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Outcomes In The Urologic Management Of Neurogenic Bladder In Spinal Cord Injured Patients

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ABSTRACT

The main objective of this study was to retrospectively report our institutional outcomes with the long-term management of neurogenic bladder in spinal cord injury patients. Specifically to: (A) report the association of recurrent urinary tract infection (UTI) with the long-term use of clean intermittent catheterization (CIC) in our population of spinal cord injury (SCI) patients. (B) Secondly, to evaluate the use of retroperitoneal ultrasound for long-term renal tract surveillance in injured patients. (C) And thirdly, to describe our experience with the use of the lowsley retractor method for suprapubic cystostmy in patients with neurogenic bladder.

Subjects were selected from patients followed by one physician at the Yale Urology Medical Group and their medical records were retrospectively reviewed. To address objectives (A) and (B), patients were identified after a search of the Financial Department's database with diagnosis codes for "neurgenic bladder" and "Spinal cord injury." Patients seen between the years 2000 to 2010 were included in the study. For objective (C), patients were identified with diagnosis code for "cystostomy" and patients seen between 1995 and 2010 were included in the study.

For objective (A), 51 male and 10 female subjects were managed with CIC. 41 (67%) subjects were placed on medical prophylaxis (PRx) for symptomatic recurrent UTI. 28 (72%) subjects were started on PRx within 2 years after initiation of CIC. 48 SCI patients were included in objective (B). Mean follow-up was 6.8 years. By final follow-up 7 (15%) subjects had moderate/minimal hydronephrosis. 4 (8%) cases were new compared to initial assessment. No severe cases of hydronephrosis were noted. For objective (C), 49 primary catheter placements were performed on 44 patients. Operation-

time documented in 19 (39%) cases was 20.2 min (±5.5) (range: 11-31 min). Blood loss was minimal and there were no intra-operative complications or cases of incorrect catheter placements.

The improved life expectancy of SCI patients in recent decades makes long-term complications of neurogenic bladder management more pertinent. Although CIC is the current standard of care following SCI, recurrent UTI remains a major complication in patients using this technique. Due to a lack of standard guidelines for long-term renal tract monitoring in injured patients, there is wide variation in surveillance strategies. Our results suggest that annual retroperitoneal ultrasound is effective for renal tract monitoring rather than subjecting patients to annual urodynamic testing. Furthermore, the improved anticholinergic therapy makes suprapubic catheters an acceptable alternative to intermittent catheterization. Our findings support the use of the lowsley retractor method of suprapubic catheter placement as a safe and effective method for isolated suprapubic cystostomy in neurogenic bladder patients.

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Abstracts

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INTRODUCTION

Renal disease resulting from neurogenic voiding dysfunction has historically been the leading cause of death in individuals with spinal cord injury (SCI). The decision to create special spinal injury units within selected hospitals during the Second World War prompted the modern era of treatment of spinal cord injured persons [1]. These regional specialized treatment units played an important role in studying and better understanding the needs of injured patients [2]. Subsequent advances in urologic management are credited for the improved survival in this patient population [3] and life-long urologic follow-up is critical to maintain quality of life and minimize urinary tract associated morbidity. The improved life expectancy in SCI patients attained by these advances in urologic care makes long-term complications of the urinary tract more pertinent, therefore mandating continued research related to urinary tract dysfunction.

The Neurogenic Bladder in Spinal Cord Injury

Neurogenic bladder (NGB) is broadly defined as the abnormal function of the urinary bladder secondary to any neurologic condition of the central nervous system or the peripheral nerves involved in the control of micturition [4]. Such neurologic conditions include spinal cord injury (SCI), neural tube defects, multiple sclerosis (MS), brain tumors as well as other diseases of peripheral nerves. In order to minimize the variability in subjects, this work specifically focuses on cases of neurogenic bladder caused by traumatic spinal cord injury.

It is estimated that about 12,000 new cases of spinal cord injury occur in the United States each year, with an estimated prevalence of 262,000 persons in the year

2009 [5]. Alteration in the function of the lower urinary tract is one of the most problematic consequences of spinal cord lesions resulting in urologic complications following SCI. Although the mortality related to such complications has been significantly reduced in recent decades [6], urinary tract problems remain a prominent cause of morbidity [7]. These problems account for the majority of hospital readmissions following SCI [8] and necessitate life-long urologic follow up as a central component in the routine care of injured patients.

The effect of spinal cord injury on the urethral sphincter and on the function of the detrusor muscle is the cause of neurogenic bladder dysfunction [9]. The degree of damage to the voiding cycle depends on the location, completeness as well as the vascular extension of the injury. A model of supraspinal bladder control is suggested by brain imaging studies. According to this model afferent signals from the lower urinary tract are received in the periaqueductal gray and relayed via the thalamus to the insula (which makes sensations accessible to conscious awareness). The cortex (via the anterior cingulate gyrus) monitors and controls micturition reflexes and also makes voluntary voiding decisions (via the prefrontal cortex) [10].

The normal micturition reflex is thought to be mediated by an area of the pons known as the pontine micturition center (PMC) or Barrington nucleus. This region coordinates the activity of the detrusor and urethral sphincter muscles [11, 12, 13]. The tip of spinal cord is located in the L1/L2 level of the vertebrae, however the detrusor muscle of the bladder and the internal urethral sphincter are innervated by parasympathetic sacral nerve roots (S2-S4) via the pelvic splanchnic nerve, in addition to some sympathetic innervation by T10-L2 nerve roots via the hypogastric nerve. On the other hand, the external urethral sphincter is innervated by somatic sacral nerve roots (S2-S4) via the pudendal nerve. Injuries to the lumbar spine can destroy the conus of the cord or the cauda equina resulting in the loss of sacral reflexes. The loss of sacral reflex activity will produce detrusor areflexia (DA), and flaccid paraplegia. Since injuries to the cervical and thoracic regions of the cord occur above the conus they typically cause detrusor hyperactivity (DH) and detrusor external sphincter dyssynergia (DESD), which describes the contraction of the bladder against a closed external sphincter. Quadriplegia may be observed if a complete cervical injury occurs.

The urologic function following SCI is generally categorized into three phases: (1) spinal shock, (2) recovery, and (3) stable phases [14]. Immediately following the initial injury, the swelling of the spinal cord fills the spinal canal and prevents oxygenation and blood flow to the spinal cord tissue. This precipitates spinal shock, which involves a temporary loss of function in the undamaged areas of the spinal cord causing the inhibition of all reflexes and function distal to the level of injury and resulting in a flaccid detrusor [15]. The recovery phase refers to the return of reflex activity and marks the end of spinal shock. Following the recovery phase, a fairly stable urodynamic picture is observed, this marks the stable phase and it represents the period when there are no further signs of neurologic recovery.

Bladder Management with Catheterization

Various modalities are employed in the management of neurogenic bladders after the stable phase is reached. Common catheterization methods include the use of clean intermittent catheters, indwelling urethral catheters, or indwelling suprapubic catheters.

