Long term results of augmentation cystoplasty and urinary diversion in multiple sclerosis

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Introduction: *There is a paucity of data about augmentation cystoplasty (AC) in multiple sclerosis (MS) patients with refractory lower urinary tract symptoms (LUTS). The aim of this study is to evaluate the long term outcomes and morbidity of these procedures in MS patients.*

Materials and methods: *This is a retrospective observational study of consecutive patients (1984-2017) with MS and refractory LUTS who underwent AC with or without a continent/incontinent abdominal stoma or urinary diversion. Pre and postoperative evaluations included routine labs, videourodynamic studies (VUDS), cystoscopy, and upper tract imaging. Long term outcomes and complications were assessed by validated questionnaires and/or chart review.*

Results: *There were 17 patients (12 women, 5 men) ranging in age from 34-77 years. Thirteen patients were wheelchair-bound (10 quadriplegics, 3 paraplegics). Indications included neurogenic detrusor overactivity (NDO) in two, low bladder compliance (LBC) in 13 and both NDO and LBC in two. One patient committed suicide at 3 months, and one was lost to follow up. Of the remaining 15, median follow up was 13 years (range 4-22), and 11 were followed up until death. Overall, 14/15 (93%) had a successful outcome based on the Patient Global Impression of Improvement (PGI-I). With respect to incontinence, 14/15 (93%) had a successful outcome based on the Simplified Urinary Incontinence Score (SUIS). Median bladder capacity increased from 180 mL to 605 mL ($p < 0.001$). Median maximum detrusor pressure decreased from 63 cm H_2O to 18 cm H_2O ($p < 0.003$). Two patients underwent stomal stenosis revisions, four patients had pyelonephritis, and two patients developed de novo bladder stones.*

Conclusions: *AC is a major surgical procedure with high potential morbidity, but these data suggest that AC is efficacious in the long term with acceptable morbidity and mortality. We believe it is an underutilized procedure for refractory LUTS in MS patients.*

Key Words: multiple sclerosis, augmentation cystoplasty, neurogenic bladder

Introduction

Multiple sclerosis (MS), often chronic and unpredictable, is a progressive neurodegenerative disorder characterized by demyelinating lesions in the brain and spinal cord. Available data suggest that 400,000 individuals are affected by MS in the United States, but this is based largely on the revision of estimates from older data. According to the National MS Society there is an approximate 2:1 predilection for women, and 32%-97% of patients have lower urinary tract symptoms (LUTS).[1,2] Overactive bladder is the most common symptom complex, and many have detrusor overactivity (DO) with or without external sphincter dyssynergia. A smaller percentage have detrusor underactivity or normal findings.[3,4] Published studies of augmentation cystoplasty (AC) in MS patients is scant in the literature.[5,6]

Most MS patients are treated empirically with medications, intermittent catheterization, intra-detrusor botulinum toxin injection, and neuromodulation, but it still remains a particular challenge for refractory patients who have progressive MS with multiple comorbidities.[7] One of the hallmarks of MS is that the lesions, and

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hence symptoms, change with time, so, many urologists have been reticent to recommend irreversible forms of treatment.

AC has shown an overall downward trend over the last decade, largely due to the popularity of neuromodulation and intra-detrusor injections of botulinum toxin to treat MS patients.[8] In highly select patients, AC offers a viable, long term solution with a high success rate; however, this benefit comes with some morbidity. The purpose of this study is to review the long term outcomes and complications in consecutive MS patients who underwent AC.

Materials and methods

Patient population

This is a retrospective, observational chart review between 1981 and 2017 of MS patients who underwent AC with or without a catheterizable abdominal stoma or continent urinary diversion (CD).

Evaluation

All patients were initially evaluated with a complete history and physical examination with special attention to neurological findings, manual dexterity, complete blood count, basic metabolic panel, cystoscopy, videourodynamic study and upper-tract imaging (computed tomography scan, intravenous pyelogram or renal ultrasound). Beginning in 1993, patients were asked to complete a LUTS questionnaire. Beginning in 2003 they were asked to complete the Patient Global Impression of Improvement (PGI-I).

