Int Urol Nephrol (2012) 44:817–827
DOI 10.1007/s11255-010-9894-5

NEPHROLOGY – REVIEW

Prevention of chronic kidney disease in spina bifida

Guido Filler · Mireille Gharib · Shelley Casier · Petra Lödige · Jochen H. H. Ehrich · Sumit Dave

Received: 13 October 2010 / Accepted: 24 December 2010 / Published online: 13 January 2011
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Abstract
Objective The prevalence of progressive chronic kidney disease (CKD) in children and adults with spina bifida is considerable, rising, and entirely preventable.
Removing the cause: prevention of spina bifida The best prevention of CKD in spina bifida is prevention of spina bifida itself through strategies that include folate supplementation, ideally before pregnancy.
The cause of CKD Dysfunctional bladder outlet causes febrile Urinary Tract Infections (UTI), even with clean intermittent catheterization (CIC), and subsequent renal scarring. The development of secondary vesicoureteric reflux (VUR) increases the risk of renal scarring and CKD.
Finding the ideal marker for measurement of renal function in spina bifida Creatinine-based methods are insensitive because of low muscle mass and underdeveloped musculature in the legs. Only Cystatin C–based eGFR can reliably assess global renal function in these patients. However, unilateral renal damage requires nuclear medicine scans, such as ^{99m}Tc DMSA.
(Video)Urodynamics studies (UDS) Early treatment is recommended based on UDS with anticholinergics, CIC, and antibiotic prophylaxis when indicated. Overnight catheter drainage, Botox, and eventually augmentation cystoplasty are required for poorly compliant bladders. A continent child or one rendered continent following surgery is at a higher risk of renal damage.
Conclusion A multidisciplinary approach is required to reduce the burden of CKD in patients with spina bifida. The right tools have to be utilized to monitor these patients, particularly if recurrent UTIs occur. Cystatin C eGFR is preferred for monitoring renal damage in these patients, and ^{99m}Tc DMSA scans have to be used to detect unilateral renal scarring.

Keywords Spina bifida · Cystatin C · Urodynamics · Chronic kidney disease · Renogram · Renal function

G. Filler (✉) · M. Gharib · S. Casier
Departments of Pediatrics, Children's Hospital at London Health Science Centre, University of Western Ontario, 800 Commissioners Road East, London, ON N6A 5W9, Canada
e-mail: guido.filler@lhsc.on.ca

S. Dave
Departments of Surgery, Children's Hospital at London Health Science Centre, University of Western Ontario, London, ON, Canada

P. Lödige · J. H. H. Ehrich
Department of Pediatrics, Hanover Medical School, Hanover, Germany

Introduction

Spina bifida aperta is the most common type of neural-tube defect (NTD) [1]. While associated issues

such as Arnold Chiari malformation, paraplegia, neurogenic bowel, and bladder are terminally differentiated at birth, children with spina bifida usually have normal renal function at birth, but often suffer a progressive deterioration of renal function due to the neurogenic bladder. Spina bifida has traditionally not been associated with a high prevalence of end-stage renal disease (ESRD) during childhood. However, older epidemiological data suggest that end-stage renal failure as a consequence of reflux nephropathy and renal scarring is not infrequent in adulthood. In a study of Scottish dialysis patients, 1.5% (both pediatric and adult) had ESRD secondary to spina bifida and spinal cord injury. In this study, they showed that the median age of renal transplantation in these patients was 27 years [2]. Despite early urological management guided by post-spinal closure video-urodynamics and institution of clean intermittent catheterization with or without anticholinergic therapy [3], there is a possibility of progressive renal damage secondary to bladder dynamics in these patients [4].

Population-based longitudinal studies on the natural history of spina bifida–associated renal damage are scarce and difficult to interpret in light of management protocols adapted and the timing of nephro-urological intervention. However, there are recent studies on the incidence and prevalence of end-stage renal disease based on national databases. A recent study based on the national health insurance database in Taiwan [5] suggested that 15% of spina bifida patients develop end-stage chronic kidney disease (CKD) over 20 years. In that study, the prevalence of end-stage CKD increased from about 2.5 to almost 10/1000 of dialysis patients over the last decade. As CKD in patients with spina bifida is completely preventable, the high prevalence of ESRD reflects a lack of proactive and timely intervention. Therefore, this manuscript will discuss the strategies for prevention of renal disease in this high-risk population.

