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ORIGINAL CLINICAL ARTICLE

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The effects of augmentation cystoplasty and botulinum toxin injection on patient-reported bladder function and quality of life among individuals with spinal cord injury performing clean intermittent catheterization

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Aims: Clean intermittent catheterization (CIC) is recommended after spinal cord injury (SCI) because it has the least complications, however, CIC has a high discontinuation rate. We hypothesized that bladder botulinum toxin injection or augmentation cystoplasty may improve satisfaction with CIC.

Methods: The NBRG registry is a multicenter, prospective, observational study asking SCI participants about neurogenic bladder (NGB) related quality of life (QoL). In this study, participants performing CIC as primary bladder management were categorized into 3 groups: (1) CIC alone (CIC); (2) CIC with botulinum toxin (CIC-BTX); and (3) CIC with augmentation cystoplasty (CIC-AUG). Outcomes included *primary*: Neurogenic Bladder Symptom Score (NBSS) and SCI-QoL Bladder Management Difficulties, and *secondary:* NBSS subdomains (Incontinence, Storage & Voiding, Consequences) and the NBSS final question (satisfaction with urinary function). Multivariable regression, controlling for multiple factors was used to establish differences between the three groups.

Results: Eight hundred seventy-nine participants performed CIC as primary bladder management and had the following characteristics: mean age 43.4 (±12.9) and years from injury 13.7 (±10.7), tetraplegia in 284 (32%), and 543 (62%) were men. Bladder management was CIC in 593 (67%), CIC-BTX in 161 (19%), and CIC-AUG in 125 (15%). Primary outcomes: CIC-AUG had associated improved total NBSS versus CIC(−3.2(−5.2 to −1.2), $P = 0.001$ and CIC-BTX(−3.9(−6.3 to −1.6), $P = 0.001$), CIC-AUG also had better SCI-QoL Difficulties scores versus CIC(−4(−5.48 to −2.53, $P < 0.001$) and CIC-BTX(−4.4(−6.15 to −2.65, $P < 0.001$). Secondary outcomes: CIC-AUG had associated improved Incontinence and Satisfaction scores versus CIC and CIC-BTX.

David Ginsberg led the peer-review process as the Associate Editor responsible for the paper.

Conclusions: Compared to patients performing CIC with or without botulinum toxin treatment, those with augmentation cystoplasty had associated better urinary function and satisfaction with their urinary symptoms.

KEYWORDS
incontinence, neurogenic bladder, patient reported outcomes, surgery

1 | INTRODUCTION

After spinal cord injury (SCI), most individuals are dependent upon some type of assisted bladder emptying. Commonly this involves urinary catheters. Physicians generally recommend clean intermittent catheterization (CIC), where a catheter is passed via the urethra or an abdominal stoma at regular intervals to drain the bladder. CIC is associated with a lower complication rate compared to indwelling catheters (IDC). For instance, SCI patients using IDCs have adverse bladder findings during urodynamic exams[1] and higher rates of upper tract abnormalities, proteinuria, and renal insufficiency.[2] In another study of thousands of patients enrolled nationally in the Model SCI system, patients with IDC had higher rates of urinary tract infection, urosepsis, hospitalizations, and sacral decubitus ulcers.[3]

Despite the lower complications associated with CIC, evidence suggests that most patients performing CIC at discharge from rehabilitation transition their bladder management to other methods, such as IDC.[3] Since very little correction is known about quality of life (QoL) related to bladder management, the reasons for this transition are not clear. No doubt, many of the reasons for switching management have roots in QoL issues and indeed in one small study of CIC discontinuation, inconvenience, and dislike were identified as important patient motivations for transition away from CIC.[4]

Botulinum toxin was approved by the US Food and Drug Agency in 2011 for use in neurogenic bladder (NGB). In NGB patients, botulinum toxin can profoundly improve urinary continence and the ability to store urine at low pressures.[5] Augmentation cystoplasty (also called enterocystoplasty) is a surgery where the bladder is widely opened and a patch of bowel is sewn onto the bladder. The surgery expands the bladder's volume and also decreases pressures and spasticity.[6] Both treatments have been demonstrated to have a profound impact on improving bladder function and lessening incontinence. Improved bladder function may decrease inconvenience, encouraging patients to continue CIC rather than transitioning to less ideal bladder managements. Prior studies, which compared QoL between patients performing CIC and those patients who perform CIC and use botulinum toxin or have undergone augmentation cystoplasty were limited by small sample sizes and were underpowered to compare between the three treatments.[7,8]

In SCI patients who manage their bladder with CIC, we hypothesized that botulinum toxin injection or augmentation cystoplasty would be associated with improvements in patient-reported bladder function and QoL compared to those patients performing CIC alone.

2 | MATERIALS AND METHODS

2.1 | Study design

This study was a multicenter, prospective, observational study, which measures NGB-related quality of life after SCI. Participants were recruited throughout the United States and Canada. The study protocol, which details recruitment methods, duration, and aims has been previously published.[9] Eligibility included: age ≥18 years, English-speaking, acquired and non-progressive SCI (eg, traumatic, spinal cord bleed/abscess/stroke, spinal cord tumor without active malignancy, transverse myelitis without progression to multiple sclerosis, and iatrogenic, such as laminectomy complication). Exclusion criteria were congenital causes of spinal cord problems, such as myelomeningocele or cerebral palsy, and progressive disorders, such as multiple sclerosis.

