one study of 25 patients with MS, 15 patients showed improvements in their symptoms that were sustained six months after implantation of the InterStim device. Of the six who had detrusor overactivity, there was a significant reduction in frequency episodes from a mean of 18 to 9 (episodes per day), post-void residuals from a mean of 127 to 33 mL, and incontinence episodes from a mean of 13 to 3 per day. Additionally, voided volumes increased from a mean of 83 to 160 mL[10]. Patients appear to have more success if their neurologic conditions are localized[11] and, while patients may have good clinical outcomes, they still may display overactivity on urodynamic testing[12].

In spite of the potential for significant benefit, sacral neuromodulation has not been adopted as a standard treatment for two reasons. First, in the small case studies assessing efficacy it has been noted that when some patients undergo a relapse or experience MS disease progression stimulation parameters could not be reprogrammed to achieve continued clinical improvement in voiding dysfunction[9]. Additionally, patients with an implanted neurostimulator cannot undergo magnetic resonance imaging (MRI) evaluation (with the exception of the head) due to the presence of metal in their body, which is the imaging modality of choice for evaluation of MS patients.

For dorsal penile or clitoral nerve stimulation electrodes are placed on dorsum of the penis or the clitoris and labia majora. In a 2006 study of eight patients with MS and detrusor overactivity, Fjorback *et al*[8] used simultaneous dorsal nerve stimulation and urodynamics to show suppression of bladder contractions and concomitant leakage in seven patients. These patients on average had fifteen minutes between the sensation of urgency and leakage with dorsal nerve stimulation, which the authors suggested was enough time to electively void. There was an increase in bladder capacity of up to 94% on average over this time period[8]. Additional studies have shown capacity to be increased by 55%[13] and conditional suppression of detrusor overactivity allowing for a delay of incontinence[14]. Although these results are promising, dorsal nerve stimulation is not available except at specialized centers and there is considerable hygienic concern with the chronic use of electrodes in the genital area.

An alternative form of neural stimulation that is gaining popularity due to its minimally invasive nature is posterior tibial nerve stimulation (PTNS). The posterior tibial nerve is a terminal branch of the sciatic nerve, which is derived from the L4 to S3 spinal nerves. The common origin of nerve fibers seems to allow for a simultaneous effect on the nerves to the bladder when the posterior tibial nerve is stimulated. In a 2008 study on acute urodynamic effects in patients with MS and overactivity treated with PTNS, Kabay *et al*[15] showed significant increases in volume at first involuntary contraction and maximum cystometric capacity (MCC) by performing urodynamics without stimulation followed by urodynamics with stimulation. Eighteen of the twenty-nine patients had a 50% increase in the bladder volume at first contraction and thirteen had a volume increase of at least 100 cc at first contraction. There was a 50% increase in MCC in 14 of 29 and 17 patients had a 100 cc increase in MCC Kabay *et al*[15]. A criticism of this evidence has been that there could be a conditioning effect of the bladder with the first filling allowing for delayed contraction even in the absence of tibial stimulation; a control group would have been helpful in this study[16].

Kabay *et al*[17] also published a study evaluating the effect of 12 wk of PTNS on 19 patients with MS and NDO utilizing repeat urodynamics and bladder diaries. They found complete clinical responses, which they defined as a 50% decrease below baseline findings, for urgency episodes in 33%, urinary incontinence episodes in 40%, daytime frequency episodes in 57%, nocturia in 75% and pad test in 90%. They also showed significant improvements in mean volume at first detrusor contraction and MCC, as well as decreases in detrusor pressure at first contraction and MCC, increase in max flow and decrease in post void residual (PVR)[17].

Gobbi *et al*[18] evaluated 21 patients with MS and overactivity that had failed anticholinergic therapy who were then treated with PTNS for 12 wk. They found significant reduction in daytime frequency, from 9 to 6

episodes, decreased PVR and increased mean voided volume. Eighty-nine percent of these patients reported a treatment satisfaction of 70%[18].