The technique of clean intermittent catheterization was introduced in 1972 [16] and involves the passage of a clean (non-sterile) straight catheter through the urethra to empty the bladder. Catheterization is typically done about 4 to 6 times daily. Indwelling urethral catheterization involves leaving a trans-urethral foley catheter in the bladder, secured by a balloon, with a drainage bag attached usually to the thigh. The catheter is typically replaced every 3 to 4 weeks. An indwelling suprapubic catheter involves the creation of a surgical vesicostomy through the lower abdominal wall to allow a catheter to be placed into the bladder suprapubically. The tube is also replaced every 3 to 4 weeks.

Individuals managed with long-term urinary catheters are at risk for many serious complications including: urethral complications such as the formation of strictures and false passages, chronic obstruction due to urinary calculi and periurethral infections including epididymitis and prostatitis. Other associated complications include life threatening complications such as pyelonephritis and bladder cancer.

The optimal catheterization method for managing the neurogenic bladder remains controversial because no randomized studies have been done to determine which method of catheterization is superior in the long-term management of spinal cord injured patients. Many studies addressing this topic have reached different conclusions. In a comparative study of 80 patients in Karachi Pakistan, Turi and colleagues found intermittent catheterization to be superior to indwelling catheterization with respect to complications and infections rates [17]. And a retrospective study of 316 posttraumatic spinal cord injured patients with a mean follow-up of 18 years concluded that CIC is the safest method of bladder management with respect to urological complications [18]. On the other hand, a comparative study in Helsinki, Finland, by Dahberg and associates found a lower incidence of UTI's in patients managed with suprapubic tapping compared to those with intermittent catheterization [19]. Other studies have not found significant differences in the incidence of urological complications between spinal cord injury patients managed with or without a bladder catheter [20].

The most recent Cochrane review addressing this issue included about 400 studies comparing these methods and found no evidence from randomized or quasi-randomized controlled trials to draw any conclusions about the use of catheters [21]. The panel of experts at the Infectious Diseases Society of America (IDSA) similarly determined, in 2009, that there was insufficient evidence to recommend whether: suprapubic catheterization was superior to indwelling urethral catheterization or whether intermittent catheterization is superior to supra-pubic catheterization for reduction of catheter associated urinary tract infection (UTI) [22].

Regardless of the lack of randomized controlled trial to determine the superior catheterization method, clean intermittent catheterization is popularly believed to be associated with fewer complications compared with indwelling catheters and it is widely accepted as the preferred method of bladder management. Hill and Davies, in 1988, proposed the use of self intermittent catheterization as the preferred bladder management method in all spinally injured patients with good hand function [23]. This technique was recommended by the international consortium on incontinence, in 2010, as the first choice for individuals that are unable to empty their bladder adequately and safely [24].

A Second Line in Bladder Management

Indwelling suprapubic catheterization is currently used as a second-line for neurogenic bladder management in appropriate patients usually after failed CIC or severe urethral damage [25]. A recent review on the role of SPC in treatment of NGB suggests that although early reports of long-term renal and bladder complications discouraged its use for long-term NGB management, current improved pharmacotherapy with anti-cholinergics and better bladder maintenance strategies may have improved its efficacy [26]. Sheriff et al. reported that 82% of patients with long-term suprapubic catheters indicated that it positively improved their quality of life [25]. The placement of suprapubic catheters in NGB patients is often done as an isolated procedure and is thought to have a low associated risk. However, the risk of intra-operative and post-operative complications has been demonstrated to be higher in patients with NGB compared to those with other lower urinary tract dysfunction. Ahluwalia et al. reported a 34% overall complication rate in NGB patients compared to 18% in patients with other forms of bladder outflow obstruction (P = 0.057) and recommended that such high-risk cases be performed in a controlled environment with senior surgeon and anesthesia present [27].

Suprapubic catheter placement can be done with an open technique or by using one of the various percutaneous or other minimally invasive methods [28]. Each approach has its limitations; the open technique is considered the definitive gold-standard but it requires a larger incision, with potentially longer operative time, and more blood loss [29]. The risk of complication using blind percutaneous technique is low but such complication can be fatal. Such risks include through and through puncture of the bladder and potential injury to the bowel [30]. Ahluwalia et al. described a 2.5% risk of bowel injury and 1.8% mortality rate in a retrospective report of their experience with 219 cases of SPC under cystoscopic guidance. The imaging guided technique was introduced to reduce the risks associated with the percutaneous approach [31]. Cronin and colleagues recently reported their experience with the imaging-guided approach in a review of SPC performed on 549 patients by skilled interventional radiologists using either the trocar or seldinger technique [32]. Their procedures involved transurethral distention of the bladder with contrast material and imaging-guided cystostomy using a combination of ultrasound and fluoroscopy. The use of ultrasonography however is limited by the skill of the practitioner and a disadvantage of fluoroscopy is the risks associated with exposing patients to ionizing radiation.

Long-Term Complications

SCI patients suffer from various degrees of detrusor dysfunction, including hyperreflexia, areflexia, detrusor sphincter dyssynergia, poor compliance and chronic urinary tract infection. Urodynamic testing is thought to be the most important predictor of the urologic outcome [33]. This test measures the pressure in the bladder and the electrical activity of the urethral sphincter to determine the effects of the neurological injury. It is used to define the type of neurogenic dysfunction and for planning the bladder management strategy. The findings of urodynamic testing after the patient is beyond the spinal-shock phase should determine the long-term bladder management strategy [14].

Amongst the most common urologic manifestations of neurogenic voiding dysfunction is the problem of recurring UTIs. The vast majority of UTIs are caused by organisms that are commonly present in the bowel and on the perineal skin, including gram-negative bacilli and enterococci [7]. Factors contributing to risk of UTI in persons with SCI include incomplete emptying of the bladder, low bladder wall compliance and insertion of urinary catheters.

Due to the widespread use of urinary catheterization, bacteriuria associated with the use of catheters is the most common healthcare-assocaited infection worldwide [22]. Long-term indwelling urinary catheterization inevitably results in lower urinary tract colonization. Significant levels of bacteria can be seen in the urine of patients managed by an indwelling catheter within 72 hours of insertion, and levels of bacteria increase 5% to 8% per day [34]. In comparison, while the likelihood of chronic bacteriuria is also increased by CIC, it is believed that this risk is offset by the benefit of not having the continued presence of a foreign object in the lower urinary tract.

There is an important distinction between asymptomatic bacteriuria and symptomatic urinary tract infections. Most neurogenic bladder patients will have bacteriuria yet they remain free from symptoms associated with a UTI and can be described as having “asymptomatic bacteriuria.” An immune response triggered by bacterial invasion of the bladder wall causes the symptoms of “clinical UTI [35].” While an increased risk of symptomatic UTI is associated with asymptomatic bacteriuria, the use of antibiotics is not indicated unless UTI symptoms develop [15].

The routine use of antimicrobial prophylaxis remains controversial due to many conflicting results from studies looking at its efficacy in preventing infections. A meta-analysis of 15 controlled trials did not find a significant reduction in symptomatic infections when prophylactic antimicrobials were administered, rather, the use of antimicrobial prophylaxis was found to double the amount of antimicrobial-resistant organisms [36]. Routine cultures in healthy asymptomatic patients are similarly discouraged since the practice causes an unnecessary treatment of bacteriuria [37].