Urodynamic evaluation included simultaneous measurements and recordings of intraabdominal pressure via a rectal catheter, vesical pressure via a 7F double-lumen catheter, perineal electromyography (EMG) with patch electrodes and simultaneous fluoroscopic voiding cystourethrography (VCUG). Cystometry was performed using room temperature radiographic contrast at 60 mL/minute. The patient was instructed to report any sensation to the examiner. Bladder capacity was defined as either a strong desire to void, uncomfortable fullness or incontinence due to involuntary detrusor contraction. Bladder compliance was defined as a change in volume divided by change in pressure over 100 mL intervals. Low bladder compliance was defined as a compliance value lower than 20 mL/cm H_2O. Maximum detrusor pressure (Pdetmax) was defined as the highest recorded detrusor pressure during the length of the study. DO was diagnosed when an involuntary detrusor contraction of any magnitude was noted during filling with or without sensation to void. If multiple studies were performed postoperatively, the most recent recordings were used for evaluation. Detrusor external sphincter dyssynergia (DESD) was diagnosed when there was an increase in EMG during an involuntary detrusor contraction and/or when there was radiographic evidence of obstruction at the middle/distal third of the urethra in women or the membranous urethra in men.

Operative procedure

All relevant operative notes were reviewed with regard to technique, type of operation, bowel segment used, and operative complications. A number of different operative techniques were utilized for AC, depending on the anatomy and the patient's functional limitations. For motivated men with a functional hand the operation of choice was augmentation cystoplasty with intermittent catheterization through the penis. If that was not practical, an ileo-vesicostomy with an incontinent stoma ("ileal chimney") was recommended. For women, the limiting factor was whether or not they could catheterize through the urethra, and that was based on hand function and the ability to sufficiently abduct the hips to expose the urethra. From 1984-1997 we preferred to use the ileocecal segment, with approximately 6 cm of terminal ileum, and a variable length of right colon, depending on the size of the cecum. If the sigmoid colon was very redundant, we used it, and if the ileocecal mesentery was too short, we used the transverse colon. The entire colonic segment was detubularized by opening it along the anti-mesenteric border and transformed into a patch by sewing the edges of the ileum to the cecum. Appendectomy was carried out concomitantly unless a continent stoma was constructed. A "U-shaped" bladder incision was made, beginning 2 cm proximal to the vesical neck, extending laterally and posteriorly to the bladder base. The flap was reflected posteriorly and fixed to the psoas major muscle on either side. The ileocecal patch was then anastomosed to the bladder using a single layer closure with 2:0 chromic running Connell stitch. The augmented bladder was drained with a Malecot cystostomy tube and/or urethral catheter. A Jackson-Pratt drain was used in the space of Retzius.

From 1997 until the present, we performed ileocystoplasty with about 30 cm of ileum opened along the anti-mesenteric border and reconfigured into a "W-shape." In patients who required a continent catheterizable stoma, the ileocecal segment was used and either an Indiana-type stoma or an appendiceal (classic Mitrofanoff or anatomic reversal re-implanting the tip of the appendix into the cecum) stoma was created.[9]

For bladder neck closure, a vertical incision was made with the cautery device extending from the bladder neck into the proximal urethra. The proximal

urethra was transected and a plane was created between the anterior vaginal wall and bladder neck. The enterocystoplasty segment was anastomosed to the bladder neck with running sutures of 2:0 chromic catgut, and an omental flap was interposed between the bladder neck and transected urethra. Cystograms were performed about 2 weeks postoperatively, and patients were started on intermittent catheterization if there was no extravasation.

Follow up and statistical analysis

Postoperative evaluation was scheduled every 3 months for the first year and every 6 months thereafter. Videourodynamic studies and upper-tract imaging were scheduled to be performed on alternating visits after the first year. Vitamin B_{12} levels were measured after 5 years. Postoperative cystoscopy was performed only for specific indications (e.g. gross hematuria, recurrent urinary tract infections, refractory incontinence).

Continence status was assessed using the Simplified Urinary Incontinence Score[10] (SUIS) questionnaire or chart review if the SUIS was not available. Success was defined as "cure" and "improved" on the SUIS. Subjective patient level of satisfaction, and long-term complications were assessed by chart review and by PGI-I. We defined success when a patient reported "very much better" or "much better" on the PGI-I or made comparable statements gleaned from the patient's medical records for those in whom a PGI-I was not available. Other outcomes included catheterization status, bladder capacity, compliance, presence of DO, Pdetmax, status of upper urinary tracts, need for reoperation, gastrointestinal symptoms, and Vitamin B_{12} deficiency.