In a multicenter study, 70 patients with MS and NDO underwent 3 mo of daily 20-min sessions of PTNS. Primary outcomes were the effect on urgency and frequency and secondary outcomes were continence, quality of life, urodynamic changes and tolerance. At the end of 90 d, 83% of the patients had significant improvements in urgency and frequency. They also found a significant decrease in overactivity on urodynamics and a trend toward increased MCC and volume at first involuntary contraction. The treatment was well-tolerated and 70% of the patients wished to continue therapy at the end of the trial[19].

Finally, in 2013, Zecca *et al*[20] published a prospective study on 83 patients with MS who underwent 12 wk of PTNS and responders were then kept on maintenance therapy and followed for a total of 24 mo. 89% of the original treatment group were classified as responders as they had a greater than 50% improvement in their symptoms as measured by the perception of bladder condition questionnaire. Maintenance therapy was one day every four, three or two weeks, depending on patient response. Most patients required treatment every two weeks. 96% of the patients who underwent maintenance therapy were still classified as responders at the end of two years with a mean reduction of frequency episodes to 7 per day from 10, nocturia to 2 times per night from 4, increase in voided volume to 268 from 171 cc, decreased PVR to 52 from 101 cc and an increase in max flow to 25 from 15[20]. It seems that PTNS has the potential to be a lasting and well-tolerated treatment for patients with MS, however there is debate throughout the urologic community as to how real these effects are. Further investigation with randomized, blinded studies of PTNS *vs* sham stimulation is necessary before incorporating this treatment into a standardized algorithm.

Botulinum toxin injections

Botulinum Toxin injections have been adopted by the urologic community and approved by the FDA as a treatment for both idiopathic and neurogenic urinary incontinence secondary to detrusor overactivity. Additionally, it can be used in the MS population for detrusor-sphincter dyssynergia, which will be discussed in more detail later. For NDO in MS patients, *Botox* has been shown to effectively reduce daytime frequency, nocturia, pad use as well as improve urodynamic parameters. In 2006, in a trial in Berlin, 16 patients underwent injection of 300 U of *Botox* into 40 sites, including the bladder base and trigone. Fourteen of these patients also had 50-100 U of the original 300 injected into the external sphincter. At three months, day time frequency decreased from 12 to 6.75, nocturia from 2.16 to 0.61 and pad use from 1.75 to 0.63 daily. Additional significant changes were noted in volume at first contraction and MCC on urodynamics. The effects in this study lasted 3-6 mo and then patients' symptoms returned to baseline[21].

Using 300 U of *Botox*, while effective, does put patients at greater risk of urinary retention requiring clean intermittent catheterization. In 2011, a pilot study in 12 patients with MS and NDO was performed, where each patient was only injected with 100 U in 10 injection sites. All 12 had significant increases in MCC and volume at first desire to void. Voiding diaries showed significant decreases in frequency, urgency episodes and pad usage with a trend to toward a decrease in mean incontinence episodes. Mean maximum flow and voided volume decreased, but only two patients required intermittent catheterization. At 12 wk, patients were beginning to experience a loss of efficacy, but average time to request for re-injection was 8 mo[22].

In 2011, Cruz *et al*[23] published a randomized, double blinded, placebo trial in 154 patients with MS and 121 with spinal cord injuries and NDO. Patients were randomized to placebo, 200 U or 300 U of *Botox*, and 30 injections were administered. The primary endpoint was change in urge incontinence episodes six weeks after treatment, with secondary endpoints of change in MCC, maximal detrusor pressure during first involuntary contraction, and Incontinence Quality of Life score. They also assessed volume at first involuntary contraction, detrusor compliance and volume per void. At week six there were significant changes in weekly urge incontinence episodes in both treatment groups compared to placebo, but no difference between the treatment arms. MCC, volume at first involuntary contraction, and detrusor compliance were all significantly increased with treatment and pressure at first involuntary contraction was significantly decreased, with no differences noted between 200 or 300 U. Median duration of effect was 42 wk for both groups. Of note, there was a higher risk of UTIs in MS patients that received *Botox* treatment. Additionally, 30% of the patients who received 200 U and 42% of the patients who received 300 U began intermittent catheterization for residuals greater than 200 cc[23].

