The Current Management of the Neurogenic Bladder in Children with Spina Bifida

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Neurogenic bladder is a complicated symptom complex that is part of many congenital and acquired disease processes. Common conditions in children include central nervous system diseases and spinal cord lesions as well as functional and structural obstructive uropathology. The neurogenic bladder does not only affect the continence status of patients but, more importantly, it also adversely affects the upper urinary tract potentially causing renal dysfunction. Because of the complexity of the illness and potential grave problems, long-term management is best performed by a specialist.

KEYWORDS
- Neurogenic bladder
- Spina bifida
- Congenital defects
- Spinal cord injury
- Bladder management
- Life quality

KEY POINTS
- Before surgery is considered, conservative protocols have to be maximized because two-thirds of patients can become continent by clean intermittent catheterization and medication alone. Fecal continence and bowel management is an integral part of spina bifida treatment.
- Reconstructive lower tract surgery remains the best-studied, most successful, permanent, and long-term satisfactory surgery to deal with urinary and stool incontinence.
- The urological care of patients with spina bifida consists of 2 components: the medical management with preservation of renal function and the quality-of-life issues with achieving dryness and independence of bladder and bowel management. Both components are equally important for patients to live a healthy and fulfilled life.
- Continuous education and care of the families and patients are necessary to motivate them for participation in treatment plans and to avoid frustration and unrealistic expectations.
- Achieving continence is a long road that requires understanding and compliance that is best delivered by a team of specialists.

Neurogenic bladder is a complicated symptom complex that is part of many congenital and acquired disease processes. Common conditions in children include central nervous system diseases and spinal cord lesions as well as functional and structural obstructive uropathology. The neurogenic bladder does not only affect the continence status of patients but, more importantly, it also adversely affects the upper urinary tract potentially causing renal dysfunction. Because of the complexity of the illness and potential grave problems, long-term management is best performed by a specialist.

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However, because the patients are commonly first encountered in the primary care community, an initial management protocol for primary providers that addresses all patients is useful until the referral takes place. It can be difficult to determine the exact reason for the neurogenic bladder and a detailed patient history and a physical examination often paired with radiographic imaging is necessary. Patients with dysfunctional elimination syndrome rarely require extensive testing and can be, most of the time, separated from patients with neurogenic bladders by careful history and examination. It is very important not to coin every child with voiding issues as a patient with a neurogenic bladder to avoid overtesting and stigmatization. Once the suspicion of a neurogenic bladder is confirmed, video-urodynamic testing is the most accurate method to objectively evaluate the lower urinary tract.

Neurogenic bladder defects are generally classified according to neurologic defects or functional impairment. Neurologic defects can be described by the Loop theory of Bradley\(^1\); in 1974, he differentiated between 4 different loops of neuronal connection. According to his theory, the disruption of each loop causes specific forms of neurogenic bladder dysfunctions.\(^1\) Other investigators based their classifications and observations on urodynamic findings.\(^2,3\) Also, anatomic and neurologic descriptions help to understand the mechanism of the defect, the functional classification systems have more use for clinical decision making.\(^4\) Especially in children, the most important question remains whether or not the bladder can empty spontaneously while maintaining safe pressures or if drainage has to be provided.

The causes and presentation of a neurogenic bladder in a child is different from adult forms. In most cases, the pediatric neurologic bladder is caused by congenital problems, and many investigators differentiate between a neurologic and a neuropathic bladder. A neurogenic bladder is one from a true neurologic deficit like spina bifida (SB), and a neuropathic bladder is one that acts like a neurogenic bladder but is not caused by an innervation problem. Examples of neuropathic bladders include those caused by a urinary obstruction, like in posterior urethral valves, or lack of bladder tissue, like bladder exstrophy. Acquired forms caused by trauma, infection, or behavioral issues are more comparable with adult clinical pictures. The timing of intervention is important because delay of treatment can cause irreversible damage, especially to the upper tracts. Many congenital defects are obvious, whereas others, like posterior urethral valves, might not be detected until problems occur. Prenatal ultrasounds (US), careful postnatal examination, and the education of primary care providers and parents all help in diagnosing problems early.