Participants were asked about their bladder management during their enrollment interview. When participants used multiple bladder managements, such as a patient using a Foley catheter overnight but CIC during the day, they were asked what they considered as their main or primary method of management. For this study, all participants used CIC as their primary bladder management. The participants were grouped into (1) those using CIC alone (CIC); (2) those that were actively using botulinum toxin (CIC-BTX); and (3) those that had an augmentation cystoplasty (CIC-AUG).

Botulinum toxin use was determined by asking "Are you using botulinum toxin injections (Botox) for your bladder?" If the answer was "yes" than patients were grouped into CIC-BTX. We did not determine the timing the last injection relative to enrollment in the study.

All participants had enterocystoplasty in the CIC-AUG group with or without creation of a catheterizable channel. Multiple bowel segments and techniques were used for augmentation cystoplasty and not all participants knew the type of augmentation that they had received. Participants with creation of a catheterizable channel without augmentation or a continent urinary pouch (ie, Indiana Pouch involving complete bypass or removal of the bladder) were excluded from the study.

2.2 | Primary outcomes

The primary outcomes were (1) the Neurogenic Bladder Symptom Score (NBSS) and (2) the Spinal Cord Injury Quality of Life Measurement System (SCI-QoL) Bladder Management Difficulties (SCI-QoL Difficulties) item bank. The NBSS has been validated in SCI and evaluates bladder function, as well as satisfaction with urinary function.[10,11] The overall NBSS has a range of 0–74 with lower scores indicating better function.

The spinal cord injury quality of life measurement system consists of many different item banks, validated specifically in SCI individuals, assessing all aspects of health and psychosocial impact of SCI.[12] We used the (SCI-QoL Difficulties) item bank, which assesses ability to carry out a bladder program, concerns about incontinence, and impact on daily life.[13] SCI-QoL questionnaires rely on item response theory and computer adaptive testing, which allows the questionnaire to adapt to a participant's answer. SCI-QoL item banks are calibrated to have a mean of 50 and a range of 0-100. Less bladder difficulties are indicated by a lower score.

2.3 | Secondary outcomes

The secondary outcomes included the three sub-domains of the NBSS: (1) Incontinence (range 0-29); (2) Storage & Voiding (range 0-22); (3) Consequences (range 0-23), and a final QoL question asking about satisfaction with urinary function (Satisfaction) (range 0-4).[10]

2.4 | Covariates

The factors we adjusted for when comparing QoL measures between the three management groups included: Demographics: (1) age (decades from injury), (2) gender, (3) obesity (body mass index>30 kg/m^2), Injury characteristics: (4) level (tetraplegia/paraplegia including cauda equina), (5) time since injury in decades, (6) complete/incomplete injury —American Spinal Injury Association Impairment Scale [ASI] "A" or if unknown participants were asked if they had a complete or incomplete injury, (7) assisted catheterization—complete reliance upon others for catheterization, and SCI complications: (8) chronic pain (asked—do you experience chronic pain?), (9) number of UTIs in the last year (categorical—0, 1–3, ≥4)—UTIs were self-defined by the patient, (10) hospitalization for UTI in last year, and (11) severe bowel dysfunction (Neurogenic Bowel Dysfunction Score>14). The Neurogenic Bowel Dysfunction Score is a validated questionnaire about bowel function in neurogenic patients.[14]

2.5 | Statistical analysis

Baseline patient characteristics were summarized and compared across the three groups: (1) CIC (reference); (2) CIC-BTX; and (3) CIC-AUG. In addition CIC-AUG was compared to CIC-BTX (reference). Continuous variables were compared using analysis of variance (ANOVA) or Kruskal-Wallis tests and categorical variables were compared using chi-squared tests. QoL outcome measures were compared across CIC management groups using univariate and multivariate linear regression models, where the multivariate models controlled for the factors described above in the "*Covariates*" section. For the CIC group (reference) we reported the predicted marginal mean of each QoL outcome with its 95% confidence interval (CI). For other management types and covariates in the model we report regression coefficients, which measured the magnitude of change in the outcome associated with that variable (negative change for the NBSS or SCI-QoL Difficulties indicated a better symptom burden or QoL), and their associated 95%CIs. Statistical analyses were conducted in R v. 3.4.1,[15] significance was assessed at the 0.05 level, and all tests were two-tailed.

3 | RESULTS

3.1 | Study participants

Over 18 months, 1479 eligible participants were enrolled and completed baseline questionnaires. From this group, 910 participants used CIC as their primary management and 879 met the inclusion criteria. Patients were excluded because of creation catheterizable channel alone without augmentation ($n = 24$), or having a continent catheterizable pouch ($n = 7$) (Figure 1). In the 125 patients in CIC-AUG group, 79 (63%) had augmentation cystoplasty alone and 46 (37%) had augmentation cystoplasty combined with creation of a catheterizable channel. The mean time since augmentation cystoplasty to enrollment in the study was 10.1 (SD 8.1) years.