Botox injections can be another form of treatment of detrusor overactivity and urge incontinence in patients with MS. It significant reduces the lower urinary tract symptoms that plague this population, but it is not a perfect solution. First, it is only effective for a limited time, requiring readministration two to four times yearly. Second, it is not without risks, mostly of having to begin intermittent catheterization, but also an increased risk of urinary tract infections. However, for many patients, the potential for improvement in quality of life will likely outweigh the inconvenience of repeat procedures and the risk of catheterization.

TREATMENT OF INCOMPLETE BLADDER EMPTYING AND URINARY RETENTION

DSD is a common manifestation of disease in patients with MS[4]. In DSD the patient is unable to completely relax the detrusor sphincter in correct timing with contracting the bladder to allow normal voiding. This is one

of the most common urodynamic findings in MS. There are multiple treatment options available to patients for DSD. Pharmacologic options include antispasmodics and alpha blockers, but these come with their own side effects and therefore surgical options have also become available for these patients. The ideal solution would be a method of voiding that allows low pressure bladder emptying[24].

When behavioral modifications, bladder training, and alpha blocker medications have not helped the following treatments may be implemented. The first of these is the use of clean intermittent catheterization (CIC). This allows the patient or caregiver to use a disposable catheter to empty the bladder on a regular schedule[2]. There are convenient packs that contain the catheter lubricant and drainage bag all in one, this facilitates things for those that are wheelchair bound or have limited dexterity. It is the treatment of choice because it allows the bladder to fill and empty completely. Patients rarely have issues with urgency or incontinence using CIC because the bladder is emptied to completion each time. Most patients can empty with CIC every 4-6 h, if patients are finding that it needs to be done more often that should prompt urodynamic evaluation to determine the bladder capacity. This will determine a safe CIC frequency. The risk of infection is lowest with CIC because there is no indwelling catheter.

In patients where CIC isn't possible patients require indwelling catheters. Urethral foleys have significant complications including urethral erosion and chronic urinary tract infections. In these cases suprapubic catheters are the next best option. Suprapubic catheters allow constant bladder drainage without urethral damage. They also decrease urinary tract infections[2].

Urethral stenting

One surgical option available to patients with DSD is a urethral stent, temporary or permanent. This is rarely used today due to the permanent nature and potential for significant complication. There are several stents available; Urolume, Memotherm and Ultraflex. All of these can be temporary but the longer they stay in the more difficult it becomes to remove them[25]. This was first used as an option in 1990, and most studies have looked at permanent urethral stents[26]. Shaw *et al*[26] investigated this option in 9 patients with DSD to allow patients to easily pass a catheter for clean intermittent catheterization or wear a condom catheter. At the time this was a new technique that allowed the bladder to empty completely relieving some of the upper tract complications that can occur in patients with DSD. There are many risks associated with temporary or permanent stents including encrustation and migration[27]. Gamé *et al*[24] in 2008 presents the outcomes of temporary stents in 147 men who underwent the procedure for neurogenic DSD. In his study the patients that underwent temporary stenting were unable to self-catheterize. Over the long term the efficacy of stenting has not been shown to be satisfactory[28].