Myelodysplasia includes a variety of neural tube defects that differ in their severity depending on site and gravity of the defect. Myelomeningocele (SB) is likely the most common congenital diagnosis for the development of a neurogenic bladder in children. The level of the defect on the spine is strongly associated with survival and the development of cognitive and motor skills, with cervicothoracic levels performing significantly lower in comparison with lumbosacral defects.\(^5,6\) In contrast to the general motor function, the bladder and bowel function do not have a direct correlation with the level of the lesion. Therefore, even patients with SB with the ability to walk often have poorly functioning bladder and bowels that prevents them from achieving spontaneous continence.

The prevalence of SB in Europe is declining because of prenatal management, but the numbers in the United States remain high, with an estimated 1 per 1000 births in 1993.\(^7\) A newer study of 10 regions in the United States demonstrated a prevalence of SB in children aged 0 to 19 years to be 3.07 per 10,000 in 2002. The total number of cases of the same age group living the United States in 2002 was estimated at 24,860.\(^8\) The aggressive promotion of folic acid supplements during all pregnancies,
but especially in families with a history of SB, plays a big role in the decline in numbers of newborns with SB. Today, infant survival rates with SB have increased to 92% in 2001 up from 83% in 1983. As a result of improved surgical treatments and early medical care, children with SB can expect longer lives today than in the past. This encouraging fact also means that primary care providers have to be more knowledgeable about the medical problems because these children not only grow in numbers but also transition into adulthood.

PRENATAL DIAGNOSIS AND FETAL SURGERY

Routine prenatal US examinations allow for earlier diagnosis of affected fetuses with SB conditions. Lately, Chaoui and colleagues reported that they identified 5 cases of SB at 11 to 13 weeks’ gestation by assessing the intracranial translucency and the posterior brain during routine US. A few months earlier, a different group found that at 11 to 13 weeks’ gestation most fetuses with SB have measurable abnormalities in the posterior brain. The early detection of SB fueled the desire for intrauterine repair to allow for regular development and improve the prognosis.

To prospectively evaluate the value of intrauterine surgery, a multicenter, randomized controlled trial was established by the National Institutes of Health and limited to 3 centers in the United States. The endpoints of this Management of Myelomeningocele Study (MOMS) included fetal and infant mortality, the need for a ventriculoperitoneal shunt at 1 year of age, and the evaluation of mental and motor development at 30 months of age.

The study began in 2003 and enrolled 183 women who were pregnant with a fetus with SB. In a randomized fashion, half of the affected individuals underwent fetal surgery, whereas the other half had standard postnatal closure of their defect. The results of the study were published in March 2011 in the New England Journal of Medicine. There were no maternal deaths and the rates of adverse neonatal outcomes were generally similar between the two groups. Two perinatal deaths occurred in each group. The rates for shunt placement were 40% in the prenatal-surgery group and 82% in the postnatal-surgery group. The prenatal surgery group had better motor function compared with the postnatal surgery group, and parent evaluation confirmed these findings. However, there was no significant differences in cognitive scores. Prenatal surgery was associated with an increased risk of preterm delivery and uterine dehiscence at delivery. The data and safety monitoring committee of the study met on December 7, 2010 and recommended termination of the trial because of the efficacy of prenatal surgery. Of great importance is that all 3 centers of the study have a multidisciplinary team of experts and followed a standard protocol to perform fetal surgery. The investigators caution: “The results of this trial should not be generalized to patients who undergo procedures at less experienced centers or who do not meet the eligibility criteria.” No comments were made concerning the effect of the prenatal surgery on the bladder development. Currently, a separate arm of the MOMS trial is looking at bladder function, and results should be available in the next 5 years.