Remove the cause: spina bifida prevention

The best prevention of renal disease associated with spina bifida is prevention of spina bifida in utero. In the embryo, the central nervous system begins to form during the third week of embryonic life as the neural plate [6]. In normal development, the neural plate folds on itself and fuses to form the neural tube [7] at the 28th day post-conception by a process called primary neurulation [8]. This neural tube will eventually differentiate into the spinal cord and the brain; however, if there is failure of this process; a myelomeningocele is formed [9].

Myelomeningocele is rather uncommon in the general population, and its incidence is difficult to quantify due to the fact that the calculations include live and stillborn babies, while excluding those that end in spontaneous or elective abortions [10].

The incidence of neural-tube defects is highly variable and depends upon age, parity, obesity, ethnic, geographic, and nutritional factors. A Northern Ireland and southeast England study shows that the incidence of NTDs ranges from one to seven per 1,000 live births [11]. The highest rates are found in China, Ireland, Great Britain, Pakistan, India, and Egypt [12]. In the United States, Hispanics were concluded to have an increased risk of NTD complications, whereas the risk for African Americans was rather low [12].

Fortunately, progress has been made to identify modifiable factors to reduce the incidence of NTD. In addition, prenatal imaging can reliably identify fetuses with spina bifida, thus allowing the option of counseling and abortion [13, 14]. However, this manuscript will not address the diagnostic tools for early identification of NTDs, but rather on its prevention. The most important strategy for the prevention is fortification of grains as well as supplementation of folate into the diets of pregnant women across the world [15–17]. The association between folate and NTD was discovered in Hungary [18]. Importantly, sufficient folate levels are required at the beginning of the pregnancy and during the formation of the neural tube. Accordingly, the US Public Health Service issued the recommendation that all women of child-bearing age who are capable of becoming pregnant should consume 0.4 mg of folic acid per day in 1993 [19]. Supplementation after 28 days of gestation will not reverse the NTD.

The incidence of NTD can be decreased further by eliminating or decreasing folic acid antagonists, such as phenytoin and sulfasalazine [20]. Molecularly, adequate folate is critical for cell division due to its essential role in the synthesis of nucleic and amino acids [21]. Folate deficiency may impede adequate

cell turnover during a critical point in neural tube closure, thereby resulting in incomplete development [21]. Therefore, it is evident from the pathophysiology that increasing folic acid intake before and during pregnancy will lower the occurrences of NTDs. In Oman, the trend of spina bifida and other NTDs before and after the implementation of the supplementation and fortification of wheat flour with iron and folate was analyzed. The annual incidence of spina bifida ranged from 2.3 to 4.0 per 1,000 births between 1991 and 1996, but fell dramatically to 0.29 per 1,000 by 2006 after the folate implementation [22].

A similar outcome was seen when a Canadian study analyzed the number of children with spina bifida in live births, stillbirths, and terminations in seven provinces from 1993 to 2002 [23]. The study period was divided into prefortification, partial-fortification, and full-fortification phases. A total of 2,446 subjects with neural-tube defects were recorded among 1.9 million births. The prevalence of neural-tube defects decreased from 1.58 per 1,000 births before fortification to 0.86 per 1,000 births during the full-fortification period, a 46% reduction. Unfortunately, despite these strategies, currently, we will still be involved in the care of spina bifida patients born every year with a neurogenic bladder and at risk of long-term renal damage.

The cause of CKD: dysfunctional bladder outlet causing urinary tract infections and renal scarring

Children with spina bifida are essentially born with normal upper tracts but are at risk of renal damage secondary to their bladder dynamics. Proactive and early institution of therapy is the key in preventing renal damage. Moreover, the lesion and its effect continue to evolve in the growing child, and as nephrologists and urologists, we have to be cognizant of this fact and monitor carefully throughout life. A multidisciplinary team ideally provides this care with expertise in pediatric subspecialties of nephrology, neurosurgery, orthopedics, neurology, urology, and rehabilitation [24]. One of the more progressive and insidious onsets that is stringently monitored is the complication of a neurogenic bladder. This may develop progressive deterioration of the upper urinary tract and ultimately lead to chronic renal disease. Therefore, it is vital to aim treatment at the reduction in bladder pressures and the minimization of urine stasis in order to prevent or at least attenuate renal disease [24]. Some of the standard management options include clean intermittent catheterization (CIC), urodynamic monitoring of bladder function, antibiotic prophylaxis when indicated, anticholinergic medication and overnight catheter drainage to reduce filling pressures and reduce the detrusor leak point pressure (DLPP), and surgical options to achieve the above-mentioned goals [25, 26].