Sphincterotomy

Another option for these patients is a sphincterotomy or bladder neck incision[27]. The bladder neck incision technique was the first treatment used for patients with DSD, beginning in the 1940s. Emmet started with transurethral resection of the bladder neck, he was not very successful but it brought up the idea of having a more permanent lasting effect by doing an external sphincterotomy[29]. An external sphincterotomy became the mainstay of treatment of DSD, the goals of treatment were the resolution of hydronephrosis, reduction in frequency of or complete resolution of UTIs, reduction in frequency of autonomic dysreflexia, reduction in post-void residual urine volume, reduction in voiding pressure, reduction in leak point pressure[27]. A conventional sphincterotomy can result in significant blood loss, this was resolved by the ability to use a laser to perform the sphincterotomy resulting in almost immediate hemostasis[30]. This is considered a permanent procedure causing urethral incontinence; however, in some situations the incision needs to be performed repeatedly due to the development of scar tissue.

Botulinum toxin for DSD

More recently the most commonly used surgical technique for treatment of DSD is intrasphincteric injection of botulinum toxin A. Interestingly, the first use of Botulinum toxin in the urologic patient was for DSD. The injection acts on the sphincter as it does on the detrusor muscle in overactive bladder allowing the sphincter to relax. It does result in urethral incontinence, which limits its use. This is a viable option in patients with MS, there are no permanent changes made and the effects of the Botulinum injection wear off. Patients with MS have a constantly changing spectrum of urologic manifestations and systemic manifestations; a reversible agent is of interest to some patients at the time of MS flare.

In a French study by Gallien *et al*[31] 86 patients were randomized to receive an injection of Botulinum Toxin A (100 U) or a placebo (normal saline). He found no significant difference in the post void residual volume in patients with MS, but the procedure was well tolerated[31]. In 2005 Smith *et al*[32] investigated the reduction in post void residual volume with urethral injections of Botulinum toxin. Patients were treated with 100 to 200 U of Botulinum Toxin-A (BTX-A) in 4 mL divided in equal doses into the four quadrants of the external sphincter or by injection into the bladder base using 100 to 300 U of BTX-A diluted in approximately 10 to 30 mL of sterile saline. Sixty eight patients, thirty two of whom have MS, underwent the procedure, it was found that there was a statistically significant difference in the post void residual and the peak voiding pressure. Both values improved after the urethral injection[32]. The study also showed that the patients overall well-being improved and they had less urinary tract infections. In another study out of Germany it was found that the injection of botulinum toxin into the sphincter for patients with

MS decreases the incidence of urinary retention after intradetrusor Botulinum toxin injection. The authors of the study feel that this is due to a degree of DSD that is found in many patients with MS[21]. This study also found that with an injection of 300 U of *Botox-A* into the bladder and sphincter the incontinence rate decreased. They found that daytime frequency was reduced by 30% at 6 mo and the use of pads was reduced by 64% after 3 mo[21].

Neuromodulation for bladder emptying

There is only one study that reports neuromodulation for use in DSD. Hohenfellner *et al*[33] used sacral nerve stimulation on 11 patients with difficulty emptying. In 8 of the 11 patients symptoms of lower urinary tract dysfunction were decreased by 50%. After the time period of 56 mo all but one of the neurostimulators became ineffective[33].

Despite the success of these few patients it is still important to remind patients that CIC is still the best option and neuromodulation has a marginal place at best in urinary retention neurogenic bladder.

URINARY DIVERSION AND BLADDER AUGMENTATION

Urinary diversion is an option available to patients with MS who have failed all other therapies and remain symptomatic with either overactive bladder symptoms, emptying symptoms, or impaired compliance. When patients experience symptoms refractory to pharmacologic agents and conservative alternatives mentioned above, major surgery becomes the next option. There are several surgical options for patients with MS including bladder augmentation, continence or incontinent urinary diversion, and catheterizable channels. The exact procedure or combination of procedures depends on the underlying bladder dysfunction that needs to be addressed. When patients are unwilling or unable to catheterize an incontinence ileal loop urinary diversion is preferred. For patients willing to catheterize an augmentation cystoplasty is the simplest procedure to increase bladder capacity, improve compliance and improve overactive bladder symptoms. For patients who have an incompetent urethral sphincter or have trouble catheterizing through their urethra and they desire continence, bladder neck closure with creation of a catheterizable channel is possible. This generally utilizes a segment of small intestine and is brought up to the skin in the right lower quadrant or at the umbilicus. A concomitant bladder augmentation is generally performed. Urethral closure should accompany these procedures only if the patient has an incompetent sphincter. As with any surgery these procedures come with their own set of morbidities and these should be weighed carefully with the patient before proceeding.