INITIAL BLADDER MANAGEMENT: EXPECTANT VERSUS PROACTIVE

The spinal defect is usually closed in the first 24 hours of life and the bladder drained for that period. Concerning the bladder function, 2 general scenarios are observed. One group of patients with SB will have an overactive sphincter and develop high detrusor leak point pressures greater than 40 cm H2O and are, therefore, at risk for upper tract damage. The other group will have little sphincter resistance with low detrusor leak point pressures, resulting in free urine flow into the diaper with little risk to the upper tract.
Depending on the policy of the treating institution, 2 different management options are followed. The expectant approach has a more observational and conservative stance, whereas the proactive approach aims to actively influence bladder development. Both options are considered safe for the development of renal function but differ in their perceived benefit for bladder development and later continence. Both approaches require a detailed physical examination, evaluating the presence of a palpable bladder or kidney. Also, a bladder and renal US is obtained to evaluate bladder filling and hydronephrosis. In the case of a negative physical examination and the absence of hydronephrosis, the expectant approach does not initiate clean intermittent catheterization (CIC), video urodynamic studies, or anticholinergic medication. Regular follow-up with examination, creatinine value, and US are initiated, and the parents educated toward the occurrence of urinary tract infections (UTI) and decreased urine output. If hydronephrosis is detected or clinical problems such as infection occur, then urodynamic studies are done to determine if initiation of CIC and pharmacotherapy is needed. The proponents of this approach argue that acting on symptoms is sufficient to protect renal function and it is not justified to have all parents perform CIC.14,15

The proactive protocol advocates for early urodynamic testing to identify high-risk patients. Patients with increased leak point pressures, detrusor sphincter dyssynergia, or noncompliant bladder muscles are placed on CIC every 3 to 4 hours during the day, and anticholinergic therapy with oxybutynin is initiated.16 The rationale is to promote detrusor muscle relaxation and development by bladder cycling and ensure bladder drainage to protect the upper tracts and prevent hydronephrosis.17–21 However, if the bladder environment is safe on urodynamics, some groups will stop CIC and move patients to the expectant protocol.22,23 Other groups prefer to continue CIC to keep the child used to catheterization and to ensure proper development. Proponents defend their approach by the fact that most patients will need to perform CIC later to achieve continence and it is easier if the child remains used to the procedure.24 Prophylactic antibiotics have not been proven to be useful in preventing infections, but no uniform treatment protocols exist.25

QUALITY OF LIFE

The initial management is centered on the primary goal of preserving renal function. As the child gets older, life quality and especially continence becomes more important. It is important for the caregiver to make the family understand that most interventions to achieve continence mean a higher level of involvement for everybody. Medical treatment has to be intensified and the child has to be much more involved. Surgical procedures will turn a previously incontinent bladder into a high-volume reservoir that will need to be catheterized. Basically, the family has to understand that surgeries can turn a current, safe incontinent bladder into a continent but very unsafe reservoir if not emptied regularly. Therefore, before initiating changes and continence procedures, patients have to have a high desire to become dry and are willing to accept a new regiment of protocols. Discussions should include the difference between complete and social continence. In the authors’ practice, social continence is defined as being continent for several hours without leaking and being continent from stool. Minimal leakage during the day or night is accepted, whereas complete continence is defined as dry for 3 to 4 hours, including nighttime dryness.

Most families have heard about available medications and procedures. The authors inform patients and families in a detailed discussion what tests, surgeries, hospital stays, recovery, postoperative teaching, and changes in their daily protocol will occur.
These consultations can take hours and often require several visits until the family is ready for change. This time is well invested for both caretakers and patients to avoid misunderstandings, frustrations, and to ensure the best possible outcome. Exposing families to social groups like the Spina Bifida Association is equally important to allow discussion and the exchange of information with peers. Often local organizations exist, such as the Greater Oklahoma Disabled Sports Association (Godsa.org), a nonprofit organization that provides sports activities, such as wheelchair basketball. The authors’ practice actively supports and promotes these groups and enrolls families into their programs.

Once the decision is made to initiate changes in the management protocol to achieve dryness, a new baseline is established, including video urodynamic testing, US for the urinary tract, and a kidneys, ureter and bladder x-ray for the bowel. CIC, anticholinergics, and bowel management are maximized and their results reevaluated. It is important to include the bowel in the continence program because constipation will adversely affect the bladder and also address the pressing problem of encopresis. Most patients and families will place the importance of continence from stool before urinary dryness. Urine leakage can usually be contained within a diaper and changed at an opportune time. Unlike urine, stool will smell immediately, causing anxiety, and might prevent families from leaving their home environment.

