Review Article

The Urologist's Role in the Management of Spina Bifida: A Continuum of Care

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Caring for the child with spina bifida necessitates lifelong care by a coordinated team of health care providers, and the urologist plays a vital role in this team. The most important management goal of the urologist is the early establishment and consistent maintenance of a lower pressure urinary reservoir. Ensuring social continence along with its attendant social independence provides some of the greatest management challenges. In those patients who fail medical therapy, surgeons, caregivers, and patients must understand the scope of lower urinary tract reconstruction, the need for strict compliance, and the possibility of future surgery. In this article, we review the recent advances in spina bifida management. UROLOGY xx: xxx, xxxx. © 2010 Elsevier Inc.

Spina bifida (SB) is among the most common congenital anomalies in the United States, affecting approximately 1000 newborns each year.[1] It results from failure of the developing neural tube to close properly during the fourth week of embryonic development.[2] SB is a multifactorial disease, but folic acid deficiency is recognized as an important contributing factor.[3] From randomized controlled data, it has become clear that significant reductions in SB incidence are possible using supplemental periconceptional folic acid.[4] Thus, in January 1998, the US Food and Drug Administration began requiring food manufacturers to fortify US wheat products with 400 μg of folic acid.[5,6] After this mandate, the number of newborns with SB declined by as much as 31%,[7,8] but more recently, further declines in newborn SB incidence have been of much lower magnitude ranging between 3% and 7%.[1,9] Despite a changing incidence, SB patients continue to comprise a considerable portion of pediatric urological practice and require a prompt newborn evaluation followed by careful lifelong surveillance. In this article, we present a review of the recent advances in SB management.

PRENATAL INTERVENTION

With continued refinement in neurosurgical management, the neonatal and childhood mortality of SB has declined dramatically, and most patients can be expected to live well into adulthood.[10] Over the last decade, considerable interest has been garnered for fetal intervention in several congenital anomalies, including SB.[11] In the late 1990s, 2 US centers performing fetal SB closure—Vanderbilt University and the Children's Hospital of Philadelphia—separately reported short-term neurologic outcomes of prenatal intervention for myelomeningocele (MMC).[12,13] The impact of fetal intervention on neurologic function was inconclusive, but both centers did observe lower rates of hindbrain herniation and ventriculoperitoneal shunt dependence after prenatal closure. These findings prompted the National Institutes of Health to begin the Management of Myelomeningocele Study (MOMS), a nonblinded, randomized, controlled trial, with the primary goal of comparing the neurosurgical outcomes of prenatal vs. postnatal MMC closure.[14] The trial began active patient accrual at 3 US centers in early 2003. As a supplement to the primary neurosurgical focus of the MOMS trial, urological evaluation will also be performed at each center specifically to determine whether prenatal closure alters the need for clean intermittent catheterization, the incidence of urinary tract infection, or the risk of death.

Before the start of the MOMS trial, however, 3 groups reported the short-term postnatal urological outcomes of prenatal MMC closure. Holmes et al. evaluated 4 boys and 2 girls after prenatal closure at the University of California, San Francisco. Urodynamic (UDS) evaluation at 1 month of age revealed sphincter dyssynergia with elevated leak point pressures (pressures >40 cm H_2O) in all patients, upper tract dilatation in 5, reduced bladder capacity in 4, and vesicoureteral reflux (VUR) in 3.[15] Holzbeierlein et al. noted similar levels of bladder dysfunction in 23 patients at Vanderbilt University. Postnatal UDS performed at a mean age of 6.5 months showed decreased compliance in 26%, decreased capacity in 34%, detrusor areflexia in 43%, and storage pressures >40 cm H_2O in 82%.[16] Finally, Koh et al. in 2006 reported the outcomes of 5 patients evaluated at their institution after prenatal MMC closure at outside institutions. At a median age of 12 months, UDS revealed detrusor overactivity and complete sphincter denervation

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in all 5.[17] In light of the short-term data provided by these studies, minimal urological improvement appears to occur after prenatal MMC closure. It is hoped that data from the MOMS trial will provide greater insight into the urological impact of fetal SB closure.[14]

NEWBORN EVALUATION AND CHILDHOOD MANAGEMENT

The initial management of the newborn SB patient requires the execution of a prompt, standardized urinary tract evaluation with appropriate intervention. A renal/bladder ultrasound should be performed within 48 hours of birth to assess the urinary tract, and prophylactic antibiotics should be prescribed if hydronephrosis is present. In addition, scheduled, clean intermittent catheterization (CIC) is often instituted before back closure and continued into the postoperative period to ensure the maintenance of a low-pressure reservoir. The frequency of catheterizations is then adjusted based on the residual urine volume obtained during CIC. Stoneking et al. highlighted the importance of this approach in their review of 53 consecutive newborn SB patients.[18] By comparing catheterized residual urine volumes before and after back closure, the authors found significantly higher urine volumes in the postoperative period. This increase was thought to be a result of postoperative spinal shock similar to that seen after spinal cord injury. Notably, in 81% of patients, the presence of elevated postoperative residual urine volumes prompted the continuation of CIC for an average of 11 days after closure.