Patients who undergo these operations are those that have run out of other options. They have usually tried multiple other modalities. In a study by Gudziak the average time from development of neurogenic bladder to ileovesicostomy was 147 mo. This is more than 10 years of suffering with urgency, incontinence, UTIs and multiple other problems that go along with neurogenic bladder[34]. The creation of an ileovesicostomy is a major surgery and there are multiple complications that can arise. Tan *et al*[35] looked at the adverse events of 50 patients who had undergone ileovesicostomy for neurogenic bladder, 19 of those 50 patients had MS. Complications included stomal complications, occurring in 38% of patients, mechanical complications occurring in 22% of patients and wound/bowel complications occurring in 54% of patients. Although the post-operative complication rate was high the urinary tract problems that these patients had preoperatively markedly decreased making ileovesicostomy a viable option for these patients[35].

Ileovesicostomy can also be done robotically, this has been shown to be equally effective in decreasing detrusor pressure while also being safe and effective with decreased hospital stays and less blood loss intraoperatively in one study[36]. In another study by Vanni *et al*[37] the only statistically significant difference between open and robotic ileovesicostomy was in the OR supply costs.

Bladder neck closure with suprapubic catheter placement is an option in patients who have urethral incontinence, decent bladder capacity and are poor surgical candidates. This procedure is simple and can be done without entering the peritoneum[38].

In a study of 9 patients with MS who underwent augmentation cystoplasty for their symptoms it was found that this procedure increases detrusor capacity and decreases intravesical pressure[39]. This is an ideal option in patients where the main problem of their voiding dysfunction is low bladder capacity, impaired compliance or detrusor overactivity with leakage. The patients who underwent the procedure all had preserved or improved renal function. An augmentation cystoplasty with a catheterizable stoma is another option that allows the patient to retain their own bladder while increasing its capacity and decreasing pressure. This is an ideal option in patients who have problems with bladder capacity as well as bladder emptying and prefer catheterization *via* a stoma. In a study by Khavari *et al*[40], 34 patients underwent the Indiana augmentation cystoplasty, 12 patients had MS as their cause for bladder dysfunction. At their final follow up all patients were continent. The patients were found to have increased bladder capacity from an average of 239.7 mL to 444.4 mL, this increase allows the patients to have more time between catheterizations, which leads to an improvement in quality of life. The rate of complications from the surgery was still high; 17% of patients had early post-operative complications including ileus, 44.1% had long-term complications including pyelonephritis and reoperations for stomal revisions[40].

The final option is an ileal conduit urinary diversion. This allows the bladder to be removed in its entirety, and diverting the ureters to a conduit made of small bowel. This is an option for MS patients with refractory neuro-

Table 1 Comparison of studies of urinary diversion for neurogenic bladder in patients with multiple sclerosis