Beyond urinary tract infections, renal deterioration is a fatal long-term consequence of poor bladder management. The goal of urologic management in SCI is to prevent upper tract deterioration and maintain continence. Renal deterioration leading to renal failure is principally caused by vesicoureteral reflux, chronic pyelonephritis, renal stone formation and hydronephrosis [38]. Normal bladder function requires urine storage at low intravesical pressure without leakage. Therefore, efforts to preserve adequate urinary tract function must maintain adequate detrusor pressures.

McGuire and colleagues in 1983 determined that high detrusor leak point pressure was related to upper tract deterioration [39]. Outlet obstruction associated with detrusor leak point pressure greater than 40 cm is now considered the major risk factor for upper tract deterioration [40, 41]. It is explained that an elevated urethral resistance causes deterioration in compliance that results in an increased detrusor pressure (Pdet). The increased Pdet is transmitted to the ureter consequently increasing the ureteral work until it reaches a limit at about 40 cm of water. At this point the delivery of urine from the ureter to the bladder ceases. It is therefore believed that the effects on the ureter seen by imaging are late rather than immediate changes of lower tract dysfunction [42].

Urinary Tract Surveillance

There are no standard guidelines established to routinely monitor the urinary tract in spinal cord injury patients due to the low availability of data relating to the value of various routine surveillance methods. This has resulted in wide variability in renal tract surveillance strategies in practices around the world [43, 44]. Most urological centers prefer annual monitoring of upper and lower urinary tract function with either an upper tract study or a compliance test [45]. The European Association of Urology (EAU) recommends video-urodynamic investigation every 2 years for patients with normal bladder compliance who do not have detrusor overactivity. And recommend annual video-urodynamics for patients with detrusor overactivity and/or low bladder compliance [46]. Although well tolerated by patients [47], conventional urodynamic testing is sometimes avoided because it is expensive and carries a risk of urinary tract infection [48]. Nosseir and colleagues retrospectively investigated the long-term results of 80 SCI patients managed at their institution with a strictly urodynamic-based treatment regime and determined that physiologic changes in bladder function can occur in the absence of changes in overall symptoms thus they recommended annual urodynamic testing in patients with detrusor overactivity [49]. It is our position that renal tract changes can be detected on routine ultrasonographic surveillance to obviate the use of regular urodynamic testing.

Statement of purpose

The primary objective of this investigation was to report outcomes related to the urologic management of our spinal cord injury patients with neurogenic bladder.

Specifically:

a) *To study the association of recurrent symptomatic urinary tract infections (UTI) with the long-term use of clean intermittent catheterization (CIC) for the management of neurogenic bladder in spinal cord injury (SCI) patients.*

b) *To report our experience with the lowsley retractor method for suprapubic cystostomy (SPC) in patients with neurogenic bladder (NGB).*

c) *To evaluate the efficacy of annual ultrasonography rather than regular urodynamic testing for upper tract surveillance in spinal cord injury (SCI) patients managed with long-term intermittent catheterization.*

METHODS

This study was approved by the institutional review board at Yale University School of Medicine. Subjects were selected from patients followed by one physician at the Yale Urology Medical Group and their medical records were retrospectively reviewed. All patient visits at the urology clinic were logged by the Patient Financial Services Department under corresponding diagnosis codes and clinic visits or phone calls were recorded in patient charts by the same physician after each encounter.

a) In order to determine the association of UTI with the long-term use of CIC in our spinal cord injury patients, the following criteria was employed (Figure 1).

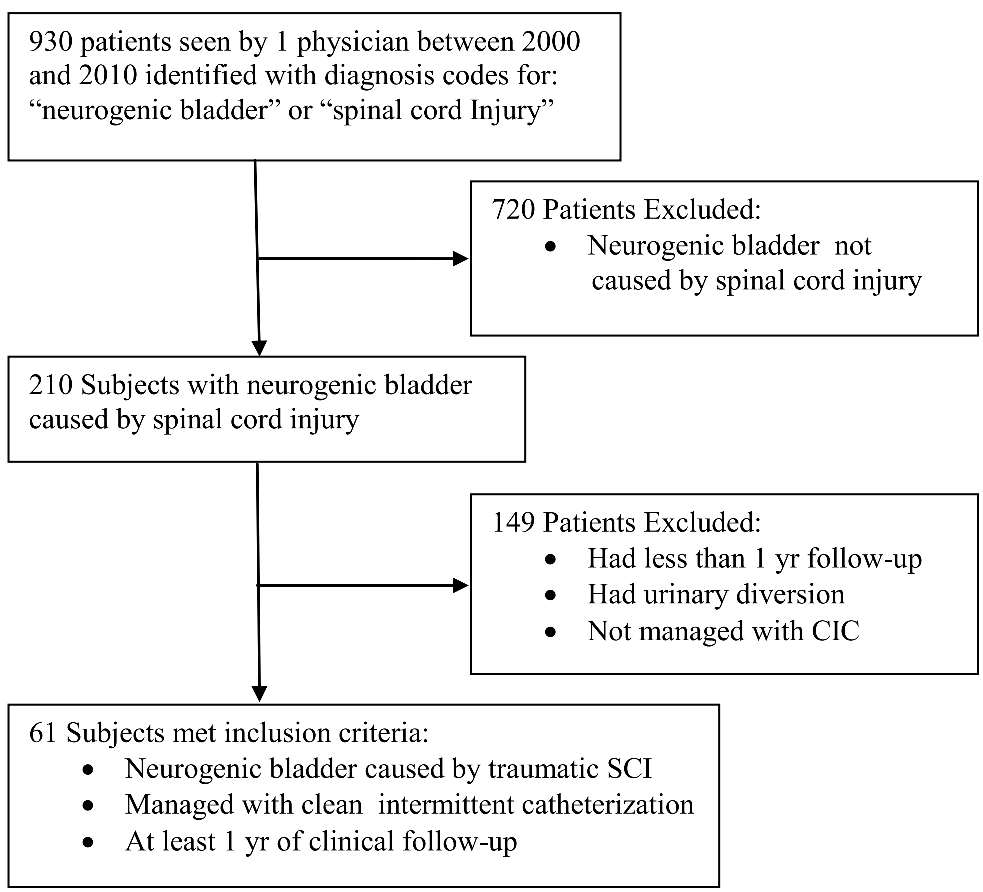

Figure 1: Application of inclusion and exclusion criteria to determine association of UTIs with the long-term use of CIC. CIC = clean intermittent catheterization; SCI = spinal cord injury; UTI = urinary tract infection.

Inclusion criteria: neurogenic bladder dysfunction; stable traumatic spinal cord injury at least one year after injury; bladder management with clean intermittent catheterization; minimum of one year follow-up by the same physician at the Yale Urology Clinic; patient seen between the years 2000 and 2010.