After repair of the spinal defect, most authors advocate for the performance of a baseline UDS assessment.[19-21] Although a few investigators have reported low rates of renal deterioration using more conservative newborn evaluation that relies on ultrasonography rather than UDS,[22,23] UDS evaluation during infancy is an important screening tool. It is particularly useful for identifying children at increased risk for upper tract deterioration caused by the presence of detrusor sphincter dyssynergia (DSD), detrusor overactivity, and elevated leak point pressures (>40 cm H_2O).[21] A critical paper by Kaefer et al. demonstrated that a proactive management strategy based on infant UDS can positively affect the ultimate need for bladder augmentation. In a population of SB patients less than 1 year of age with high-risk UDS parameters at baseline (DSD, fixed bladder outlet, or elevated storage pressures), the authors compared proactive management (immediate institution of CIC and anticholinergics) to a more expectant approach (CIC and anticholinergics initiated at the first sign of sonographic renal deterioration or urinary incontinence). Among patients who were managed aggressively, 17% subsequently required augmentation compared with 41% who were managed expectantly.[20] Kessler et al. reached a similar conclusion in a cohort of SB patients undergoing initial UDS evaluation over a spectrum of ages. Routinely, in the authors' practice, the presence of detrusor overactivity and a spastic external sphincter prompted treatment with anticholinergics and CIC, respectively. With an average follow-up of >9 years, patients undergoing initial UDS evaluation before 2 years of age were significantly more likely to maintain normal upper tracts and significantly less likely to need surgery for upper tract protection.[24]

After the initial infant evaluation, the childhood management of SB is predicated on meticulous surveillance of the urinary tract for signs of bladder hostility or upper tract deterioration. An important risk factor for such deterioration is the development of secondary spinal cord tethering, which occurs in 15%-25% of patients and commonly presents between the ages of 2 and 8 years.[25-29] Secondary cord tethering is caused by adhesions between the spinal cord itself and the repaired dura mater. During phases of rapid somatic growth, the tethered spinal cord is subjected to mechanical and oxidative stress, leading to neurologic deterioration.[2] The tethered spinal cord presents in a variety of ways, most commonly with a combination of neurologic, orthopedic, and urological findings. Fewer than 10% of patients present with isolated urinary tract symptoms.[25,29]

The key question surrounding secondary spinal cord tethering from the urologist's perspective is to what extent detethering procedures will affect bladder function. Several recent retrospective series have reported improvements in bladder dysfunction after cord release, particularly in children diagnosed at a younger age.[25,27] Tarcan et al. identified 56 patients with secondary tethering of the spinal cord. All had undergone preoperative and postoperative UDS evaluation. At initial presentation of cord tethering, hydronephrosis and VUR were present in 20% and 30%, respectively. After cord release, postoperative UDS demonstrated significant improvements in both total cystometric bladder capacity and detrusor leak point pressure. In addition, low-grade hydronephrosis (Grades 1 or 2) and VUR (Grades 1-3) were improved or resolved in 73% and 100% of cases, respectively. More importantly, children treated before the age of 7 years demonstrated the greatest functional improvements.[27] Abrahmsson et al. followed 20 SB patients with routine UDS before and after spinal cord detethering. In the cohort, only 1 patient demonstrated isolated urinary symptoms, whereas most presented with neurologic or orthopedic abnormalities. Two sets of UDS studies were analyzed in each patient before surgery a baseline evaluation before symptom onset and a preoperative study after the presentation of secondary cord tethering. In the interval between these 2 studies, notable deterioration in bladder function, as evidenced by an increase in detrusor leak point pressures, occurred in 6 patients, whereas the remainder had abnormal but stable bladder function. Overall, postoperative bladder function improved in 35% and remained stable in the rest. The authors found the 6 patients demonstrating obvious preoperative changes in bladder function derived the greatest benefit from release

of the tethered cord. These studies suggest that routine follow-up with UDS is critical to the timely diagnosis and treatment of secondary cord tethering when acute deterioration in bladder function is most likely to be reversed.[25]

