Chronic Urinary Retention in Multiple Sclerosis Patients

Physiology, Systematic Review of Urodynamic Data, and Recommendations for Care

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KEYWORDS

• Multiple sclerosis • Urinary retention • Neurogenic bladder • Urodynamics

KEY POINTS

- Urinary retention is common in patients with multiple sclerosis (MS). Cross-sectional self-reported survey data show that 1 in 4 MS patients performs intermittent catheterization.
- Urinary retention in patients with MS can be caused by neurogenic underactive bladder and/or bladder outlet obstruction from detrusor sphincter dyssynergia (DSD). Pooled urodynamic data (1997–2017) show that 53% of patients with MS have detrusor overactivity, 43% have DSD, and 12% have atonic bladder.
- It is recommended that urinary retention in patients with MS be defined as post–void residual volume greater than 300 mL. Prospective studies are needed to validate this threshold value.
- Relationship between elevated post–void residual and risk of urinary tract infection or upper tract pathophysiology has not been well defined.
- Treatment algorithm for management of MS-related urinary retention is proposed based on stratifying patients by risk of morbidity from chronic urinary retention and then bothersome symptoms. Low-risk, asymptomatic patients with MS with chronic urinary retention should not be followed conservatively and not treated until they become symptomatic.

INTRODUCTION

Multiple sclerosis (MS) is an inflammatory autoimmune disease that affects approximately 100 per 100,000 people.[1] The disease more commonly affects younger women and can be characterized into relapsing versus progressive disease types. Urinary symptoms are highly prevalent among patients with MS. The 2005 North American Research Committee on Multiple Sclerosis (NARCOMS) survey collated responses from almost 10,000 patients with MS and reported that 65% of the responders experienced at least one moderate to severe urinary symptom.[2] Over time, MS urinary symptoms tend to increase in severity. Tepavcevic and colleagues[3] recently studied 93 patients with MS over a 6-year timeframe, and demonstrated symptoms of bladder dysfunction were reported by approximately 50% of men and women with MS on presentation

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and by 75% of men and women after 6 subsequent years with the disease.

Over the past 10 years, there have been significant improvements in diagnosing and treating MS. The McDonald criteria for diagnosing MS were revised in 2010 and now provide a greater degree of standardization for identifying patients with MS through clinical symptoms, MRI findings, and cerebral spinal fluid evaluations.[4] These revised criteria have resulted in earlier diagnosis of MS.[5] New treatment methodologies have also expanded care and support options for patients with MS. Compared with past treatments, contemporary treatment algorithms now include escalating disease-modifying therapies[6] and shared decision making in a team-based care environment.

Urologic care for the MS patient has also improved. Urologic symptom-specific treatment algorithms have been developed in the British, French, and Italian Health Systems.[7–9] Advances have occurred in understanding the efficacy of anticholinergic medications[10] and botulinum toxin[11] in treating MS-related overactive bladder. Similarly, studies have demonstrated significant improvement of MS-related nocturia for the patient taking desmopressin.[12] Published outcomes on surgical interventions for patients with MS with refractory neurogenic bladder symptoms are likewise becoming more common in the literature.[13,14]

However, despite these advances, there is uncertainty regarding the optimal strategy for managing MS-related urinary retention. The prevalence and impact of urinary retention among patients with MS are significant; Mahajan and colleagues[15] reanalyzed responses from the NARCOMS survey and found that approximately 1 in 4 MS patients performs some type of catheterization. Furthermore, the patients catheterized reported consistently lower quality of life across multiple domains. The purpose of this review is to describe the physiology, presentation, diagnosis, and treatment of MS-related urinary retention. A systematic review of MS-related urodynamic data was also performed.

PHYSIOLOGY OF URINARY RETENTION

The bladder detrusor consists of 3 layers of overlapping smooth muscle, which have no insertion or origin points. An extracellular matrix surrounds the detrusor muscle and acts a scaffold of support. It is a constantly remodeled matrix and consists of collagen (type 1 and 3), elastic fibers, adhesive proteins, glycans, and glycoproteins.[16] Bladder storage requires sympathetic nervous system stimulation of alpha- and beta-adrenergic receptors to close the bladder outlet and relax the detrusor muscle. There are 3 subtypes of α1 receptors (α1a, α1b, and α1d), but the α1a subtype in the prostate and urethra is primarily responsible for contraction of the bladder outlet.[17] There are 3 subtypes of beta-receptors, and stimulation of β2- and β3-receptors facilitates detrusor smooth muscle relaxation and bladder storage.[18] Bladder contraction and emptying is facilitated by parasympathetic stimulation of the muscarinic cholinergic receptors. Although there are 5 known subtypes of muscarinic receptors (M1 to M5), the human detrusor has a preponderance of M2 (70%), M3 (20%), and M1 (10%) receptors.[19] M3 receptors are principally responsible for detrusor contraction, but inactivation of M3 in knockout mice models shows that M2 receptors can also stimulate detrusor activity. M2/M3 receptors may also trigger some afferent reflex activity based on a neurogenic bladder rat model, which may result in uninhibited contraction of the detrusor muscle.[20] It is unclear how muscarinic receptors function in an acontractile bladder, but mice models suggest that M3 receptors become dysregulated and not coupled to detrusor stimulator.[21]

When the bladder fills, afferent sensory nerves are stimulated. The bladder neck and proximal urethra have the greatest concentration of afferent nerve bundles, and the bladder dome has the lowest concentration.[22] In a rat model, 2 types of afferent nerves, myelinated A-delta and unmyelinated C fibers, carry sensory information from the bladder to the spinal cord through the pelvic and pudendal nerves. Delta fibers are located mostly in the detrusor muscle and are activated with bladder stretching. C fibers are located closer to the urothelium and respond to stimulus such as pain and temperature stimuli. C fibers are thought to have a higher threshold of activation.[23] It is postulated that some urinary retention may be related to detrusor muscle decompensation and/or poor afferent signaling.[24]

Afferent sensory nerves enter the dorsal spinal cord through the S2-S4 nerve roots. Sensory information is carried cephalad by the spinothalamic tract in the spinal cord to the periaqueductal gray (PAG) region in the midbrain region. In some cases, overstimulation of urethral afferent nerves may inhibit bladder afferent nerves and thus cause urinary retention through a loss of communication to the central nervous system.[25] When the bladder fills, the PAG activates and inhibits the pontine micturition complex (PMC) in the brainstem. The PMC is held in a state of inhibition by the PAG