Table 1 summarizes the cohort's characteristics. Overall, there were 543 (62%) men and the mean age and years from injury were 43.4 (SD 12.9) and 13.7 (SD 10.6) years. Compared to the CIC-alone and CIC-BTX groups, the CIC-AUG group was significantly more likely include female and

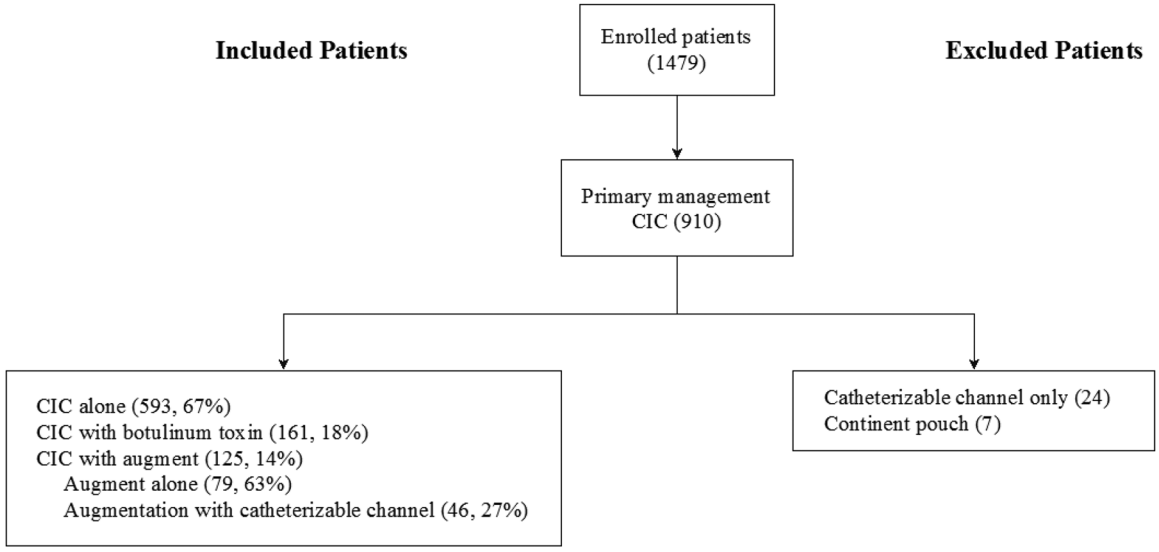

FIGURE 1 Study flow for patient enrolled in the Neurogenic Bladder Research Group SCI registry

quadriplegic patients. Some other significant differences existed between the CIC groups including: age, years since injury, chronic pain, and severe bowel dysfunction. There were no differences in the rate of UTIs or hospitalization for UTI between groups. The unadjusted primary and secondary outcome measures are compared between groups in Table 2.

3.2 | Primary outcomes

The CIC-AUG group had an associated better Global bladder function (total NBSS), compared to CIC and CIC-BTX (Table 3). Multiple variables were associated with improvement in the total NBSS, including: older age, male sex, tetraplegia, and increased years since injury. A worse score was significantly associated with obesity, chronic pain, UTIs (both 1–3 and ≥ 4 per year), and severe bowel dysfunction.

There was also a better associated SCI-QoL Difficulties score in the CIC-AUG group compared to both CIC and CIC-BTX (Table 3). Similar to the NBSS, better scores were associated with: older age, male sex, tetraplegia, and increased years since injury; while obesity, UTIs (both 1–3, and ≥ 4 per year), and severe bowel dysfunction were all associated with worsened scores. There were no differences in either of the primary outcomes between CIC-BTX and CIC.

3.3 | Secondary outcomes

In the NBSS subdomains, CIC-AUG had associated better scores in the Incontinence subdomain and with Satisfaction compared to CIC and CIC-BTX (Table 4). The other subdomains, Storage & Voiding and Consequences, showed no differences between CIC-AUG and CIC or CIC-BTX. There were no differences between CIC-BTX and CIC in any of the subdomains.

4 | DISCUSSION

The best overall bladder function and satisfaction was associated with participants who had undergone augmentation cystoplasty compared to those performing CIC or those performing CIC and having current treatment with botulinum toxin. The improvements in bladder function were evidenced in global function (total NBSS), improved continence, and satisfaction with urinary system. In addition, SCI patients with augmentation cystoplasty had less bladder management difficulties, although the magnitude of change was smaller than changes in the NBSS, when compared to the marginal means in the multivariable model. There were no differences in any patient-reported outcomes between patients treated with botulinum toxin and those doing CIC alone.