The addition of specialized pediatric nurse practitioners who work with the families extensively is also helpful. This work includes not only explaining the medications and techniques but also providing individualized CIC sessions that address the specific dexterity needs of the child. Catheter type and size is tailored to the specific needs of patients, and bowel management is maximized with oral and rectal options. Regular follow-up in the clinic and on the telephone is provided. This individualized program is time intensive for families and providers, making them understand what it takes to become dry. Investing time and manpower at this stage will deal with anxiety and frustrations early. This investment will not only save time and money later but will also ensure better health and superior postoperative outcomes if surgery does become necessary. This conservative management will be successful in a large number of patients to achieve complete or at least social continence. However, next to continence, independence from caregivers will play a big role as patients become older. Self-catheterization via the urethra can be difficult depending on body shape and genital anatomy. Applying enemas to one self-effectively is almost impossible even for the most mobile patients. The discussion about available surgeries is initiated at this time.

**SURGICAL OPTIONS**

Generally two-thirds of patients can get socially dry with CIC, whereas the remaining one-third will require surgery. Surgery is divided between well-established traditional surgical reconstruction and the more recent bladder function modulation with medication or neuromodulation.

**MINIMAL INVASIVE TREATMENTS AND NEUROMODULATION**

*Botulinum Toxin*

The intravesical injection of botulinum toxin (Botox) is a good temporary measure to enhance bladder capacity and decrease intravesical pressures. Botox is injected into the detrusor muscle endoscopically using a cystoscope under anesthesia. It is performed as an outpatient procedure, is generally well tolerated, and the effects last for several months. Next to its positive effect on the bladder detrusor muscle, many patients report an improvement in bowel function and continence. However,
the procedure is not approved by the Food and Drug Administration (FDA). Botox injection can be repeated safely, but because of its temporary effect, it is not a final measure and will require additional procedures later. Neuromodulation therapy aims to treat the abnormal innervation of the bladder, trying to retrain the nerve-muscle interaction to attain more normal bladder function. The available treatments include nonsurgical therapies, such as transurethral electrical bladder stimulation; minimally invasive procedures, such as implantation of a sacral neuromodulation pacemaker device; and operative procedures that reconfigure sacral nerve root anatomy.

Transurethral Electrical Bladder Stimulation

The results of transurethral electrical bladder stimulation have varied. The technique begins with detailed bladder capacity measurements followed by refilling the bladder via an electrocatheter. During the first 90-minute session, various electric parameters, such as intensity of current and frequency, can be adjusted to the individual patient. A series of treatment consists of twenty 90-minute sessions. Follow-up sessions are tailored to the individual patient. In general, bladder stimulation therapy will provide volitional voiding in less than 10% of patients but can be an effective form of treatment for up to 60% of patients. If present, the beneficial effects are generally permanent but the therapy is labor intensive and requires a dedicated family. It is hoped that a better understanding of the mechanism of action will lead to more effective forms of bladder stimulation therapy in the future.

Sacral Neuromodulation

Sacral neuromodulation (InterStim, Medtronic, Minneapolis, MN, USA) is a reversible implantable device that is thought to improve bladder function either by consistent stimulation of the efferent fibers of the sacral nerve roots or by providing rhythmic contractions of the pelvic floor. First, a temporary test system is placed and, if proven successful, replaced by a permanent device. The device consists of a pacemaker, placed in the area of the buttocks, and a neurostimulator lead that is tunneled under the skin to electrically stimulate the S3 nerve root. A prospective randomized study enrolled 42 patients with SB and compared urodynamic outcomes and incontinence. The implanted group demonstrated significantly improved leak point pressure; however, the control group developed significantly improved bladder capacity at 12 months. Some patients in the treatment group also reported improvement in bowel function and a new sensation of a full bladder. Further studies will be necessary to evaluate the true advantage for patients with SB.