Exclusion criteria: other etiology for neurogenic bladder such as multiple sclerosis, parkinson's disease, spina bifida or diabetes; other methods of bladder management including other catheterization methods, crede maneuver or patients with urinary diversion.

A list of 930 potential subjects was generated by a search of the Financial Services records using diagnosis codes for "neurogenic bladder (596.54)" or "Spinal Cord Injury (952.9)." The search was limited to patients seen by the same physician at the Yale Urology Medical Group between the years 2000 and 2010. Initial review of the clinical records eliminated 720 potential subjects who had neurogenic bladder from other etiology but did not have traumatic spinal cord injury. Of the 210 spinal cord injury patients with neurogenic bladder, another 149 subjects were excluded either because they had neurogenic bladder managed by methods other than clean intermittent catheterization or had undergone urinary diversion. Only 61 traumatic spinal cord injury subjects with neurogenic bladder managed by intermittent catheterization and followed for at least one (1) year after spinal cord injury were included in this study (Table 1).

Table 1. Patient characteristics	
Age (y)	43.4 ± 16.3
Sex (n)	
Male	51 (84)
Female	10 (16)
Injury level (n)	
Cervical	24 (39)
Thoracic	24 (39)
Lumbar	12 (20)
Sacral	1 (2)
Independence (n)	
Paraplegic	35 (57)
Tetraplegic	18 (30)
Independent	8 (13)
Duration of catheterization (y)	
Before initiating PRx	2.7 ± 3.3
Subjects not requiring PRx	7.2 ± 3.8
Duration of follow-up (y)	5.8 ± 4.1
Use of UTI PRx	
Yes	41 (67)
No	20 (33)

Data presented as mean ± SD, unless noted otherwise; data in parentheses are percentages. PRx = prophylaxis; UTI = urinary tract infection.

Data Gathering

For each research subject the following data points were recorded on Excel:

- Age
- Gender
- Level of spinal injury
- Amount of independence
- Mean years of follow-up at Yale
- Time elapsed since initial injury
- Frequency of catheterization
- Presence of incontinence
- Ultrasound findings
- Number of positive urine cultures
- Use of UTI prophylaxis
- Years after injury before using prophylaxis
- Type of UTI prophylaxis
- Number of symptomatic UTIs in last year
- Number of positive cultures in the year prior to starting prophylaxis
- Urodynamic findings
- Pharmacologic control of detrusor
- Surgical control of detrusor
- Number of symptomatic UTIs in last year

All complications of bladder management were recorded based on the status of subjects at the time of their last urologic follow-up at Yale.

Outcome model

Patients experiencing recurrent UTI were identified by their continued use of medical UTI-prophylaxis (PRx) at the time of last clinical follow-up. Medical PRx in this case is defined as the use of either oral antibiotics or methenamine with ascorbic acid to decrease the frequency of UTIs. Subjects were started on PRx when they had experienced ≥ 3 UTIs within a one (1) year period. For subjects on UTI prophylaxis, the recurrent and symptomatic nature of their infections was verified by the number of positive cultures occurring within a year prior to starting prophylaxis. Subjects were not placed on PRx if they have not had at least three episodes of symptomatic UTI within a one year period. For each subject not placed on UTI prophylaxis, the number of symptomatic UTIs occurring in their final year of follow-up was recorded based on the number of times patients complained of UTI symptoms including cloudy/malodorous urine, increased incontinence, fever, chills and bladder spasms. Where available the number of positive cultures was also recorded. All cultures were done only after subjects complained of UTI symptoms and were considered positive when subjects had greater than 10^3 colony forming units (cfu)/ml of ≥ 1 organism.

b) Regarding the use of renal ultrasonography rather than regular urodynamic testing as a routine surveillance method in spinal cord injury patients, data was extracted from subjects identified in specific objective (a) who met further inclusion and exclusion criteria.

Subjects included in this objective had received initial urodynamic testing to guide their pharmacologic and catheterization regimen. After a safe system had been established, routine upper tract surveillance was done annually with ultrasonography of the renal tracts and bladder to monitor urinary tract stability. Urodynamic testing was repeated only when patients presented with new symptoms such as persistent urinary tract infections, increased leakage between catheterization, or with abnormal findings on ultrasonography.

Data was gathered retrospectively from the medical records of 48 subjects (40 males and 8 females) who were included in the study. The inclusion criteria were: NB secondary to SCI; a minimum of one year follow-up at our institution; NB management with IC; and annual upper tract surveillance with retroperitoneal ultrasound. The primary endpoint was the presence or absence of abnormal ultrasound findings at the time of last renal tract surveillance. Specifically the finding of hydronephrosis/pelvicaliectasis, renal/ureteral calculi, and renal cortical scarring/thinning were noted. The duration of ultrasound follow-up, degree of disability, and baseline ultrasound and urodynamic findings were also noted.

c) In order to report our institutional experience with the lowsley retractor method for suprapubic cystostomy, cases were evaluated as follows:

Subjects were selected from patients undergoing suprapubic cystostomy by one surgeon at the Yale Urology Medical Group. A search of the billing department database was conducted with the procedure code for “cystostomy.” A list of 90 patients was generated and the medical records of these patients were retrospectively reviewed. Patients with neurogenic bladder, who underwent elective suprapubic cystostomy using the lowsley retractor method between the years 1995 and 2010 were included. Patients who underwent cystostomy as part of other surgical procedures were excluded. The age and gender of subjects as well as the indication, anesthesia type, catheter size, blood loss, fluids administered, complications and duration of the procedure were recorded.

Statistical Analysis

All analyses were done with SPSS statistics version 17.0. For comparisons of the mean age in males and females the student's *t*-test was used. Data were represented as counts and percentages for categorical variables. Means and standard deviations were used for continuous variables. $P < 0.05$ was considered statistically significant.

RESULTS

a) Of 210 SCI patients with neurogenic bladder only 61 subjects, (51 males and 10 females met the inclusion criteria for specific objective (a).

The mean age of the 61 subjects was 43.4 years (± 16.3) (range: 12-86 years). The age were similar for male and female subjects; 43.5 years (± 16.5) and 43.2 years (± 15.5) respectively. The mean duration of follow-up for all subjects was 5.8 years (± 4.1) (range: 1-16 years). 18 (30%) subjects were quadriplegic, 35 (57%) were paraplegic and 8 (13%) subjects were fully independent; having neurogenic bladder with preserved upper and lower limb functions (Table 1).

Figure 1 illustrates the proportion of male, female and all subjects requiring prophylaxis at the time of last follow-up.