All statistical analyses were performed using SPSS Statistics v.22.0 software (SPSS Inc., Chicago, IL, USA). Wilcoxon signed rank test was used to calculate any statistically significant change in bladder capacity, maximum detrusor pressure, and bladder compliance. A p value < 0.05 was considered statistically significant.

TABLE 1. **Clinical data**

	Median years (range)
Age	53 (34-77)
	n (%)
Sex	
Women	12/17 (71)
Men	5/17 (29)
Multiple sclerosis type	
Secondary progressive	11/17 (65)
Relapsing-remitting	4/17 (24)
Primary progressive	2/17 (12)
Wheelchair	13/17 (76)
Quadriplegic	10/17 (59)
Paraplegic	3/17 (18)
Preop continence status	
Incontinent	15/17 (88)
Continent (urinary retention)	1/17 (6)
Stoma	1/17 (6)
Preop incontinence management	
Indwelling catheter	10/17 (59)
Diapers	4/17 (24)
Clean intermittent catheter	2/17 (12)
Stoma	1/17 (6)
Indications	
Neurogenic detrusor overactivity	2/17 (12)
Low bladder compliance	13/17 (76)
Both	2/17 (12)
Detrusor external sphincter dyssynergia	12/17 (71)
Neurogenic detrusor overactivity	4/17 (24)
Low bladder compliance	8/17 (47)

Results

Demographics, clinical data and indications for surgery are listed in Table 1. One patient was lost to follow up, and a severely depressed 78-year-old quadriplegic woman committed suicide 3 months postoperatively. Of the remainder, four patients are alive and well, and 11 died of causes unrelated to the lower urinary tract Figure 1.

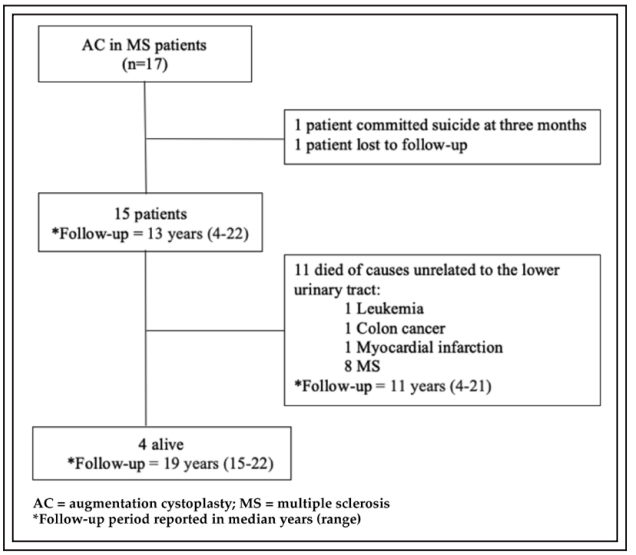

Figure 1. Current status of patients.

TABLE 2. **Type of augmentation cystoplasty**

Type of procedure	**n (%)**
Bowel segment	
Colonic	
Transverse colon	2/17 (12)
Sigmoid	1/17 (6)
Ileocecal	6/17 (35)
Ileal	8/17 (47)
Concomitant procedures	
Continent stoma	8/17 (47)
Mitrofanoff	1/17 (6)
Indiana	7/17 (41)
Incontinent stoma	5/17 (29)
Pubovaginal sling	2/17 (12)
Bladder neck closure	4/17 (24)
Nephrectomy	1/17 (6)

TABLE 3. **Complications**

Complication	**n (%)†**
Pyelonephritis	4/15 (27)
De novo bladder stones	2/15 (13)
Stomal stenosis	2/10 (20)*
Urosepsis	1/17 (6)
Stitch abscess	1/16 (6)
Nephrogenic adenoma	1/15 (7)
Bowel obstruction treated	
Conservatively	1/15 (7)
Requiring surgery	1/15 (7)
Chronic diarrhea	1/15 (7)
Postop dehydration	2/17 (12)

†complete complications were recorded for all but 1 patient who was lost to follow up and 1 patient who committed suicide a 3 months follow up; the respective denominator values reflect this
*reported value is limited to the 10 patients with stomas