Xiao Procedure

Recently, another exciting neurosurgical technique has been developed in which a new neuronal loop is created. This technique was pioneered by Xiao and colleagues in China and has gained international interest. This so-called Xiao procedure describes a limited laminectomy between L4 and S2 and the nerve roots are exposed. The L5 ventral root is identified by electrostimulation producing plantar flexion of the foot and transected at the orifice. The S3 ventral root is transected near the cord. The proximal stump of the ventral root of L5 is then anastomosed to the distal stump of the S3 ventral root. This procedure is performed unilaterally. The originators of this method first reported their successes in adults with spinal cord injuries, showing that via percutaneous electrical stimulation or scratching the skin in the L7 (in animals, humans do not have L7) dermatome, a detrusor contraction could be initiated.
The follow-up data after 3 years showed that 10 of the 15 patients (67%) regained satisfactory bladder control and residual urine decreased from an average of 332 to 31 mL. Overflow incontinence and UTI were no longer clinical issues for these patients. Hence, this same group decided to apply this neurosurgical technique to the SB population. The cohort consisted of 20 children (average age, 11 years); 17 (85%) attained increased bladder storage capacity and emptying functions, including the ability to sense fullness and to initiate bladder emptying with L5 dermatome stimulation, and they were dry 6 months after the procedure. The negative of this trial was that 5 of the 17 children who had success also had signs of partial loss of L5 motor function. In the 3 patients who had no improvement, 2 were noted to have significant scarring in the spinal canal caused by their previous surgeries and, therefore, had inadequate neural rootlet identification. These results are still promising, demonstrating that surgical alteration of the sacral innervation of patients with SB can have significant beneficial effects on bladder function.\textsuperscript{35} In 2010, Peters and colleagues\textsuperscript{36} published their 1-year results in the first United States trial on 9 patients. Most patients had an improvement in bowel function, but none achieved complete urinary continence. Two patients could stop CIC, and antimuscarinic medication was safely stopped in all. Temporary weakness of lower-extremity muscle groups occurred in 89%, 1 child had persistent foot drop. The investigators concluded that more patients with longer follow-up are needed before the procedure can be universally recommended. To the authors’ knowledge, only 2 centers in the United States, 1 in Detroit and 1 in Tampa, are currently offering the procedure.

\textit{Reconstructive Bladder and Bowel Surgery}

Traditional bladder reconstruction includes enlargement of the bladder with a piece of intestine to increase bladder capacity and lower intravesical pressures permanently. Access of the resulting reservoir can be accomplished either by the native urethra or by a newly created catheterizable channel connecting the bladder with the abdominal skin (cutaneous appendicovesicostomy/Mitrofanoff procedure). At the same time, a cutaneous stoma can be created that allows access to the cecum for the application of antegrade enemas (antegrade continent enema [ACE] procedure). If incontinence persists, additional surgeries might be necessary to achieve long-lasting success.\textsuperscript{37}

\textit{Bladder Augmentation and Catheterizable Bladder Stoma}

Bladder augmentation with a piece of reconfigured intestinal tract will transform a high-pressure low-capacity bladder into a low-pressure reservoir capable of holding 400 to 500 mL of urine. The surgery is a long but standardize procedure offered at most major pediatric urological institutions. Improvements in surgical technique and preoperative and postoperative management have made the procedure safer and reduced the complications. However, short- and long-term complications remain common and include infection, stone formation, intestinal obstruction, electrolyte imbalances, metabolic disturbances, bladder perforation, and possible tumor development.\textsuperscript{38} Bladder augmentation will allow patients to store large amounts of urine but also makes it mandatory to empty the reservoir regularly. Because many patients with SB have difficulty accessing their native urethra for CIC, the simultaneous creation of a catheterizable channel is often performed. Several techniques are described depending on patient size and intestine availability. All techniques create a continent channel that connects the bladder with skin via a stoma that can be accessed by patients or caretakers in a sitting position without leaving the wheelchair.
ACE Procedure

This ACE procedure allows patients to empty the bowels on a daily basis via bowel irrigation, therefore, remaining stool continent.\textsuperscript{39} Similar to the bladder stomas, a connection between the cecum and the skin is created via a continent channel. These stomas are placed in the umbilicus or lower abdominal wall in a cosmetically hidden position.\textsuperscript{40} Patients or caretakers catheterize the cecum via the stoma and infuse normal saline while sitting on the toilet. The amount of fluid and time needed until the bowels are emptied are individually different and need to be tailored to the individual patient’s needs.