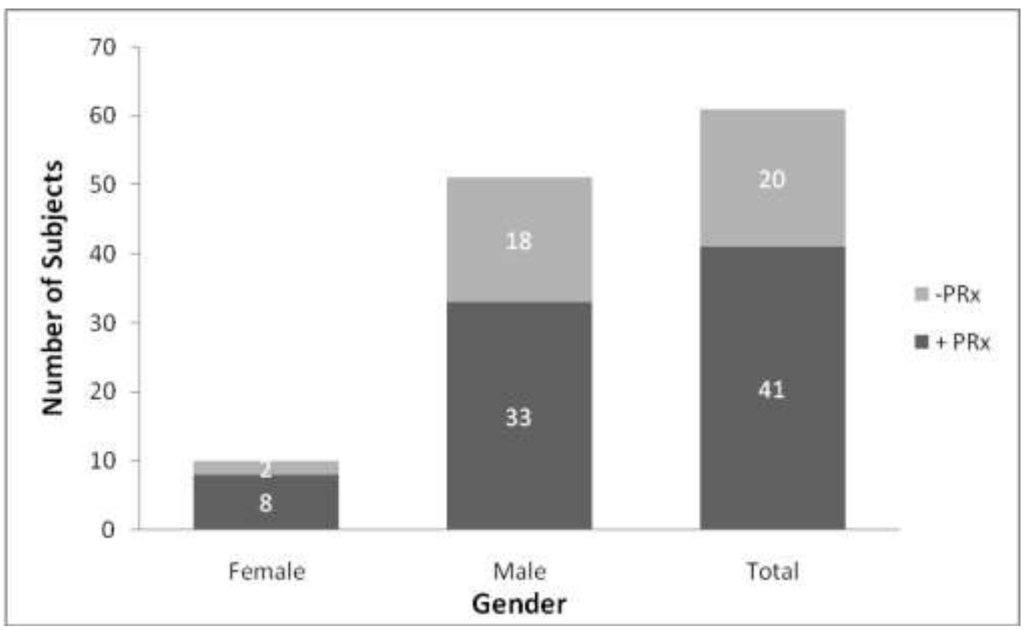

Figure 1. ***Subjects on PRx by Gender.*** *Bar graph illustrates number of subjects on UTI prophylaxis by gender and by total number of subjects. +PRx = subjects using prophylaxis; -PRX = Subjects not using prophylaxis; UTI = urinary tract infection*

The initial date of PRx use was noted in 39 of 41 subjects and the results demonstrate that 28 (72%) were started on PRx within 2 years after initiation of CIC (Figure 2). The mean duration of follow-up for subjects on PRx as well as for those not using PRx are provided in Table 1. The date of initial catheter use was noted in 18 of the 20 (90%) subjects not requiring PRx.

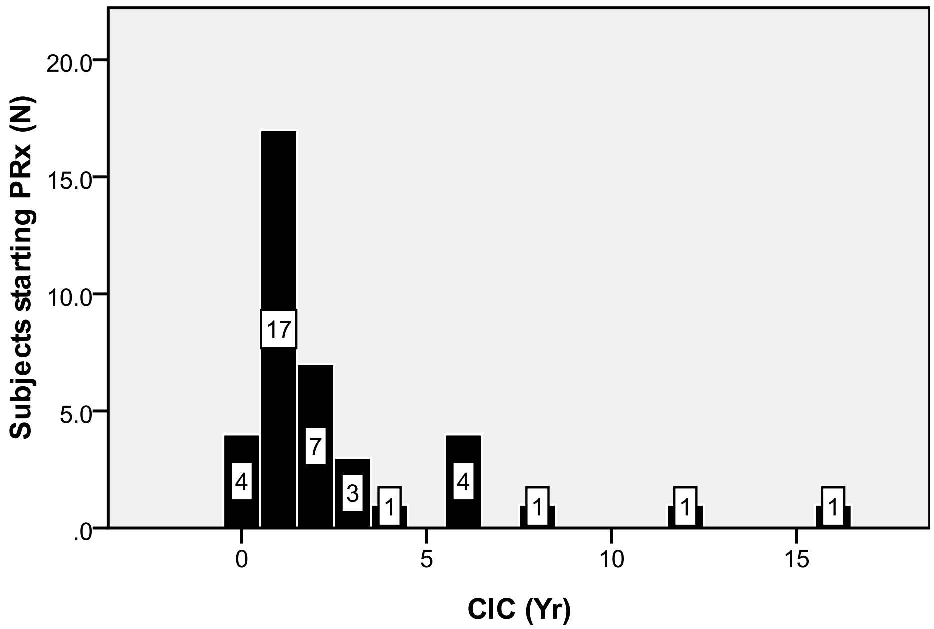

Figure 2. ***Subjects on PRx by years after starting CIC.*** *Bar graph illustrates number of subjects started on UTI prophylaxis based on the number of years after starting CIC. CIC = clean intermittent catheterization; PRx = prophylaxis; UTI = urinary tract infection.*

Table 2 lists the number and percentage of subjects on UTI PRx with the number of positive cultures, $\geq 10^3$ cfu/ml, available within the year prior to starting them on PRx. Culture results were not available for 11 (27%) of these subjects. Of the 20 subjects not placed on UTI PRx, 15 had no complaints of UTI symptoms in the final year of follow. The remaining 5 subjects were each noted to have had only one complaint of symptomatic UTI. Three of these subjects had a positive culture, ≥ 10^3cfu/ml, each. Culture results were not available for the other 2 subjects.

Table 2. Culture Results for Subjects on UTI PRx	
Cx ≥ 10^3 cfu	*n* (%)
≥3	17 (41)
2	7 (17)
1	6 (15)
Cx = cultures; cfu = colony forming units; UTI = urinary tract infection; PRx = prophylaxis.	

b) Of the spinal cord injury patients identified in specific objective (a), 48 subjects met criteria for inclusion in the evaluation of renal tract ultrasonography as a long-term surveillance method.

The mean age of these subjects was 44.8 years (range: 13-84 years) (**Table 3)**. Included subjects had been followed for a mean duration of 6.8 years (±3.7) (range: 2-16 years). 26 (54%) subjects were paraplegic, 16 (33%) subjects were quadriplegic and 6 (13%) subjects had adequate function of all extremities. On average subjects were followed with ultrasonography for 5.2 years (±2.6) (range: 1-9 years) and the average time between the most recent urodynamic testing and the last ultrasound follow-up was 4.8 years (±3.3).

Table 3. Patient Characteristics	
Age (y)	44.8 (range: 13-84)
Sex (n)	
Male	40 (83)
Female	8 (17)
Injury level (n)	
Cervical	22 (46)
Thoracic	16 (33)
Lumbar	10 (21)
Disability (n)	
Paraplegia	26 (54)
Quadriplegia	16 (33)
Independent	6 (13)
Duration of follow-up (y)	6.8 (±3.7)
Duration of U/S follow-up (y)	5.2 (±2.6)

Data presented as mean ± SD, unless noted otherwise; data in parentheses are percentages. U/S = ultrasound.

Table 4 shows the results of the most recent urodynamic testing in 45 (94%) subjects. Results of recent urodynamic testing were not available for three subjects.

Table 4. Most recent urodynamic findings	
DO	36 (80)
DA/DU	9 (20)
Pseudo-DSD	1 (2)
DSD	9 (20)
Decreased bladder compliance	9 (20)

Data presented as counts (n); data in parenthesis are percentages. DO = detrusor overactivity; DA = detrusor areflexia; DU = detrusor underactivity; DSD = detrusor sphincter dyssynergia.