The research published about QoL with different bladder management methods among SCI patients is heterogeneous and mostly relies upon general QoL measures rather and bladder specific patient-reported outcome measures. There are very few studies evaluating the influence of surgery on QoL. One of the few studies looking at the influence of surgery, by Adriaansen et al,[7] used the short form of the Qualiveen NGB QoL questionnaire to evaluate differences in bladder management in SCI patients.[7] This questionnaire is similar to the SCI-QoL Difficulties used in our study, and assess feelings and limitations related to NGB.[16] The authors found on univariate analysis that patients having surgery, either continent ($n = 8$) or incontinent urinary diversion ($n = 8$), had improved QoL compared to patients performing

TABLE 1 Characteristics of the 879 participants who performed CIC

Variable	All patients	CIC	CIC-BTX	CIC-AUG	*P*-value
Number of participants	879	593 (67%)	161 (18%)	125 (14%)	
Surgery					
Augmentation				79 (63%)	
Augmentation+catheterizable channel				46 (27%)	
Demographics					
Age—Mean (SD)	43.4 (12.9)	44.3 (12.9)	41.4 (13.4)	41.8 (11.9)	0.014
- Median (IQR)	43 (33, 53.2)	44.3 (34.3, 53.6)	39.5 (30, 51.9)	40.7 (31.3, 51.8)	-
- Range	(18, 86)	(18, 78.5)	(18.4, 86)	(19, 67.9)	-
Sex-Male	543 (62%)	408 (69%)	97 (60%)	38 (30%)	<0.001
Obese (BMI>30 kg/m^2)	194 (22%)	135 (23%)	28 (18%)	31 (25%)	0.22
Injury characteristics					
Level tetraplegia	284 (32%)	172 (29%)	57 (35%)	55 (44%)	0.003
Paraplegia	595 (68%)	421(71%)	104 (65%)	70 (56%)	-
Years since injury—mean (SD)	13.7 (10.6)	13.9 (11)	10.6 (8.5)	16.5 (10.4)	<0.001
- Median (IQR)	10.4 (5.1, 20.8)	10.7 (4.9, 21.8)	8.1 (4.5, 13.8)	15.1 (8.2, 23.2)	-
- Range	(0, 50.4)	(0, 48.3)	(0.7, 36.8)	(1, 50.4)	-
Complete injury	375 (43%)	236 (40%)	78 (49%)	61 (49%)	0.049
Assisted catheterization	94 (11%)	54 (9%)	28 (17%)	12 (10%)	0.010
SCI complications					
Chronic pain	596 (68%)	395 (67%)	104 (65%)	97 (78%)	0.041
Number of UTIs					
0	209 (24%)	141 (24%)	32 (20%)	36 (29%)	0.52
1-3	428 (49%)	291 (49%)	81 (50%)	56 (45%)	-
≥4	242 (28%)	161 (27%)	48 (30%)	33 (26%)	-
Hospitalization for UTI	89 (10%)	59 (10%)	19 (12%)	11 (9%)	0.68
Severe bowel dysfunction	333 (40%)	204 (36%)	68 (45%)	61 (52%)	0.002

CIC (clean intermittent catheterization), CIC-BTX (CIC with current use of botulinum toxin), CIC-AUG (CIC with prior augmentation cystoplasty with or without catheterizable channel), BMI (body mass index), complete injury—American Spinal Injury Association Impairment Scale [ASI] "A" or if unknown participants asked if they had a complete or incomplete injury, assisted catheterization—complete reliance on others for catheterization, chronic pain—participants asked "do you experience chronic pain?", UTI (urinary tract infection), number of UTIs and hospitalization in last year, severe bowel dysfunction—Neurogenic Bowel Dysfunction Score ≥ 14. Missing data: Obese ($n = 11$), Assisted Catheterization ($n = 1$), Chronic Pain ($n = 2$), Severe Bowel Dysfunction ($n = 46$).

CIC. The study results were limited by the small number of patients.

Another study, by Anquetil et al,[8] evaluated differences in QoL between patients with a history of augmentation cystoplasty and those receiving botulinum toxin using the full Qualiveen questionnaire to compare groups. Patients with augmentation ($n = 16$) had improved overall QoL, as well as improvement in the subdomain of Limitations and Constraints compared to those using botulinum toxin ($n = 14$). These were substantial differences and represented improved scores ranging between 29 and 56%. In comparison, we found the improvement in augmentation patients in the SCI-QoL Difficulties was only an approximately a 7% improvement (−4.4 on a scale of 0–100, with marginal means of 58.3 [CIC reference]). However, in the study by Anquetil et al, 13% of patients in the botulinum toxin group did not perform CIC and relied on condom catheters, IDCs or leakage into diapers. Poor QoL associated with these managements within the botulinum toxin group might have created a much larger gap in QoL between treatment groups compared to our study where all patients were performing CIC. Again this study was limited by small numbers in comparison groups. Among the potential confounding variables, we included dependence upon others for catheterization. Independence is valued by SCI individuals[12] and so there is an intuitive link between worse QoL and dependence upon others. One study by Akkoc et al, noted that QoL, measured by the King's Health Questionnaire, was worse among CIC patients that are reliant on others for catheterization.[17] On our multivariate analysis, we found no association between assisted catheterization and worse bladder function or QoL. Our patients on average were 14 years from injury and SCI patients probably developed mature resources for assistance over-time. One can infer from our data, that if a patient has reliable help and desires to continue or to start CIC, reliance upon others for catheterization should not be a barrier to treatments to optimize CIC, such as botulinum toxin injection or even augmentation cystoplasty.

