ORIGINAL PAPER

A snapshot of the adult spina bifida patient – high incidence of urologic procedures

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Introduction To describe the urologic outcomes of contemporary adult spina bifida patients managed in a multidisciplinary clinic.
Material and methods A retrospective chart review of patients seen in our adult spina bifida clinic from January 2004 to November 2011 was performed to identify urologic management, urologic surgeries, and co-morbidities.
Results 225 patients were identified (57.8% female, 42.2% male). Current median age was 30 years (IQR 27, 36) with a median age at first visit of 25 years (IQR 22, 30). The majority (70.7%) utilized clean intermittent catheterization, and 111 patients (49.3%) were prescribed anticholinergic medications. 65.8% had urodynamics performed at least once, and 56% obtained appropriate upper tract imaging at least every other year while under our care. 101 patients (44.9%) underwent at least one urologic surgical procedure during their lifetime, with a total of 191 procedures being performed, of which stone procedures (n = 51, 26.7%) were the most common. Other common procedures included continence procedures (n = 35, 18.3%) and augmentation cystoplasty (n = 29, 15.2%). Only 3.6% had a documented diagnosis of chronic kidney disease and 0.9% with end-stage renal disease.
Conclusions Most adult spina bifida patient continue on anticholinergic medications and clean intermittent catheterization. A large percentage of patients required urologic procedures in adulthood. Patients should be encouraged to utilize conservative and effective bladder management strategies to reduce their risk of renal compromise.

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Key Words: adult ‹› spina bifida ‹› neurogenic bladder ‹› lithotripsy ‹› transitional care

INTRODUCTION

There is a growing adult spina bifida population, with 75–85% of children with spina bifida expected to survive into adulthood with advances in their care [1, 2, 3]. Bladder disturbances are common in spina bifida patients, affecting 24–98% of patients [3–7]. Without adequate urological management, the upper urinary tract can be adversely affected; as many as 48% of spina bifida patients with untreated urologic problems have evidence of kidney damage [8, 9]. This makes early initiation of urological management key in the preservation of renal function [10]. Early and appropriate bladder management of spi-

na bifida patients is essential not only to maintain a healthy upper urinary tract, but also to improve the quality of life. Although uncommon, this ideally occurs in the setting of a multi-disciplinary spina bifida clinic, of which urologists play an integral role. As patients transition from pediatric to adult clinics, many practitioners are faced with the challenge of treating this medically complex group of patients. The transition from a well-known and trusted pediatric clinic to an unfamiliar adult clinic can be difficult, and the ideal protocol for transition or establishment of care in an adult spina bifida clinic, and subsequent follow-up, is not clearly defined or standardized. Currently, there is a scarcity of published

literature regarding urologic features and management of adults with spina bifida. One of the steps necessary to optimize our care for this growing population is to better define their patient characteristics as a group. We aim to describe the population of the adult spina bifida patients in our own experience in the setting of a multi-disciplinary clinical practice, including demographics, urologic management and co-morbidities throughout life, in order to better understand how we can more effectively care for, reduce mortality and improve quality of life.

MATERIAL AND METHODS

We performed an Institutional Review Board approved retrospective review of patients seen in our multidisciplinary adult spina bifida clinic by the same physician (SJK) between January 1, 2004 and November 1, 2011. Patients with the diagnosis of neural tube defects (e.g. myelomeningocele, spina bifida occulta, tethered cord syndrome), as identified through the Northwestern Enterprise Data Warehouse by CPT code and age over 18 years were included in the analysis. Chart review was performed using our Electronic Medical Record for progress notes, operative reports, lab values, pathology and imaging studies.

Demographic information, urologic medications, prior urologic surgery, bladder management techniques, and co-morbidities were reviewed based on inpatient and outpatient history, physical findings, progress notes and patient reported surgical history. History of urologic procedures and surgeries over the patient lifetime were reviewed for indication, patient age and outcomes. Stone procedures were reviewed for stone location. When multiple stone surgeries were performed on the same patient, this was documented as a separate procedure, but notation to indicate the number of procedures on unique patients was also recorded. Mann-Whitney U and Fischer's exact tests were used to evaluate statistically significant differences between procedures performed in pediatric versus adult patients. For all statistical analyses, $P < 0.05$ was considered statistically significant. Analysis was performed using IBM SPSS, version 21.