The results of initial and final ultrasonography exams are illustrated in **Figure 3**. At the time of initial retroperitoneal ultrasound, a small renal calculus was present in 1 (2%) subject, 6 (13%) subjects were noted to have cortical scarring and moderate to minimal hydronephrosis/caliectasis were found in 5 (10%) subjects. 2 of the 5 cases of upper tract dilation that were present on initial ultrasound had completely resolved by the final follow-up exam.

At the time of last follow-up, final ultrasonography demonstrated small renal/ureteral calculi in 5 (10%) subjects of which one case was stable compared to the initial exam. No new cases of renal cortical scarring/thinning were noted and 3 cases of scarring were stable compared to the initial, while the other 3 cases that were previously noted on initial ultrasound were not reported in the final ultrasound exams.

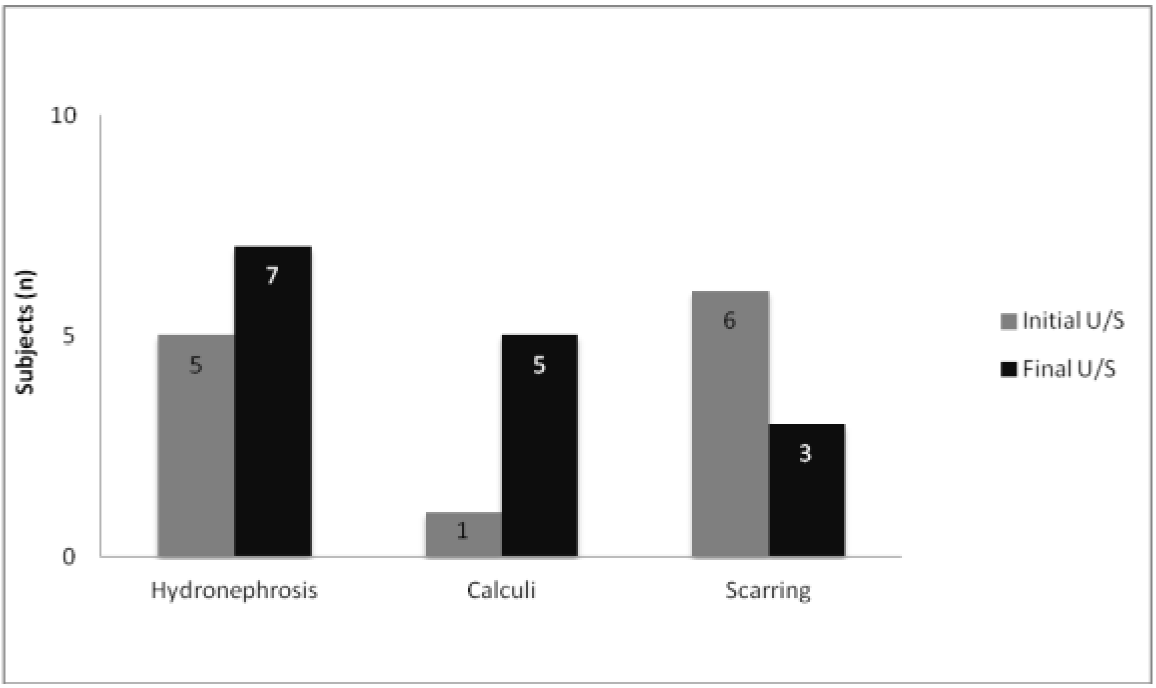

Figure 3*.Comparison of Initial vs Final Ultrasound Findings.* *Bar graph illustrates the changes in retroperitoneal ultrasound findings between the initial ultrasound and the final ultrasound at last follow-up. Hydroneph = hydronephrosis; U/S = ultrasound.*

Moderate to minimal hydronephrosis/caliectasis was present in 7 (15%) subjects at the time of the final surveillance. Of these, 3 cases were stable and 4 (8%) cases were new compared to the initial assessment. 3 of the 4 new cases of mild hydronephrosis were secondary to obstruction by ureteral calculi in 2 cases and by an enlarged prostate in the third. The three subjects were treated with laser lithotripsy, extra-corporeal shockwave lithotripsy and finasteride respectively. No cases of severe hydronephrosis occurred.

c) For suprapubic cystostomy using the lowsley retractor method, 49 elective cases of primary suprapubic catheter placements were performed on 44 patients with neurogenic bladder using a curved lowsley retractor. 23 (52.3%) males and 21(47.7%) females underwent the procedure (Table 5).

Table 5. Patient characteristics

Age (Yr)	44.7 (± 18.0) (range: 18-86)
Sex (n)	
Female	21 (47.7)
Male	23 (52.3)
NGB Etiology (n)	
Spinal cord injury	29 (65.9)
Multiple sclerosis	9 (20.5)
Cerebral palsy	1 (2.3)
Spina bifida	1 (2.3)
Spinocereballar ataxia	1 (2.3)
Amytropic lateral sclerosis	1 (2.3)
Parkinson’s disease	1 (2.3)
Anticholinergic side effect	1 (2.3)

Data presented as mean ± SD, unless noted otherwise; data in parentheses are percentages. NGB = neurogenic bladder

The etiology of neurogenic bladder was spinal cord injury in 29 (65.9%) subjects and multiple sclerosis in 9 (20.5%) subjects. The other 6 (13.6%) patients had neurogenic bladder from spina bifida, spinocereballar ataxia, cerebral palsy, amyotropic lateral sclerosis, parkinson’s disease and anticholinergic medication side effect. The mean age for all subjects was 44.7 years (± 18.0) (range: 18-86 years). The mean age was similar for males and females, 41.5 years (± 17.2) and 47.7 years (± 18.5) respectively, *P* = 0.23.

8 (16.3%) cases were successfully performed with local and monitored anesthesia care (Table 6).

Table 6. Operative experience

Anesthesia type (n)	
General anesthesia	41 (83.7)
Local + MAC	8 (16.3)
Operation time (min.)	20.2 (± 5.5) (range: 11-31)
Blood loss	minimal
IV Fluids (mL Crystalloids)	461.2 (± 222.0)
Foley catheter size (Fr)	range: 16-22 Fr
Complications (n)	
Hematuria	1 (2.0)

Data presented as mean ± SD, unless noted otherwise; data in parentheses are percentages. MAC = monitored anesthesia care

All other cases were performed under general anesthesia. The mean operation time documented in 19 (38.7%) cases was 20.2 min (± 5.5) (range: 11-31 min). Blood loss was reported as zero or minimal in all cases and records indicate a mean fluid administration of 461.2 mL crystalloids (± 222.0) in 31 (63.3%) cases. The median catheter size inserted was 20-Fr Foley catheter (range: 16-22 Fr). There were no cases of incorrect catheter placement and no intra-operative complications. One patient returned with significant hematuria a day following the procedure; Clavian Grade I. No other minor or major complications were noted.

DISCUSSION

Urologic advances are credited for the reduced mortality observed in spinal cord injury patients in recent decades. The improved life expectancy now makes long-term complications of urinary tract management more pertinent therefore mandating the need for continued research in this arena. This research retrospectively reports our institutional outcomes in the long-term management of neurogenic bladder in patients with traumatic spinal cord injury.