TABLE 2 Summary of primary and secondary outcomes and comparison between three groups

	All patients	CIC	CIC-BTX	CIC-AUG	*P*-value
Primary outcomes					
NBSS—Mean (SD)	25 (10.1)	24.9 (10.2)	26.6 (9.6)	23.3 (9.7)	0.020
– Median (IQR)	24 (17.5, 32)	24.0 (17.0, 32.0)	27.0 (20.0, 33.0)	24.0 (15.0, 30.0)	
– Range	(1, 63)	(3.0, 63.0)	(1.0, 55.0)	(3.0, 48.0)	
SCI-QoL difficulties—mean (SD)	58.3 (7.4)	58.6 (7.3)	59.5 (7.1)	55.3 (7.3)	<0.001
– Median (IQR)	58.8 (54.4, 62.9)	59.9 (54.4, 62.9)	59.9 (56.6, 64.1)	56.6 (49.6, 60.1)	
– Range	(37.6, 82.1)	(37.6, 81.5)	(37.6, 82.1)	(37.6, 74.3)	
Secondary outcomes					
NBSS Incontinence—Mean (SD)	10.4 (6.8)	10.5 (6.8)	11.6 (6.6)	8.8 (6.6)	0.002
– Median (IQR)	11 (6, 15)	11.0 (6.0, 15.0)	12.0 (8.0, 16.0)	9.0 (2.0, 13.0)	
– Range	(0, 28)	(0.0, 28.0)	(0.0, 25.0)	(0.0, 25.0)	
NBSS storage & voiding—mean (SD)	7.8 (3.3)	7.8 (3.4)	7.9 (3.3)	7.7 (3.1)	0.90
– Median (IQR)	8 (5, 10)	8.0 (5.0, 10.0)	8.0 (6.0, 10.0)	7.0 (6.0, 10.0)	
– Range	(0, 19)	(0.0, 19.0)	(1.0, 17.0)	(2.0, 18.0)	
NBSS Consequences—Mean (SD)	6.8 (2.9)	6.6 (3.0)	7.2 (2.6)	6.8 (3.1)	0.12
– Median (IQR)	7 (5, 8.5)	6.0 (5.0, 8.0)	7.0 (6.0, 8.0)	7.0 (5.0, 9.0)	
– Range	(0, 20)	(0.0, 19.0)	(0.0, 20.0)	(0.0, 13.0)	
NBSS Satisfaction—Mean (SD)	2.1 (1.2)	2.2 (1.2)	2.2 (1.1)	1.4 (1.1)	<0.001
– Median (IQR)	2 (1, 3)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	1.0 (1.0, 2.0)	
– Range	(0, 4)	(0.0, 4.0)	(0.0, 4.0)	(0.0, 4.0)	

CIC (clean intermittent catheterization), CIC-BTX (CIC with current use of botulinum toxin), CIC-AUG (CIC with prior augmentation cystoplasty with or without catheterizable channel), NBSS (Neurogenic Bladder Symptom Score), SCI-QoL (Spinal Cord Injury Quality of Life Measurement System), SCI-QoL Difficulties (SCI-QoL Bladder Management Difficulties).

Botulinum toxin has been associated with dramatic improvements in QoL in SCI patients. The two landmark randomized trials leading to approval of botulinum toxin in Europe and the United States assessed QoL of life and bladder function with the Incontinence Quality of Life score (IQOL).[5,18] This is a bladder specific questionnaire focused upon incontinence and has been validated in NGB.[19] These studies showed that after botulinum toxin injection IQOL scores were dramatically improved, as well as urodynamic parameters and incontinence episodes. In these studies, there was significantly better QoL in participants that received botulinum toxin compared to those that did CIC and received placebo. In contrast, we did not find any differences between these groups; however, the studies are very different and patients entering the randomized controlled trials presumably were having bladder difficulties and electing to enter a clinical trial to try to improve their bladder function. This is evidenced by the very high rate of incontinence episodes at baseline in the study as well as the very low IQOL scores. In contrast, our study was a crossectional survey that presumably captures patients with a spectrum of bladder function including many patients doing very well with their current management. Despite the lack of differences, in our study, in bladder function or QoL in patients using botulinum toxin compared to patients doing CIC with standard NGB management, the efficacy of botulinum toxin is evidenced by the fact that a full 21% of patients in our study that not had augmentation cystoplasty were actively using botulinum toxin.

Our data are cross-sectional and unlike the randomized trials of botulinum toxin efficacy, we are not able assess pre and post interventions. One of the best ways to use our data are in shared decision making with SCI patients who are seeking help for urinary problems and want to continue to perform CIC. These patients, if they are appropriately chosen, can be counseled that their bladder related function after botulinum toxin injection should approximate on average patients that are doing well with CIC and standard NGB management. Those patients that are not good candidates for botulinum toxin or if the drug loses its positive effects, and elect to undergo augmentation cystoplasty can expect to have comparable or even better bladder function and QoL than individuals that are performing CIC with or without the use of botulinum toxin. It needs to be acknowledged that NGB management is not static in time and individuals may do well with standard management for a variable time period and then worsen and progress to needing botulinum toxin and in some cases augmentation cystoplasty. Our data does not indicate the SCI individuals should have augmentation cystoplasty, but rather indicates that when patient progress to the need for augmentation cystoplasty they will have excellent bladder function and QoL associated with the surgery.