RESULTS

A total of 225 patients were identified and included in the analysis. Demographic information and neurologic lesions are detailed in Table 1. Median current age of patients was 30 years (range 16-72, IQR 27, 36). Median age at time of presentation to the adult spina bifida clinic was 25 years (IQR 22, 30). Mean time of follow up was 37.9 (SD ±29.2) months,

with an average frequency of 2.4 clinic appointments per year. The majority of patients in our cohort had a diagnosis of myelomeningocele (86.7%). The associated co-morbidities of our patient population can be found in Table 2. 21.5% of patients were identified as having one or more of the comorbidities referenced in Table 2. The most common co-morbidities

Table 1. *Patient demographics*

Patient characteristic	n=225
Age at initial evaluation in clinic (years)	Median (IQR) 25 (22, 30)
Age at time of study (years)	Median (IQR) 30 (27, 36)
	n (%)
18 to ≤25	123 (54.7)
>25 to ≤35	71 (31.6)
>35 to ≤55	25 (11.1)
>55 to ≤65	5 (2.2)
>65	1 (0.4)
Gender	
Male	95 (42.2)
Female	130 (57.8)
Diagnosis	
Myelomeningocele	195 (86.7)
Lipomeningocele	12 (5.3)
Spina bifida occulta	6 (2.7)
Syringomyelia	4 (1.8)
Arnold-Chiari malformation	3 (1.3)
Sacral agenesis	2 (0.9)
Tethered cord	2 (0.9)
Encephalocele	1 (0.4)
Neurological level*	
Thoracic/high lumbar (T and L1-L3)	50 (28.4)
Low lumbar (≥L4)	90 (51.1)
Sacral	36 (20.5)
Associated shunted hydrocephalus**	148 (69.8)

*Documented in 176 of 213 (82.6%) patients with diagnoses of myelomeningocele, lipomeningocele and spina bifida occulta. **Documented in 212 of 225 patients (94.2%).

Table 2. *Patient comorbid conditions*

Comorbidity	n (%)
Hypertension	25 (11.1)
Gastroesophageal reflux	12 (5.3)
Epilepsy	12 (5.3)
Diabetes mellitus	9 (4.0)
Obstructive sleep apnea	8 (3.6)
Chronic kidney disease	8 (3.6)
Asthma	7 (3.1)
Depression	5 (2.2)
Deep vein thrombosis	5 (2.2)
Bladder cancer	2 (0.9)
End-stage renal disease	2 (0.9)

were hypertension, gastro-esophageal reflux and seizure disorders. Eight patients, or 3.6%, had documented chronic kidney disease, while one patient (0.9%) had end-stage renal disease. Regarding bladder management, 23 patients (10.2%) voided spontaneously, 7 (3.1%) voided by Valsalva, 11 (4.9%) into diapers, 159 (70.7%) utilized clean intermittent catheterization (CIC) (with 10 (4.4%) catheterizing through continent stomas), 4 (1.8%) used indwelling urethral catheters, 3 (1.3%) suprapubic catheter, and 8 (3.6%) had an ileal conduit. Anticholinergics were prescribed for 111 patients (49.3%), including oxybutynin (24.0%), solifenacin (18.7%), darifenacin (4.4%), and tolterodine (2.2%). Additionally, 65.8% underwent urodynamics at least once during their care in the spina bifida clinic. Serum creatinine was available in 180 patients (80%), with a median creatinine of 0.67, and 93.3% having a Cr <1.3.

Unique urologic procedures were analyzed (reported in Table 3). One hundred and one patients (44.9%) had at least one urologic procedure during their lifetime, with a total of 191 procedures performed. Continence procedures, including pubovaginal sling, ileal conduit, urethral bulking agent, artificial urinary sphincter, male Stamey sling, and suprapubic catheter placement, were 18.3% of procedures performed. Other common bladder procedures included augmentation cystoplasty and botulinum injections. Procedures for vesicoureteral reflux (VUR) were documented in 24 patients (12.6%). Twelve patients (6.3%) underwent procedures involving the urethra and bladder outlet, including urethral dilation or incision, transurethral resection bladder neck, urethral diverticulectomy and urethrovaginal repair. Most procedures were performed after 18 years of age (62.6%), while 20.7% were performed before age 18, and 16.7% were performed at an unknown age from the available documentation.