Study	Year	Location	Patient	Outcome
Urinary diversion/reconstruction for cases of catheter intolerant secondary progressive multiple sclerosis with refractory urinary symptoms[43]	2011	Lahey Clinic	26 MS patients (22 female) 15 ileovesicostomy, 7 enterocystoplasty and 4 ileal loop procedures	Improved continence and fewer UTIs
Management of neurogenic bladder dysfunction with incontinent ileovesicostomy[34]	1999	Wayne State	Thirteen patients incontinent ileovesicostomy 8 SCI, 4 MS, 1 TB Meningitis	Safe and effective at providing low pressure urinary drainage
Augmentation cystoplasty in patients with multiple sclerosis[38]	2003	Czech Republic	9 MS patients (7 females, 2 males)	Increased detrusor capacity and decreased pressure
Bladder neck closure and suprapubic catheter placement as definitive management of neurogenic bladder[39]	2011	Tulane	35 patients, 11 male 24 female 27 SCI, 5 MS, 4 other	97% continent, 8 requiring reprocedure to achieve continence
Functional outcomes after management of end-stage neurological bladder dysfunction with ileal conduit in a multiple sclerosis population: A monocentric experience[42]	2011	France	53 MS patients, 6 men 47 women	Statistically significant improved QOL
Robotic-assisted ileovesicostomy: Initial results[36]	2009	Lahey	8 MS patients	Safe and effective with minimal blood loss and shorter LOS
Prospective evaluation of laparoscopic assisted cystectomy and ileal conduit in advanced multiple sclerosis[41]	2012	France	44 MS patients, 34 women 10 men	Decrease in limitations and constraint scores and an increase in autonomy scores
A modification to augmentation cystoplasty with catheterizable stoma for neurogenic patients: Technique and long-term results[40]	2012	Methodist Hospital	12 MS patients	Safe and effective, no ureteral reimplants, no need for cystectomy

MS: Multiple sclerosis; UTI: Urinary tract infection; SCI: Spinal cord injry; TB: Tuberculosis; QOL: Quality of life; LOS: Length of stay.

genic bladder symptoms and poor functional status and dexterity. The indications for an ileal conduit are recurrent febrile urinary tract infections in the setting of poor bladder emptying, chronic retention or an indwelling catheter, urinary incontinence refractory to conservative treatment affecting patients' quality of life (QOL), chronic renal failure secondary to poor bladder compliance, and recurrent urethral bleeding or erosion due to urethral trauma in patients with indwelling catheters[41]. One key aspect of this procedure is the necessity to do a cystectomy at the same time as the diversion due to the risk of pyocystitis[42]. A study was done to determine the potential benefit of laparoscopic-assisted surgery on the cystectomy and ileal conduit procedure. The prospective study by Guillotreau showed that patients had improved QOL scores by decrease in limitations and constraint scores and an increase in autonomy scores. The study was also important in showing that the morbidities were similar to open cystectomy in terms of long term complications but immediate complications were less, *i.e.*, less blood transfusions, shorter hospital stay. In addition, a finding of the study was that patients the longest length of disease duration had significantly more complications, therefore it may be important to consider ileal conduit surgery earlier on in the management of these patients. These studies are summarized in Table 1[41].

There are other surgical options that are available depending on the patients' age and symptoms but these are much less common, including ileal chimney, appendicovesicostomy, and Indiana Pouch. There is very little data to support the use of these options in MS. Augmentation has the benefit of preserving the native ureteral insertion over ileal loop diversion. The ureteral stricture rate is approximately 10%, making this a large consideration[2].

CONCLUSION

MS is a debilitating disease, which can have significant effects on patients' quality of life. Bladder dysfunction is a common symptom experienced by MS patients. There are multiple treatments available if pharmacologic treatments fail. They key is understanding what the underlying bladder dysfunction is, how it may impact the kidneys over time, and what the patients treatment goals are. Minimally invasive options such as clean intermittent catheterization, external condom catheters in men. Neuromodulation, botulinum toxin, and major bladder surgery are available to address patient symptomatology. Sacral nerve stimulation has become a proven technique to treat bladder overactivity in the setting of MS with the possibility of also improving emptying function; however, it requires implantation of metal precluding future MRI. *Botox* was FDA approved to treat neurogenic detrusor overactivity in 2011 and has had a major impact on the treatment algorithm of these patients; however, intermittent catheterization is generally needed for adequate bladder emptying. Major surgery is a final option for patients suffering from bladder dysfunction due to MS. It is usually reserved for patients with deteriorating upper urinary tract function due to impaired bladder compliance and those with intolerable incontinence.

With the many options available it is important to review all of the options with the patient so they are well prepared for the option they have chosen and understand all the risks and benefits.

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