Finally, the importance of routine UDS assessment is further underscored by a recent review of SB patients with normal infant UDS evaluations. In this report, from Chidren's Hospital Boston, the authors defined normal UDS as normal bladder compliance, capacity, sphincter electromyography, sustained bladder contraction with complete emptying, and the absence of uninhibited detrusor contractions. In this cohort, 32% eventually developed neurourologic changes requiring cord release and, postoperatively, 25% reported improvements in bladder function.[26] Because of the commonality and interdisciplinary involvement of patients with secondary cord tethering, careful follow-up through a combined SB clinic comprised of orthopedists, neurosurgeons, and urologists allows for the prompt symptom recognition, diagnosis, and treatment.[30]

SOCIAL CONTINENCE

As the SB patient progresses from childhood to adolescence, the goal of the urologist is to facilitate social continence of both the bowel and bladder while preserving renal function. CIC, introduced by Lapides in the 1970s, helped to revolutionize the management of the child with neurogenic bladder.[31] As a result, CIC has become a vital component for the nonsurgical management of SB, and when combined with anticholinergic medication, urinary continence can be achieved in as much as 90% of patients.[32-34] In general, CIC is well tolerated by patients and relatively free of complications.[35-37] On average, most children are able to perform CIC independently and do so beginning between the ages of 8 and 12 years, with girls learning to perform this task sooner than boys.[35-37] Recently, a pair of studies from Swedish investigators reviewed the outcomes of patients performing CIC for more than 10 years. In 31 female patients performing CIC more than 370 patient-years, 20 episodes of difficult catheterization occurred, and only 4 patients reported developing gross hematuria. In the comparison population of 28 males with more than 430 patient-years of performing CIC, difficult catheterization episodes occurred only 42 times. Interestingly, in the males, the onset of puberty did not result in an appreciable increase in catheterization complications.

Yet, despite the success of medical management for neurogenic bladder, a substantial percentage of patients will ultimately require bladder augmentation.[33] Indications for bladder augmentation are variable and typically include upper tract deterioration secondary to elevated storage pressures (>40 cm H_2O), persistent urinary incontinence, detrusor overactivity, and poor compliance.[38] Bladder augmentation is typically reserved for patients older than 5 years of age when social continence becomes important, and in contemporary series, the average age at the time of surgery ranges between 8 and 12 years of age.[39-41] A variety of tissues can be used for augmentation including ureter, small bowel, colon, and stomach.[39,42,43] But regardless of the tissue used, the augmentation must adhere to the basic principle of creating a capacious, lower-pressure reservoir. Studies with long-term follow-up after enterocystoplasty confirm its efficacy in reversing deterioration of the upper tracts and improving urinary continence. Lopez Pereira et al. reported 11 year follow-up in 29 patients undergoing enterocystoplasty. Preoperatively, nearly three-quarters of the patients had upper tract changes consisting of VUR and/or hydronephrosis. After augmentation, hydronephrosis resolved in all patients and VUR resolved in 76% without need for reimplantation. All patients had normal glomerular filtration rates at last follow-up.[43] Medel et al. performed a review of 19 incontinent SB patients after isolated bladder augmentation. At a mean follow-up of 4 years, 79% were dry between catheterizations without the need for pads.[44] Despite such positive results, a recent review of the published enterocystoplasty literature revealed that current knowledge regarding bladder augmentation surgery is derived entirely from a single-institution, retrospective series. The review further noted the relative paucity of studies accurately defining both the surgical indications and appropriate outcome measures of enterocystoplasty.[38] Certainly more controlled data are needed to gain true scientific perspective on the benefits of bladder augmentation.

Considerable thought is necessary before embarking on lower urinary tract reconstruction in the child with SB. All parties involved, including the surgeon, must understand the ramifications of the procedure, the need for strict patient compliance, the potential for complications, and the need for additional surgery. Metcalfe et al. addressed some of these concerns in a comprehensive review of 500 bladder augmentations performed at Indiana University over a 25-year period.[39] MMC was the most common diagnosis, constituting 54% of the cohort, and 40% also had concomitant bladder neck or catheterizable channel procedure performed. After an average of 13.3 years, 34% of patients required additional surgery. Surgical interventions included repair of spontaneous bladder perforation in 8.2%, laparotomy for bowel obstruction in 3%, and cystolithalopaxy in 15%. Repeat bladder augmentation was ultimately required in nearly 10%.[39] Another important consideration in patients undergoing pediatric bladder augmentation is the risk of future malignancy. Clear data regarding this issue are lacking, but available evidence suggests that invasive urothelial cell carcinoma occurs in approximately 1%-2% of patients after bladder augmentation. In 2 recent studies, the median length of time from augment to tumor development ranged between 19 and 32 years.[42,45] The role of environmental carcinogens in this process is unclear, but the development of malignancy in the aug-

mented bladder is likely multifactorial and is likely to increase with longer follow-up. Present recommendations suggest that patients should undergo annual cystoscopy beginning 10 years after augmentation surgery.[39]