Over the course of follow-up in our cohort of 225 patients, 181 patients (80.4%) completed upper urinary tract imaging (renal ultrasound, computed tomography abdomen/pelvis or magnetic resonance imaging abdomen/pelvis) at least once. One hundred twenty-six (56.0%) obtained imaging at least every other year and 64 (28.4%) did yearly. Thirty-eight patients underwent surgical intervention for stone disease. Surgery for stone disease was more commonly performed in the adult SB patient (80.4% of stone surgeries) than those <18 years of age (19.6%) (p <0.001). Of the surgical interventions, 31.1% were performed for bladder stones, 11.5% for ureteral stones, and 57.4% for renal stones (Table 4). Two patients (0.9%) were diagnosed with bladder cancer during the course of follow-up, the details of which are described in a recently published case se-

Table 3. *History of procedures and surgeries in adult spina bifida patients. STING = subureteric transurethral injection; TURBT = transurethral resection of bladder tumor; TUR = transurethral resection; MACE = Malone antegrade continence enema. Procedures without age available were included in total procedure count. Mann-Whitney U and Fischer's exact tests were used to evaluate significant difference between procedures performed in pediatric (<18 years) versus adult (≥18 years) patients*

Procedure	n	Pediatric	Adult	p value
Continence and urethral surgery				
Augmentation cystoplasty	29	8 (27.6)	16 (55.2)	0.07
Continent catheterizable stoma	10	2 (20.0)	6 (60.0)	0.08
Ileal Conduit	9	3 (33.3)	6 (66.7)	0.18
Botulinum Injection	7	n/a	7 (100.0)	n/a
Pubovaginal Sling	14	n/a	11 (78.6)	n/a
Urethral bulking agent	5	n/a	3 (60.0)	n/a
Artificial urinary sphincter	5	1 (20.0)	3 (60.0)	0.2
Male Stamey	2	n/a	2 (100.0)	n/a
Urethral dilation or incision	8	n/a	6 (75.0)	n/a
Sacral nerve stimulator	2	2 (100.0)	n/a	n/a
Kidney and ureteral surgery				
Ureteral reimplant	14	5 (35.7)	2 (14.3)	0.12
STING	10	4 (40.0)	3 (30.0)	0.52
Partial ureterectomy	3	n/a	2 (66.7)	n/a
Nephrolithiasis	51	10 (19.6)	41 (80.4)	<0.001
Nephrectomy	6	2 (33.3)	3 (50.0)	0.58
Renal Transplant	3	1 (33.3)	1 (33.3)	n/a
Oncologic surgery				
TURBT	2	n/a	2 (100.0)	n/a
Radical cystectomy	2	n/a	2 (100.0)	n/a
Other urologic surgery				
MACE	6	3 (50.0)	1 (16.7)	0.2
Orchiectomy	2	1 (50.0)	n/a	n/a
Penile prosthesis	1	n/a	1 (100.0)	n/a

Table 4. *Urinary tract stone procedures performed in the adult spina bifida patient*

Location of stone	Patient count n (%)	Procedure count n (%)
Bladder	17 (44.7)	19 (31.1)
Ureteral	5 (13.2)	7 (11.5)
Renal	16 (42.1)	35 (57.4)

ries [11]. Briefly, both patients were young women, aged 34 and 46 years, who managed their native bladders with clean intermittent catheterization for over 20 years and were otherwise healthy prior to their diagnosis. Both patients were found to have high grade, muscle-invasive malignancy (T2), with one case of urothelial carcinoma and the other with squamous cell carcinoma.

DISCUSSION

SB is a chronic disease process that requires care from a number of medical sub-specialties and social

services. One of the obstacles to cohesive care is the effective transition from pediatric to adult care. Our results demonstrate a median age of presentation of 25 years (IQR 27, 36), similar to reported presentation in adult spina bifida clinics of 26.8 years in the literature [12]. These findings suggest the existence of a 'coverage gap' in the appropriate care of SB patients as they transition to adult clinics. Factors impeding the timely transition of care were outside the realm of our study, although proposed factors include inability of pediatric care providers to "let go" of their patients, lack of planning, delay in readiness of transfer, little incentive for patients to transition and inability of parents to relinquish control [13].

Neurogenic bladder in spina bifida patients can be associated with compromised renal function with elevated bladder pressures, urinary tract infections and stone formation [14]. Patients utilizing clean intermittent catheterization have a significantly lower incidence of urinary tract dilation and vesicoureteral reflux when compared to patients voiding with Valsalva, reflex voiding, or incontinence to pads [15, 16]. The majority (70.7%) of patients in our cohort managed their bladders with clean intermittent catheterization, comparable to reported 61-85% clean intermittent catheterization rate reported in the literature for adults with myelomeningocele [1, 17]. Though the majority of our patients have a serum Cr within the normal range, the decrease in body muscle mass in this population may lead to an over-estimation of renal function based on serum Cr, which may limit our detection of renal insufficiency. Historically, many young patients with spina bifida and dysfunctional voiding were treated early with urinary diversion in hopes of preventing renal pathology. However, studies have shown that more conservative management (clean intermittent catheterization and anticholinergic medications) may be as effective and pose significantly fewer risks [18, 19]. Clean intermittent catheterization was the primary bladder management technique in 70.7%, with anticholinergic use reported in 49.3%. Nine patients (4.0%) in our study had an ileal conduit and 29 patients (12.8%) had undergone augmentation cystoplasty. Recent research assessing the quality of life in spina bifida adults suggests that the bladder management technique and history of urologic reconstruction did not translate into a significant change in health-related nor incontinence-related quality of life [20]. This highlights the importance of balancing both patient goals and quality of life related to urologic care as well as renal preservation. While the minority of patients had undergone reconstructive surgery to reduce bladder storage pressures, a large proportion of patients with spina bifida