The first objective addressed the association of recurrent urinary tract infections with the long-term use of CIC in identified spinal cord injury patients followed by the same physician at the Yale Urology medical group. CIC is a common bladder catheterization method used in the years following spinal cord injury [50]. Some studies looking at its efficacy have observed an increased frequency of UTI raising the need for prophylactic antibiotics [50]. Oral antimicrobials, methenamine compounds and bladder instillations of providone iodine and chlorhexidine preparations are often used and have been shown to postpone bacteriuria for short periods in patients managed with CIC [51, 52]. Daily use of low-dose systemic antimicrobials such as trimethoprim-sulfamethoxazole has also been shown to be effective in reducing bacteriuria and symptomatic UTI in persons with acute SCI [53]. The routine use of methenamine products or systemic antimicrobials for prophylaxis in long-term intermittent catheterization is controversial and not recommended [22], however in carefully selected subjects with frequent recurrent symptomatic UTIs this may help improve quality of life.

Our results demonstrated that 67% of our subjects were on UTI prophylaxis at the time of last follow-up (Figure 1). And that most of these patients were started on prophylaxis within two years of initiating bladder management with CIC (Figure 2). UTI prophylaxis in this case was defined as the use of oral antimicrobials or methenamine combined with ascorbic acid. In an acidic environment methenamine forms formic acid which serves as a bladder antiseptic. Ascorbic acid is used to lower the urine pH sufficiently for generation of formic acid. Theoretically the combination is effective in reducing UTI without leading to antibiotic resistance.

Our patients were placed on prophylaxis only after they complained of three or more episodes of symptomatic UTIs within a one year period and where available, urine culture results were used to confirm the need of PRx in those subjects using PRx. The diagnosis of UTI is usually based on the quantification of uropathogens in voided urine, with significant bacteriuria defined as the amount of uropathogens in urine which distinguishes true infection or colonization of the urinary tract from contamination [54]. The National Institute on Disability and Rehabilitation Research (NIDRR) defines UTI by the presence of significant bacteriuria with tissue invasion and resultant tissue response with signs and/or symptoms of UTI [55]. The criteria for significant bacteriuria in SCI patients are dependent on the method of bladder management being used. To be diagnosed with catheter associated UTI, patients managed with intermittent catheterization require $\geq 10^3$ cfu/ml in addition to UTI symptoms un-attributable to other sources [56]. This cut-off for positive cultures was used to confirm the need for PRx in the subjects included in this study.

Urine culture results were found for 31 of 41 (76%) subjects placed on PRx however culture results were not available for those subjects that were started on PRx at initial follow-up after they have been referred to our institution for management of frequent recurrent infections. In addition, culture results were not available for other subjects since patients are often treated outside the purviews of our office with cultures done by their primary care providers. Of all subjects included in the study, 17 had at least three positive cultures within the year prior to starting UTI PRx confirming that at least 28% of our SCI patients were experiencing recurrent symptomatic UTI. These results suggest that symptomatic UTIs remain a frequent, recurrent complication of clean intermittent catheterization.

Due to the small number of females included in our study we could not determine whether the difference in the percentage of male and female subjects requiring UTI PRx was statistically significant. The issue of sex as an independent risk factor for UTI in SCI patients remains unresolved. It is well known however that females have a higher incidence of UTI compared to males in otherwise healthy individuals with normal bladder function. Since females represent a minority of those with spinal cord injury only a few studies have compared complication outcomes in male and female SCI patients. Waites and colleagues did not find sex to be an independent risk factor for UTI in a prospective study of 61 SCI patients [57]. However a comparative study by Bennett and associates demonstrated a higher incidence of UTI in females, especially with bowel organisms [58, 59]. Another study of 302 SCI patients on CIC found a significantly higher rate of clinical UTI in women even though men and women had equal rates of bacteriuria [60].

Most of our patients on UTI PRx required it within 2 years of initiating bladder management with CIC. However, the 20 patients not placed on UTI PRx had been followed for a mean of 7 years without the need for PRx. These results suggests that patients who will be placed on PRx are started on it early in the course of management, while those not needing PRx could go on without PRx almost indefinitely. Future studies will be needed to address what factors influence why certain patients do not experience frequent recurrent UTI while undergoing long-term bladder management with CIC.

The finding that 67% of our SCI patients are placed on PRx within 2 years of starting CIC is high and may not be generalizable to the average SCI population since patients are often referred to our institution for management because they have been experiencing frequent symptomatic infections. Previous studies have reported that up to eighty to ninety percent of persons with acute SCI have bacteriuria within 2 to 3 weeks of starting intermittent catheterization [53]. Esclarin and colleagues found an incidence of 2.75 episodes of bacteriuria/100 Person-days, with 0.41 episodes/100 person-days incidence for UTI in a retrospective study of adults with acute SCI [61]. Unlike previous reports, our study investigates the association of symptomatic UTI with long-term CIC in stable rather than acute SCI. Our results demonstrate that recurrent UTI remains a major complication of long-term bladder management with clean intermittent catheterization. An increased incidence of symptomatic UTI has been reported when CIC is performed at home by a caregiver rather than by the person with SCI [62]. However most of the factors contributing the increased risk of UTI in patients with CIC remain controversial and future studies are needed to fully define the risk factors.

The second specific objective evaluated the efficacy of retroperitoneal ultrasonography as a long-term surveillance method in injured patients managed with CIC. All patients included in this study were managed with CIC and the results of their most recent video urodynamics revealed detrusor overactivity in 80%, detrusor sphincter dyssynergia in 20% and decreased bladder compliance was also present in 20% of those included. The standard first line therapy in patients with neurogenic detrusor overactivity is intermittent catheterization along with oral anticholinergic treatment for detrusor relaxation [63] because upper tract dilation is caused by a poorly compliant bladder with high pressure whether or not vesicoureteral reflux is present [64]. Consequent hydroureteronephrosis in neurogenic bladder patients may cause renal deterioration, renal failure and death [65].

Study subjects with detrusor overactivity who reported having incontinence or those with inadequate storage pressures were managed initially with oral anticholinergic medications to suppress the involuntary contractions, prevent urinary incontinence and protect the kidneys from high pressures. Urodynamic testing was repeated if patients presented with new symptoms including recurrent urinary tract infections, incontinence or increased frequency of catheterization and their management regimen was modified. Modifications to management strategies in study subjects included optimization of anticholinergic medication dose, addition of another anticholinergic such as imipramine or surgical intervention with augmentation cystoplasty.

We retrospectively assessed our population of spinal cord injury patients with neurogenic bladder for the long-term results of a management regime based on annual ultrasonography. Urodynamics were repeated only after patients presented either with new symptoms or with abnormal findings on ultrasonography. Our series demonstrated that compared to initial ultrasonography, by the time of last follow-up there were 4 (8%) new cases of moderate or minimal hydronephrosis/caliectasis and 4 (8%) new cases of small renal/ureteral calculi. 3 of the 4 cases of upper tract dilation however was secondary to distal obstruction from calculi and prostatic hyperplasia and no cases required modification of the bladder management regime. Furthermore, no cases of severe upper tract dilatation or large stone burden were observed in any of our patients. All cases of upper tract dilation noted on initial ultrasonography had either resolved or remained stable by the time of last follow-up after initial management was modified either by increasing the dosage of anticholinergics or after augmentation cystoplasty was performed.