Nonetheless, to achieve urinary continence, many children will also require a procedure to increase the resistance of the bladder outlet, and a variety of different modalities exist for this purpose. Long-term results have shown that the artificial urinary sphincter can provide reliable urinary continence in as much as 90% of patients.[46] A bladder neck sling is also efficacious in bolstering the bladder outlet and can be performed using autologous rectus fascia or synthetic materials such as porcine small intestine submucosa.[47] Long- and short-term reports have demonstrated continence rates >80%.[48] The results of minimally invasive techniques for bulking the bladder neck with injected collagen have been disappointing and for that reason are not recommended as first-line treatment of urinary incontinence because of sphincter deficiency.[49]

Most series reporting outcomes after bladder outlet procedures include many patients who have already undergone bladder augmentation. Therefore, the impact of the bladder outlet procedures on urinary continence is difficult to discern.[39,41,50-52] Snodgrass and colleagues reported their experience in 30 patients with neurogenic bladder receiving a bladder neck sling without concomitant augmentation. After short follow-up of 22 months, 83% of patients achieved satisfactory continence (defined as ≤2 damp pads per day), but only 56% of patients were considered dry. Postoperatively, anticholinergic therapy remained unchanged in 20 patients and was initiated or increased in 8.[50] In their follow-up study comparing 18 patients undergoing bladder neck sling and enterocystoplasty to 23 patients undergoing bladder neck sling alone, urinary continence (61% and 52%) was similar regardless of augmentation status. The group undergoing augmentation required significantly less frequent catheterizations and lower doses of anticholinergic mediations.[41] In contrast, Dave et al. reviewed the outcomes of an isolated bladder neck sling procedure in 15 patients with neurogenic bladder. After surgery, 11 patients were dry and 4 patients had persistent incontinence. After a mean follow-up of more than 11 years, 9 of the 11 dry patients presented with recurrent incontinence, and eventually all 15 required augmentation cystoplasty. Comparison of UDS before and after bladder neck sling noted significant increases in mean detrusor leak point pressures and significant decreases in mean compliance and capacity. Furthermore, new-onset hydronephrosis and VUR occurred in 40% and 33% of patients, respectively.[51]

With the integral role played by CIC in SB care, many patients are unable to perform self-catheterization via the native urethra because of a host of factors including previous bladder neck surgery, manual dexterity, and body habitus. As a means to improve both continence and facilitate CIC, catheterizable channels may be created surgically. Using the Mitrofanoff principle, a patient's appendix can be interposed between the abdominal wall and the bladder to create a continent catheterizable bladder channel.[53] In patients without suitable appendix, other segments of bowel may be substituted, or a portion of the bladder may be configured into a tube and brought to the skin.[54-56] Chronic constipation caused by neurogenic bowel is also a significant source of morbidity and requires patients and their families to adhere to a daily bowel regimen consisting of various enemas, suppositories, and rectal stimulation to maintain normal bowel function and prevent stool accidents. With principles similar to that of catheterizable bladder channels, Malone and colleagues described the antegrade continence enema in 1990 to improve the management of neurogenic bowel.[57] Since that time, urologists have embraced this procedure and used a variety of bowel segments to create a continent catheterizable channel between the abdominal wall and the colon.[54,55,58] Via this channel, enemas can be administered daily, significantly reducing the number of stool accidents while obviating the need for rectal bowel regimens.

Surgical outcomes of catheterizable bowel and bladder channels have been favorable and patient acceptance of these procedures has been high.[58,59] Among the most common complications of both bowel and bladder channels is stomal stenosis, which typically occurs in 5%-18% of patients, requiring channel revision in 8%-27%.[54,56,58,60] Bani-Hani et al. recently reported their large experience with the Malone antegrade continence enema. After median follow-up of 50 months in 236 patients, the authors observed a fecal continence rate of 94%.[58] Clark et al. similarly reported a 95% fecal continence rate after Malone antegrate continence enema creation in 20 patients.[54] Stomal leakage from continent catheterizable channels to either bowel or bladder is rare, occurring in approximately 2%-3% of patients.[54,56,58,60] In addition, when compared with staged procedures, the creation of catheterizable channels for both the neurogenic bladder and bowel can be completed in 1 operation without adverse effects on continence, complications, or need for revision.[55] Regardless of the channel being created or the type of tissue used, patients and families must receive adequate preoperative counseling regarding the importance of diligent compliance with daily catheterizations. Research has clearly shown that in patients undergoing surgery to create catheterizable bowel and bladder channels, the incidence of infection, stomal stenosis, and surgical revision is significantly more likely to occur in patients who are not compliant with routine follow-up visits and daily catheterization.[54]