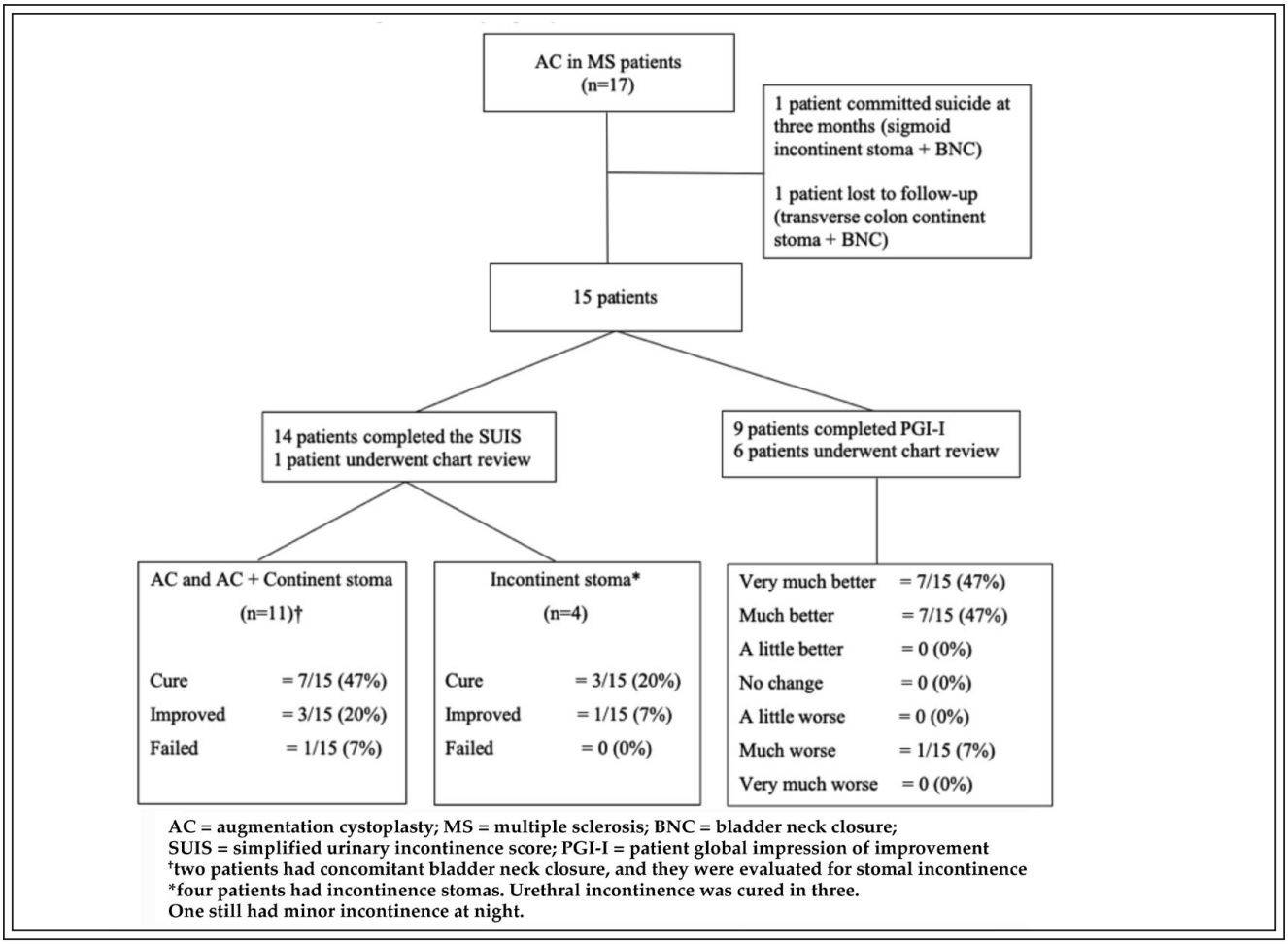

Figure 2. Outcomes of augmentation cystoplasty.