TABLE 3 Primary Outcomes: Multivariate linear regression comparing the NBSS and SCI-QoL Difficulties between patients performing CIC-BTX versus CIC, CIC-AUG vs. CIC, and CIC-AUG versus CIC-BTX adjusting for patient characteristics. Unless otherwise specified, results include the regression coefficient, 95% Cis, and *P*-values, indicating the change in the outcome associated with each predictor

Variables	NBSS total	*P*-value	SCI-Qol difficulties	*P*-value
Bladder management				
CIC[a]	24.8 (23.9-25.7)		58.3 (57.6-58.9)	-
CIC-BTX	0.7 (−1-2.4)	0.44	0.4 (-0.87-1.67)	0.54
CIC-AUG	−3.2 (−5.2 to −1.2)	0.001	−4 (−5.48 to −2.53)	<0.001
CIC-AUG vs CIC-BTX[b]	−3.9 (−6.3 to −1.6)	0.001	−4.4 (−6.15 to −2.65)	<0.001
Demographics				
Age	−0.7(−1.3 to −0.1)	0.014	-0.64(-1.05-−0.22)	0.003
Sex-Male	−3.7(−5.1 to −2.3)	<0.001	−1.8(-2.85 to −0.75)	<0.001
Obese (BMI>30 kg/m^2)	1.8 (0.2-3.4)	0.026	1.23 (0.06-2.4)	0.039
Injury characteristics				
Level tetraplegia	−2.5 (−4.1 to −0.9)	0.002	−2.27 (−3.45 to −1.09)	<0.001
Years since injury	-0.9(-1.5 to −0.2)	0.013	−0.9 (−1.41 to −0.4)	<0.001
Complete injury	−0.3 (−1.6 to 1.1)	0.69	−0.38(−1.39 to 0.64)	0.47
Assisted catheterization	1.7 (−0.6 to 4)	0.15	0.02 (−1.7 to 1.74)	0.98
SCI complications				
Chronic pain	1.7 (0.3-3.1)	0.014	0.87 (−0.16 to 1.9)	0.10
Number of UTIs				
1-3	1.9 (0.3-3.5)	0.020	1.26 (0.07-2.45)	0.038
≥4	5.7 (3.8-7.5)	<0.001	2.96 (1.57-4.34)	<0.001
Hospitalization for UTI	1.7 (−0.5 to 3.9)	0.13	−1.12 (−2.75 to 0.52)	0.18
Severe bowel dysfunction	1.7 (0.3 to 3)	0.013	1.18 (0.2 to 2.15)	0.018

NBSS (Neurogenic Bladder Symptom Score), SCI-QoL (Spinal Cord Injury Quality of Life Measurement System), SCI-QoL Difficulties (SCI-QoL Bladder Management Difficulties), CIC (clean intermittent catheterization), CIC-BTX (CIC with current use of botulinum toxin), CIC-AUG (CIC with prior augmentation cystoplasty with or without catheterizable channel), age (in decades), BMI (body mass index), Years since injury (decades from injury), complete injury—American Spinal Injury Association Impairment Scale [ASI] "A" or if unknown participants asked if they had a complete or incomplete injury), assisted catheterization—complete reliance on others for catheterization, chronic pain—participants asked "do you experience chronic pain?", UTI (urinary tract infection), number of UTIs and hospitalization in last year, severe bowel dysfunction—Neurogenic Bowel Dysfunction Score ≥ 14. Multivariate linear regressions were used to compare NBSS score and each of its subdomain scores (Incontinence, Storage & Voiding, and Consequences), as well as Satisfaction across CIC types adjusting for covariates. For CIC (reference level of management type), predicted marginal means were reported with 95% confidence intervals (CIs), reflecting an average of model predictions when management type is CIC, at all combinations of levels of other categorical predictors weighted by the frequencies of these combinations in the data set with continuous variables set to their sample means. For other predictors in the model, regression coefficient, 95% CIs and *P* values were reported, indicating change in the outcome associated with the predictor.

[a]Predicted marginal means for CIC were reported with 95% confidence intervals (CIs), reflecting an average of model predictions when management type is CIC, at all combinations of levels of other categorical predictors weighted by the frequencies of these combinations in the data set with continuous variables set to their sample means.

[b]Estimated from the same model but switching the reference level to CIC-BTX.

One limitation of this study is that the nature of the survey data may have introduced inclusion bias into those responding and enrolling into the study. The study obviously involved bladder management problems and people with SCI and urinary problems may have enrolled in the study at higher rates in hopes of learning more about NGB. In addition, those participants with a history of augmentation cystoplasty may have confirmation bias, which might influence their bladder related QoL positively. Another limitation is that we lacked information about the timing of the last injection of botulinum toxin. Participants in the CIC-BTX group stated they were actively using botulinum toxin, however, it was not possible for us to determine whether they were in a therapeutic window of time to be considered actively treated with the drug. We also did not have any objective data on the function of the patients' bladders, such as bladder journals or urodynamic studies. This type of data could not be practically collected on such a diverse population of participants from across the United States and Canada. An additional limitation was the exclusion of patients that had creation of a catheterizable channel alone without augmentation cystoplasty. We were unsure if these patients would have QoL more like augmented patients or those never having had augmentation. After creation of a catheterizable channel nothing is fundamentally done to the bladder, which would eliminate spasticity or high pressures; however, patients may have had substantial improvements in QoL associated with facilitating their ability to catheterize. There were too few patients