QUALITY-OF-LIFE OUTCOMES

Recently, increasing focus has been directed towards quality-of-life (QOL) outcomes in a number of pediatric patient groups, including SB. In general, SB patients

appear to have lower self-image than their healthy counterparts. Moore et al., using a validated psychological assessment tool, demonstrated lower overall scores of self-concept among adolescent SB patients when compared with gender-specific controls.[61] However, when continent SB patients were compared with the healthy controls, self-concept scores did not differ. In contrast, a recent French study was unable to demonstrate a correlation between continence and health-related QOL in 160 adolescents with SB.[62] With these conflicting results, understanding the impact of surgical reconstruction on continence and subsequent QOL outcomes is even more important. Unfortunately, only limited retrospective data has shown that lower urinary tract reconstruction leads to improvements in QOL.[63] In a prospective fashion, Parekh et al. administered the validated PedsQL™4.0 health-related QOL instrument to SB patients and their parents before and after lower urinary tract reconstruction. SB patients demonstrated significantly lower QOL scores compared with their healthy counterparts. However, preoperative child-reported scores were significantly higher than those reported by their parents. Postoperatively, surgery did not impact QOL negatively and the disparity between child- and parent-reported scores lessened. Unfortunately, a true QOL benefit from surgical reconstruction could not be demonstrated.[64] In another recent prospective analysis, MacNeily et al. also addressed the QOL impact of lower urinary tract reconstruction in 31 consecutive SB patients. Administration of a validated QOL instrument preoperatively and postoperatively showed significant improvements in continence after surgery, but the authors were unable to detect any significant changes in health-related QOL because of the operation. Taken at face value, these studies suggest that surgical intervention for bowel and bladder continence does little to improve QOL. Yet, urologists must continue to critically evaluate the impact of lower urinary tract reconstruction on patient QOL by developing better instruments for assessing and capturing these important postoperative outcomes.

NEW FRONTIERS

The future of the surgical management pediatric SB lies in technologic advancement. With the advent of laparoscopy and robotic-assisted laparoscopy, minimally invasive approaches for lower urinary tract reconstruction, including enterocystoplasty, catheterizable channel creation, and bladder neck procedures, are being reported with increasing frequency.[65-67] Tissue engineering is another of intense interest in patients with neurogenic bladder. In an attempt to eliminate the morbidity associated with interposing bowel into the urinary tract, the search is ongoing to find alternative tissue for augmenting the bladder. In a remarkable 2006 report, researchers from Children's Hospital Boston presented the preliminary results of 7 children undergoing augmentation cystoplasty using a tissue-engineered augment grown in a laboratory from a sample of the patient's own bladder.[68] Based on this initial experience, a phase II open-label, multicenter trial of augmentation using autologous bladder tissue is currently underway.[69] Finally, Xiao et al., in a promising 2005 study, reported their experience with a surgically created somatic-autonomic reflex pathway in patients with SB. Building on their experience in patients with spinal cord injury, 20 incontinent SB patients underwent the performance of a limited lumbar laminectomy followed by microsurgical anastomosis of lumbar and sacral ventral nerve roots. Postoperatively, 17 of the 20 patients were able to initiate volitional voiding by stimulating the L5 dermatome on the thigh. Included among the 17 responders to treatment were 14 patients with preoperative UDS demonstrating detrusor areflexia. The authors additionally noted improvements in bladder sensation after surgery.[70]

CONCLUSIONS

SB is a multifaceted disease that requires lifelong care by a coordinated team of health care providers. The urologist plays a vital role in this care team and must be involved early and often. The paramount goal of managing the neurogenic bladder is the early establishment and maintenance of a lower-pressure urinary reservoir followed by frequent, meticulous follow-up with appropriate intervention. Ensuring social continence along with its attendant social independence provides some of the greatest management challenges. In those patients who fail medical therapy, surgeons, caregivers, and patients must understand the scope of lower urinary tract reconstruction, the need for strict compliance, and the possibility of future surgery. SB care in the future will benefit not only from technologic advances in minimally invasive surgical technique and tissue engineering but also from advances in understanding how current management strategies affect patient QOL.

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