required at least one urologic surgical procedure during their lifetime (44.9%), with the majority of these procedures performed after the age of 18 (127/191 procedures, 66.5%). We report on the lifetime incidence of urologic procedures in spina bifida patients, demonstrating both a significant frequency as well as a proportion of urologic surgeries performed over the age of 18. The most common urologic procedures performed were urinary tract stone treatment (26.7%), reconstructive surgery (25.1%), and continence procedures (18.3%).

The incidence of stone disease in individuals with neural tube defects (6.1%) is significantly higher than the general population (1.0%) [21]. The high incidence of stone procedures (51/191 procedures, 26.7%) in our population of adult spina bifida patients may be higher than that reported for neural tube defects due to inclusion of only spina bifida patients, a group with risk factors including an indwelling catheter or clean intermittent catheterization and selection bias for routine imaging while being followed by a urologist. A higher incidence of stone procedures occurred in the adult spina bifida population (80.4%) when compared to pediatric (19.6%) patients. This is the largest series of its kind in the adult spina bifida population, reporting a significant number of stone procedures in adult spina bifida patients that has not been previously well characterized. We follow our adult spina bifida patients regularly and counsel them regarding urinary tract stone risk, presentation, management options and serial imaging.

Patients with neurogenic bladder have an increased incidence of bladder cancer (2.3–10%) that typically presents at a younger age with more aggressive and advanced disease, compared to a 2% incidence in the general population [22, 23, 24]. This is consistent with our two female patients, with high grade, muscle-invasive bladder cancer (squamous cell and urothelial) [11]. Hematuria should be promptly assessed with close follow-up with cystoscopy and upper tract imaging. In addition to the need for longitudinal urologic care, appropriate medical management of comorbid conditions is essential. Analysis of our patient population indicated that 11.1% were diagnosed with hypertension and 5.3% suffered from gastro-esophageal reflux disease, compared to the ultrasound prevalence of 30.4% and 10–20%, respectively [25–28]. In our cohort, 3.6% of patients were found to have chronic kidney disease with 0.9% of our patients requiring dialysis. The relative high incidence of chronic, comorbid conditions in this cohort draws attention to the need for early and regular evaluation by primary care physicians for the optimization of general medical management, in addition to the

need for close urologic follow-up. It should be noted that these medical comorbidities were culled from reviewing multiple provider's clinical notes and medication history and may therefore, under-represent incidence of comorbid conditions in this population. There are a few limitations of this study that deserve mention. As a retrospective review our findings represent only a snapshot in time of our patient population and is limited in its design for analyzing individual patient trends over time. However, all patients were seen by the same physician, minimizing inconsistency. Incomplete patient memory and the unavailability of pediatric records hindered our ability to collect complete information regarding pediatric procedures performed. Furthermore, analyses of pediatric versus adult surgeries and history of interventions should be considered within the context of the number of years within each category. This is the first report showing the breadth of bladder management methods in an adult multidisciplinary clinic population for spina bifida. Future work is planned to investigate long-term outcomes for bladder and renal health, as well as general health outcomes in adults with spina bifida. There is a need for longitudinal, prospective studies to better characterize the medical and urologic needs of the adult spina bifida population, their ideal management and the long-term outcomes from medical and surgical intervention.

CONCLUSIONS

The results presented here are the first report showing the span of modern medical and surgical management strategies utilized in a large single center sample of adult spina bifida patients managed in an adult multidisciplinary clinic. There is a need for organized and efficient transfer of care to an adult clinic. The multi-disciplinary clinic may be a promising start for the appropriate care of patients, given the systemic pathology seen in spina bifida. Stone procedures were the most common urologic procedure performed, with a large proportion occurring in adulthood. Future directions of research and areas for concern include optimization of quality of life, long-term outcomes, stone management and prevention and malignancy risk.

CONFLICTS OF INTEREST

None of the contributing authors have any conflict of interest, including specific financial interests or relationships and affiliations relevant to the subject matter or materials discussed in the manuscript.

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