TABLE 4 Secondary outcomes: Multivariate linear regression comparing NBSS subdomains, and the final question about satisfaction between patients performing CIC-BTX versus CIC, CIC-AUG versus CIC, and CIC-AUG versus CIC-BTX adjusting for patient characteristics

	NBSS Subdomains							
Variables	**Incontinence**	***P*-value**	**Storage & voiding**	***P*-value**	**Consequences**	***P*-value**	**Satisfaction**	***P*-value**
Bladder management								
CIC[a]	10.3 (9.7-10.9)		7.8 (7.5-8.1)		6.7 (6.4-6.9)		2.2 (2.1-2.3)	
CIC-BTX	0.39 (−0.77 to 1.54)	0.51	0.01 (−0.6 to 0.62)	0.97	0.3 (−0.2 to 0.7)	0.23	−0.16 (−0.36 to 0.04)	0.12
CIC-AUG	−2.75 (−4.09 to −1.42)	<0.001	−0.41 (−1.11 to 0.3)	0.26	−0.1 (−0.6 to 0.5)	0.81	−0.81 (−1.05to −0.58)	<0.001
CIC-AUG vs CIC-BTX[b]	−3.14 (−4.72 to −1.56)	<0.001	−0.42 (−1.25 to 0.41)	0.32	−0.3 (−1 to 0.3)	0.29	−0.65 (−0.93 to −0.37)	<0.001
Demographics								
Age	−0.3 (−0.67 to 0.08)	0.12	−0.21 (−0.4 to −0.01)	0.038	−0.2 (−0.3 to 0)	0.013	0 (−0.07 to 0.06)	0.95
Sex-Male	−2.85 (−3.8 to −1.91)	<0.001	−0.81 (−1.31 to −0.31)	0.002	−0.1 (−0.4 to 0.3)	0.78	−0.25 (−0.42 to −0.09)	0.003
Obese (BMI >30 kg/m^2)	1.34 (0.28-2.4)	0.013	0.3 (−0.26 to 0.86)	0.29	0.1 (−0.3 to 0.6)	0.49	−0.02 (−0.2 to 0.17)	0.85
Injury characteristics								
Level Tetraplegia	−2.99 (−4.06 to −1.92)	<0.001	0.27 (−0.3 to 0.83)	0.35	0.3 (−0.2 to 0.7)	0.25	−0.13 (−0.32 to 0.06)	0.18
Years since injury	−0.81 (−1.26 to −0.35)	<0.001	−0.21 (−0.4 to −0.01)	0.038	00.1 (−0.1 to 0.2)	0.49	−0.3 (−0.38 to −0.22)	<0.001
Complete injury	0.73 (−0.18 to 1.65)	0.12	−1.01 (−1.49 to −0.53)	<0.001	0 (−0.4 to 0.4)	0.98	−0.14 (−0.3 to 0.02)	0.09
Assisted catheterization	1.05 (−0.51 to 2.6)	0.19	−0.16 (−0.98 to 0.66)	0.70	0.8 (0.2-1.4)	0.013	0.08 (−0.19 to 0.36)	0.55
SCI complications								
Chronic Pain	0.72 (−0.21 to 1.66)	0.13	0.59 (0.1-1.08)	0.019	0.4 (0-0.8)	0.028	0.14 (−0.03-0.3)	0.10
Number of UTIs								
1-3	−0.02 (−1.09-1.06)	0.97	0.26 (−0.31 to 0.83)	0.37	1.7 (1.2-2.1)	<0.001	0.22 (0.03-0.41)	0.023
≥4	1.54 (0.29-2.79)	0.016	0.58 (−0.08 to 1.23)	0.09	3.5 (3-4.1)	<0.001	0.57 (0.35-0.78)	<0.001
Hospitalization for UTI	−0.11 (−1.57 to 1.35)	0.92	0.82 (0.04-1.59)	0.038	1 (0.4-1.6)	0.001	−0.22(−0.48 to 0.04)	0.09
Severe bowel dysfunction	0.86 (−0.02 to 1.74)	0.06	0.37 (−0.09 to 0.84)	0.12	0.4 (0.1-0.8)	0.019	0.25 (0.09-0.4)	0.002

NBSS (Neurogenic Bladder Symptom Score), CIC (clean intermittent catheterization), CIC-BTX (CIC with current use of botulinum toxin), CIC-AUG (CIC with prior augmentation cystoplasty with or without catheterizable channel), age (in decades), BMI (body mass index), Years since injury (decades from injury), complete injury—American Spinal Injury Association Impairment Scale [ASI] "A" or if unknown participants asked if they had a complete or incomplete injury), assisted catheterization —complete reliance on others for catheterization, chronic pain—participants asked "do you experience chronic pain?," UTI (urinary tract infection), number of UTIs and hospitalization in last year, severe bowel dysfunction—Neurogenic Bowel Dysfunction Score ≥ 14. Multivariate linear regressions were used to compare NBSS score and each of its subdomain scores (Incontinence, Storage & Voiding, and Consequences), as well as Satisfaction across CIC types adjusting for covariates. For CIC (reference level of management type), predicted marginal means were reported with 95% confidence intervals (CIs), reflecting an average of model predictions when management type is CIC, at all combinations of levels of other categorical predictors weighted by the frequencies of these combinations in the data set with continuous variables set to their sample means. For other predictors in the model, regression coefficient, 95% CIs and *P* values were reported, indicating change in the outcome associated with the predictor. Unless otherwise specified, results include the regression coefficient, 95% Cis, and *P* values, indicating the change in the outcome associated with each predictor.