TABLE 4. **Preoperative and postoperative urodynamic characteristics**

	n = 15*	Preop median (IQR)	Postop median (IQR)	p value
Bladder capacity (mL)	AC and AC + continent stoma (n = 11)	180 (123-296)	605 (562-750)	< 0.001
	Incontinent stoma (n = 4)	229.5 (87.5-304.57)	316 (124.25-693.75)	n/a†
Max detrusor pressure (cm H_2O)	AC and AC + continent stoma (n=11)	63 (25-75)	18 (3-28)	< 0.003
	Incontinent stoma (n = 4)	50 (21-73.75)	6.5 (3.5-9.5)	n/a†
Bladder compliance (mL/cm H_2O)	AC and AC + continent stoma (n = 11)	6 (3-7)	38 (31-132)	< 0.001
	Incontinent stoma (n = 4)	6 (1.25-14.5)	40.5 (18.75-204.75)	n/a†

AC = augmentation cystoplasty; IQR = interquartile ranges (quartile 1 to quartile 3)
*two patients were excluded (one committed suicide, and one was lost to follow up)
†the sample size for incontinent stoma was too small to allow for a reliable calculation of the Wilcoxon signed-rank statistic

Table 2 depicts the types of procedures performed. Two women underwent concomitant pubovaginal sling procedures, and four women had concomitant bladder neck closures. One man underwent concomitant nephrectomy for chronic pyonephrosis.

Based on the PGI-I (and chart review in 6 patients) overall success was 14/15 (93%) and incontinence, based on the SUIS and chart review, incontinence was cured or improved in 14/15 (93%) as seen in Figure 2.

Complications are reported in Table 3. There was one failure: a 48-year-old morbidly obese woman who had been treated with an indwelling catheter for 18 years and subsequently underwent an AC, with concomitant bladder neck closure, and continent stoma procedures. She had multiple kidney stones that passed into the bladder. She later developed recurrent urosepsis and stomal incontinence.

Two patients with preoperative hydronephrosis improved after surgery, and one patient with bilateral vesicoureteral reflux had improvement on the right side and complete resolution on the left. One patient developed hydronephrosis secondary to urethral obstruction from metastatic colon cancer 5 years postoperatively. Two patients developed stomal stenosis 4 and 6 years after surgery, respectively, and both underwent successful operative revision. Four patients developed bladder stones (two passed upper tract stones, two had de novo stones) but were successfully treated with electrohydraulic lithotripsy. Two patients experienced small bowel obstruction 3 and 7 years after surgery, respectively, one of whom required lysis of adhesions. Chronic diarrhea developed in one patient that was treated with anti-diarrheal medication. None of the patients developed vitamin B_{12} deficiency. Fifteen patients completed postoperative urodynamic studies, and the results are summarized in Table 4.

Discussion

Patients with MS and refractory neurogenic voiding dysfunction present considerable therapeutic challenges. Proper management of the lower urinary tract is important from both health and quality-of-life standpoints. The goal of treatment is to create a low pressure reservoir that can be emptied either by voiding or by intermittent catheterization. A low pressure reservoir may be accomplished by "paralyzing" or modulating detrusor activity (e.g. anticholinergics, beta-3 adrenergic blockers, intra-detrusor botulinum toxin injections, neuromodulation).[11]

For patients who are refractory to these treatments, aggressive treatment is important not only for their quality of life but also for protection of their upper urinary tracts and prevention of hydronephrosis, stones, urosepsis and kidney failure.[3] It is well accepted that DO, DESD, and low bladder compliance are major risk factors for the development of these complications. Augmentation cystoplasty with or without a continent abdominal stoma, urinary diversion or an indwelling catheter are the only remaining options for these patients.[12-14]

Traditionally, there has been considerable reluctance to recommend irreversible, lifestyle-altering procedures, such as AC, in MS patients because of the concern that their LUTS and urodynamics may change over time and may actually improve. Ciancio et al quantified this idea and found that 55% of patients with new

or persistent symptoms, followed for a mean of 42 months, had a significant change in their urodynamic classification of compliance over time.[15] None of these patients, however, converted to a normal pattern on repeat evaluation. Of particular interest, DESD, once diagnosed, almost invariably persists on subsequent evaluations.[16] While it is true that these patients' urinary tract function may change over time, it is our belief that once patients get to the point where an augmentation or diversion is considered, they are unlikely to improve to the degree where they would no longer benefit from a reconstructive procedure.

Our group of patients represents the most severely affected of MS patients who have failed all other treatment options including intermittent catheterization and indwelling catheters. More than half were quadriplegic, and three-quarters were wheelchair-bound. Most had multiple comorbidities. Despite this, the overall subjective success rate was 93%. The upper urinary tract remained normal or improved in all but one patient; bladder capacity and detrusor pressures were dramatically improved in all but the same patient. Only one patient developed urosepsis. Two patients developed de novo bladder stones that were easily extracted.