The surgeries are traditionally accomplished via a long midline incision from below the sternum to the symphysis pubis. With the asset of laparoscopy and robotic assisted laparoscopy, much progress has been made to perform part or the complete surgery with minimal invasive techniques.\textsuperscript{41,42}

Bladder Neck Procedures

The bladder neck can either be competent or have little resistance requiring a bladder neck procedure to avoid postoperative urine leakage. Bladder neck procedures either aim to tighten the bladder outlet by creating a muscular channel or by placing a sling to tighten and elevate the bladder neck region. Both procedures create a controlled obstruction to prevent urine flow under low pressures but still allow leakage of urine if the intravesical pressures are high because of excessive bladder filling. Because most patients do not have an adequate native bladder, providing them with a sufficient low-pressure reservoir simultaneous with bladder augmentation is often necessary. However, Snodgrass and colleagues\textsuperscript{43} reported the possibility of performing a bladder neck procedure without augmentation. The group observed that in their patients, the bladder usually will eventually gain enough compliance to prevent unsafe intravesical pressures that could harm the upper tracts. As with all major congenital conditions, various management protocols exist and are defended by their proponents passionately. These controversies and educated discussions are highly desirable because they spark more research and advance the field.

Tissue Engineering

Research will continue with the ultimate goal to replace intestinal segments for bladder augmentation. Many groups, including the authors’ institutions, pursue possibilities of tissue engineering for bladder regeneration. Bladder augmentation and replacement using laboratory-engineered tissue has been successful in animal models; however, no long-lasting successful human models have been reported. Active laboratory studies creating bladder tissue suitable for transplantation involve biodegradable scaffolds, stem cells, and nanotechnology.\textsuperscript{44–47} Intensive collaboration between basic researches and physicians ensures that the balance between basic science and clinical application is assured. This bench-to-bedside approach will keep research focused on the goal to improve the health and long-term life quality of our patients.

TRANSITION OF PEDIATRIC PATIENTS INTO ADULTHOOD

The success in improving the health and life quality of patients with SB has resulted in a new set of problems for patients and their families as well as for the treating physicians. Reconstructive surgery and management protocols require regular and lifelong follow-up. In the past, most patients did not reach adulthood and had been taken care of by pediatric specialties. With improving patient care, patients with SB can expect a normal lifespan but continue to be taken care of by pediatric specialties. Often, tight
relationships have been built over the years between the families and the physicians, and surgeons accustomed to the procedures and management have provided care. However, as the patients reach adulthood, transition into adult clinics is necessary. Therefore, models have to be created for pediatric and adult disciplines to work together to streamline care and guarantee high-quality follow-up.\textsuperscript{48} Several centers instituted specialized clinics for adult patients cared for by an adult urologist. Exchanges concerning past procedure, new surgeries, management protocols, and research are granted by regular clinics and conferences. However, transition has to occur because adult urologist are more suited to deal with upcoming problems concerning sexuality, benign urological disease, or cancer.

SUMMARY

Much progress and alterations have been made to improve the management, outcome, recovery, and cosmetics of the traditional treatment and continence procedures for patients with SB. Before surgery is considered, conservative protocols have to be maximized because two-thirds of patients can become continent by CIC and medication alone. Fecal continence and bowel management is an integral part of SB treatment. Reconstructive surgery remains the best studied, most successful, permanent, and long-term satisfactory surgery to deal with urinary and stool incontinence. However, complications are common and the families and patients have to understand the need for lifelong management and observation of the created continent reservoir.

The urological care of patients with SB consists of 2 components: the medical management with preservation of renal function and the quality-of-life issues with achieving dryness and independence of bladder and bowel management. Both components are equally important for patients to live a healthy and fulfilled life. Continuous education and care of the families and patients are necessary to motivate them for participation in treatment plans and to avoid frustration and unrealistic expectations. Achieving continence is a long road that requires understanding and compliance best delivered by a team of specialists.

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