[a]Predicted marginal means for CIC were reported with 95% confidence intervals (CIs), reflecting an average of model predictions when management type is CIC, at all combinations of levels of other categorical predictors weighted by the frequencies of these combinations in the data set with continuous variables set to their sample means.

[b]Estimated from the same model but switching the reference level to CIC-BTX.

undergoing creation of a catheterizable channel to perform a sub-analysis of QoL.

5 | CONCLUSIONS

Among patients performing CIC, those who underwent augmentation cystoplasty had better associated bladder function, fewer bladder management difficulties, and higher satisfaction than those performing CIC with or without botulinum toxin use. Our study provides reassuring data that as surgeons we are providing our patients with therapy that they rate as having positive impact upon bladder related function and QoL.

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CONFLICTS OF INTEREST

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REFERENCES

1. Weld KJ, Graney MJ, Dmochowski RR. Differences in bladder compliance with time and associations of bladder management with compliance in spinal cord injured patients. *J Urol*. 2000;163:1228–1233.
2. Weld KJ, Dmochowski RR. Effect of bladder management on urological complications in spinal cord injured patients. *J Urol*. 2000;163:768–772.
3. Cameron AP, Wallner LP, Forchheimer MB, et al. Medical and psychosocial complications associated with method of bladder management after traumatic spinal cord injury. *Arch Phys Med Rehabil*. 2011;92:449–456.
4. Lane GI, Driscoll A, Tawfik K, Chrouser K. A cross-sectional study of the catheter management of neurogenic bladder after traumatic spinal cord injury. *Neurourol Urodyn*. 2017.
5. Ginsberg D, Gousse A, Keppenne V, et al. Phase 3 efficacy and tolerability study of onabotulinumtoxinA for urinary incontinence from neurogenic detrusor overactivity. *J Urol*. 2012;187:2131–2139.
6. Quek ML, Ginsberg DA. Long-term urodynamics followup of bladder augmentation for neurogenic bladder. *J Urol*. 2003;169:195–198.
7. Adriaansen JJ, van Asbeck FW, Tepper M, et al. Bladder-emptying methods, neurogenic lower urinary tract dysfunction and impact on quality of life in people with long-term spinal cord injury. *J Spinal Cord Med*. 2017;40:43–53.
8. Anquetil C, Abdelhamid S, Gelis A, Fattal C. Botulinum toxin therapy for neurogenic detrusor hyperactivity versus augmentation enterocystoplasty: impact on the quality of life of patients with SCI. *Spinal Cord*. 2016;54:1031–1035.
9. Patel DP, Lenherr SM, Stoffel JT, et al. Study protocol: patient reported outcomes for bladder management strategies in spinal cord injury. *BMC Urol*. 2017;17:95.
10. Welk B, Morrow S, Madarasz W, Baverstock R, Macnab J, Sequeira K. The validity and reliability of the neurogenic bladder symptom score. *J Urol*. 2014;192:452–457.
11. Welk B, Lenherr S, Elliott S, et al. The Neurogenic Bladder Symptom Score (NBSS): a secondary assessment of its validity, reliability among people with a spinal cord injury. *Spinal Cord*. 2018;56:259–264.
12. Tulsky DS, Kisala PA, Victorson D, et al. Overview of the Spinal Cord Injury-Quality of Life (SCI-QOL) measurement system. *J Spinal Cord Med*. 2015;38:257–269.
13. Tulsky DS, Kisala PA, Tate DG, Spungen AM, Kirshblum SC. Development and psychometric characteristics of the SCI-QOL Bladder Management Difficulties and Bowel Management Difficulties item banks and short forms and the SCI-QOL Bladder Complications scale. *J Spinal Cord Med*. 2015;38:288–302.
14. Krogh K, Christensen P, Sabroe S, Laurberg S. Neurogenic bowel dysfunction score. *Spinal Cord*. 2006;44:625–631.
15. R Core Team, *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing; 2017.
16. Costa P, Perrouin-Verbe B, Colvez A, et al. Quality of life in spinal cord injury patients with urinary difficulties. Development and validation of qualiveen. *Eur Urol*. 2001;39:107–113.

17. Akkoc Y, Ersoz M, Yildiz N, et al. Effects of different bladder management methods on the quality of life in patients with traumatic spinal cord injury. *Spinal Cord*. 2013;51:226–231.
18. Cruz F, Herschorn S, Aliotta P, et al. Efficacy and safety of onabotulinumtoxinA in patients with urinary incontinence due to neurogenic detrusor overactivity: a randomised, double-blind, placebo-controlled trial. *Eur Urol*. 2011;60:742–750.
19. Schurch B, Denys P, Kozma CM, Reese PR, Slaton T, Barron R. Reliability and validity of the Incontinence Quality of Life questionnaire in patients with neurogenic urinary incontinence. *Arch Phys Med Rehabil*. 2007;88:646–652.

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