The type of operation and need for additional procedures (usually anti-incontinence) should be individualized depending on urodynamic findings, sphincteric function, manual dexterity, willingness to catheterize, upper tract status and availability of bowel for reconstructive purposes. We believe that augmenting the native bladder is preferable, in most instances, to urinary diversion as it avoids two ureteral anastomoses. In patients with vesicoureteral reflux, ureteral reimplantation is generally not necessary because the creation of a low pressure system will usually prevent complications secondary to reflux.[17] The choice of bowel segment used in the augment depends on patient anatomy, surgeon preference and the need for a catheterizable stoma. There are inherent advantages and disadvantages to using different bowel segments that is beyond the scope of this discussion.

Presently, there are no accepted criteria for determining the need for an anti-incontinence procedure at the time of enterocystoplasty.[18] Most of the literature involves myelodysplastic children, who may not be applicable to adult patients with MS. Kreder and Webster suggested that videourodynamic evaluation was crucial to operative planning in these patients and, based on their study with 30 patients, concluded that an anti-incontinence procedure was necessary when the bladder neck and distal sphincter mechanisms are incompetent in the absence of a detrusor contraction.[19]

Our current practice has changed considerably over the years; we recommend simultaneous anti-incontinence procedures only in patients with severe sphincteric incontinence like that described by Kreder et al.[19] Because there is a reported incidence of fistulas from bladder neck closures ranging from 8%-40%, we reserve this procedure only for those patients in whom it is not technically possible to perform an autologous fascial sling (in women) or urinary sphincter prosthesis (in men), which are our procedures of choice.[20] When bladder neck closure is chosen, we recommend buttressing it with an omental flap, transecting the urethra just below the bladder neck, and incorporating the bowel anastomosis into the bladder neck closure.

There is a paucity of studies about AC in patients with MS. Khavari et al reported on 34 neurogenic patients after ileocecal augmentation with a continent stoma, 10 of whom had MS.[21] Minor complications and the need for additional interventions have traditionally been between 30%-44% and 15%-20%, respectively, but despite the high complication rate, overall patient satisfaction has been excellent according to the authors.[22]

The most constant and difficult to manage complication involves stomal stenosis or difficulty catheterizing, and most of that data comes from the pediatric age group. In a large single surgeon series of 50 appendicovesicostomies, 10% developed stomal stenosis and 16% required stomal revision at a median time of 13 months. At a mean follow up of 51 months, 96% continued to catheterize the stoma, and all except 1 patient was continent.[23] De Ganck et al reported a 36% stomal complication rate in 53 patients who underwent either a Mitrofanoff or Monti-type continent stoma.[24] Reported stomal stenosis rates are highly variable and dependent on the type of stoma, technique, and patient factors. Our rates of stomal revision, bowel obstruction and UTI's are comparable to those reported in the literature. In addition, no patient developed de novo upper tracts stones or hydronephrosis, and all patients with pre-existing hydronephrosis showed improvement. None developed vitamin B_{12} deficiency. Bladder rupture is a specific risk of AC and was estimated to occur in 5%-13% of patients.[25,26] None of the patients in our study had a bladder rupture.

Soergel et al discussed concern about the risk of bladder cancer after AC. They reported the incidence to be about 1%, and the associated lag time is generally greater than 10 years. The most common histology is adenocarcinoma, followed by transitional cell carcinoma. While there is no consensus about screening, the recommended annual surveillance cystoscopy starts approximately 10 years after AC. Also, hematuria should always prompt an evaluation.[27]

Limitations

The strengths of this study, albeit with only 17 patients, are: 1) it is the largest series that we could find in the literature involving MS patients, 2) it has one of the longest follow ups, and 3) the fact that videourodynamics were done pre and postoperatively in all but 1 patient. There are a number of limitations: 1) this is a retrospective and observational chart review with all of the attendant weaknesses, most importantly, 2) outcomes such as patient-reported quality of life was not measured, and 3) there were no detailed records of the cause of death in any of the patients; it was gleaned from medical records and discussed with family members.

Conclusion

For MS patients with refractory LUTS, AC is an efficacious treatment option; it reliably decreases detrusor pressure, increases bladder capacity, improves urinary continence, and protects the upper tracts. The majority of patients need to rely on intermittent self-catheterization or on an external urinary appliance. It is not without complications, but we believe the morbidity is acceptable and that it is a vastly underutilized procedure. □

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