Patients managed on an annual urodynamics based regime by Nossseir and colleagues had no cases of upper tract damage; their series included 51 patients managed with intermittent catheterization and anticholinergic pharmacotherapy [49]. Although a significant number of their patients, 10 (20%), suffered from recurrent urinary tract infections renal ultrasound demonstrated morphologically unaffected upper urinary tract in all patients. In our series however patients were followed with annual ultrasonography rather than urodynamics and 8% of our subjects developed mild cases of upper tract dilation. Most of these cases however were early manifestations of acute obstructive processes rather than late manifestations of inadequate bladder pressures. And it is unlikely that a more frequent bladder surveillance regime would have prevented the development of minimal caliectasis in these subjects.

We propose that after the initial treatment regime is implemented and a safe system is established, SCI patients managed with intermittent catheterization can be monitored regularly with retroperitoneal ultrasound alone; and further urodynamic testing reserved only for patients presenting with new symptoms, to prevent long-term upper tract damage. Our results demonstrate that bladder management based on annual surveillance with ultrasound is sufficient to prevent upper tract damage in our population of SCI patients and future studies are needed to demonstrate the frequency of surveillance necessary to maintain upper tract function in the general SCI population managed with intermittent catheterization.

Since neurogenic bladder (NGB) patients have been shown to be at increased risk of injury during suprapubic catheter placement, the third specific objective described our experience with a safe technique for suprapubic cystostomy (SPC) known as the lowsley retractor method. Suprapubic cystostomy is used to manage patients in acute urinary retention, those undergoing lower urinary tract operations as well as persons with neurogenic bladder. Various percutaneous and minimally invasive methods for suprapubic cystostomy have been described but the open approach under general and spinal anesthesia is still accepted as the definite gold-standard [26]. NGB patients have been shown to have a higher risk of complication during SPC procedures [27]. Zeidman and colleagues in 1988 introduced a safe technique for suprapubic catheter placement using the lowsley retractor designed for perineal prostatectomy [66]. In reporting their institutional experience they noted no cases of incorrect catheter placement and had no major or minor complications. However their patient characteristics were not described in detail and their technique is sometimes avoided for concern of possible urethral injury and potential difficulty in obese patients [67, 29]. To our knowledge no other institutional experiences with this approach has been published since its initial introduction. This report describes our institutional experience with the lowsley retractor method for isolated primary suprapubic catheter placement in NGB patients.

In their initial description of the technique, Zeidman and associates did not detail patient characteristics or their operative experience. They reported the use of the procedure in 125 female and 25 male patients needing cystostomy either as an isolated procedure or as part of a more extensive surgery. They only report the exclusion of male patients suffering from a fixed pelvic floor after radiation therapy due to difficulty of the procedure in this group of patients. Their approach was successful in all patients with no major or minor complications. In this report we describe our experience with the lowsley retractor method for SPC as an isolated procedure in NGB patients. Our operative experience regarding operative time, blood loss, and fluids administered are reported in detail to fully describe the safety and ease of utilizing this technique.

Surgical Technique

Similar to the technique previously described by Zeidman, the patient is placed in dorsal lithotomy position. A curved lowsley retractor is advanced through the urethral meatus into the bladder and pointed to the anterior abdominal wall. A small suprapubic incision is carried through the subcutaneous tissues and the abdominal wall using sharp dissection or electrocautery until the head of the lowsley retractor is met. The retractor is advanced through the incision and a 2-0 silk tie is used to tie a Foley catheter (of desired size) to the head of the lowsley retractor. The catheter is withdrawn into the bladder and out the urethral meatus using the retractor. The silk tie is cut releasing the end of the Foley catheter. The catheter is then pulled back through the meatus into the bladder. The balloon is inflated (10-15 cc), then a rigid cystoscope is introduced into the bladder confirming appropriate inflation of the catheter within the bladder. The bladder is allowed to drain spontaneously via the catheter and the catheter is sutured to the skin using interrupted 2-0 nylon suture.

The procedure was fast and effective. The operative time was recorded in 19 of 49 cases with a mean of 20.2 minutes (range: 11 – 31 min). All patients had minimal blood loss and on average required about 500 mL of intravenous crystalloids during the operation. In the 8 cases where general anesthesia was not used, the patients tolerated the procedure well under local anesthesia with monitored anesthesia care. There were no cases of incorrect catheter placements and no intra-operative complications. Our only complication was in a female spinal cord injury patient who returned to the emergency department a day following catheter placement with significant hematuria and hypotension. This complication occurred after her suprapubic catheter was inadvertently tugged-on at an outpatient care facility. Her hematuria resolved with conservative management and her pressures normalized after intravenous administration of fluids and fresh frozen plasma. The lack of other major or minor complications using this technique is consistent with the outcomes reported by Zeidman in 1988. We did not have any cases of urethral injury and to our knowledge no cases of urethral injury using the lowsley retractor method have been published. This suggests that the theoretical risk of possible urethral injury may be easily avoidable. Also, attempts should be made in future reports to address outcomes in obese patients undergoing this method of SPC.

CONCLUSION

Although intermittent catheterization is widely viewed as the healthiest bladder management option, many patients managed with long-term CIC will frequently experience recurrent symptomatic urinary tract infections. Our results highlight the continued need for improvements in bladder management methods to reduce rates of symptomatic infections in these patients. Future studies are needed to determine the benefit of UTI prophylaxis in these patients and to address what factors influence why certain patients managed with long-term CIC continue to experience frequent symptomatic infections when others do not.

While the combination of CIC and oral anticholinergic therapy is a successful first line regimen in SCI patients with neurogenic bladder, these patients will often require a variety of treatment modifications and interventions in long-term follow-up to prevent upper tract deterioration [41]. This retrospective analysis of patients monitored with annual retroperitoneal ultrasound rather than regular urodynamics demonstrates that an ultrasound based surveillance regime is efficacious. Future studies are needed to determine the optimal surveillance interval with ultrasonography to prevent upper tract deterioration in spinal cord injury patients managed with clean intermittent catheterization.

Due to improved pharmacotherapy with anticholinergics, SPC is emerging as an effective alternative for the long-term management of NGB patients [26]. Patients using this bladder management method report a high level of satisfaction as well as an improved quality of life [25]. Various percutaneous procedures have been demonstrated for suprapubic catheter placements, but patients with NGB have been demonstrated to have a higher risk of complications following the procedure [27]. This report describes our experience with SPC using the lowsley retractor method introduced by Zeidman et al. in 1988. Our findings demonstrate that the technique is easy and safe for performing primary cystostomy as an isolated ambulatory procedure in patients with neurogenic bladder.

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