Renal damage in NTD is secondary to a combination of high bladder filling and emptying pressures, presence of detrusor sphincter dyssynergia and the secondary vesicoureteric reflux this induces along with recurrent urinary tract infections (rUTI) that results in renal scarring [27, 28].

Few studies have evaluated the natural history of spina bifida–related renal damage over time. We report here an unpublished study that enhances the understanding of the progressive nature of renal damage in spina bifida patients. After obtaining approval by the institutional ethics board, we studied the prevalence of rUTI and renal damage in a cohort of 159 spina bifida patients treated at a single centre in a multidisciplinary clinic during the time interval of 1972–1992. At the last investigation, 88 female and 71 male patients had a mean age of 11.5 ± 6.1 years standard deviation. Mean observation time was 5.7 years (range 0.1–18.2 years). In our manuscript, urinary tract infections were defined as febrile or otherwise symptomatic urinary tract infections with a positive urine culture. This definition is not ideal; however, as this was a retrospective chart review, any documented infection meeting these criteria was captured. Ultimately, we appreciate that not all urinary tract infections may have been captured. Serial renal ultrasounds, voiding cystograms (VCUG), nuclear medicine renal scans, and serum creatinine measurements were analyzed retrospectively. Bladder configuration, kidney size, location, shape and echogenicity and dilatation of the urinary tract were studied using standard ultrasound criteria. Normal creatinine was defined by values below 60 μmoles/L in children less than 8 years and below 100 μmoles/L in children older than 8 years. Increased pathological post-void residual bladder volume was defined as >15 mL in infants, >20 mL in children aged 2–8, >50 mL in children aged

8.1–13 years, and >100 mL in adolescents >13 years of age [29]. VCUG documented VUR grade as described by Dwoskin and Perlmutter [30]. The methods of Jafri et al. [31] were implemented using ^{123}J-hippurate Isotope scans and IVP scans using IV Omnipaque. Forty to 60% unilateral differential renal function of the total renal function was considered to be normal, while 30–40% was mild and <30% was categorized as severe unilateral renal impairment. It is important to note that in today's studies, a 20% variation is to be considered too large and that hence a 10% variation (45–55%) is within normal limits. Due to this difference, the results presented here may underestimate the degree of unilateral renal damage.

In our cohort of 159 patients, we observed progressive worsening of renal damage over time. As this was a historical study, it was not surprising to find a high prevalence of manual bladder expression (73%) in the first year of life, 16% were able to void spontaneously, and only 1% performed CIC in the first year of life, while the remainder were not recorded. Over time, the proportion of CIC increased to 23% at age 7. Furthermore, a variety of urinary diversions, ranging from vesicostomy to Mainz pouch, were performed in 11%. In these 159 patients, incidence to first UTI was studied by life-table analysis (Fig. 1). Fifty percent of children developed at least one UTI by the age of 15 months. By the age of 15 years, 81% of patients developed at least one UTI. There was also a high prevalence of rUTIs: more than 5 episodes were seen in 44% of patients

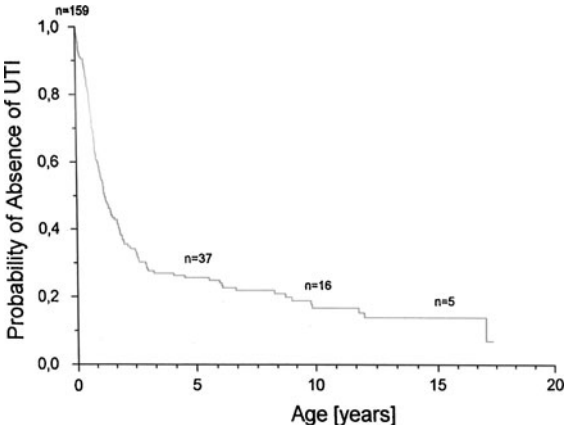

Fig. 1 Life-table analysis of the probability of absence of urinary tract infection in 159 children with spina bifida, followed between 1972 and 1992

and more than 20 occurrences in 9%. rUTIs were caused by E-coli (31%), Proteus (30%), and unidentified or other bacteria (39%). There was a high prevalence of Pseudomonas infections in patients with more than 20 febrile urinary tract infections. For the fifth UTI, 32.1% had E.coli, 7.1% had proteus vulgaris, and 5.4% had other proteus species, and one patient grew yeast when diagnosed with the 5th UTI. 15.7% of patients had up to 10 UTIs, and in these cases, pseudomonas aeruginosa was found in 24%. 8.6% of patients had twenty or more documented UTIs, and in these cases, 36.4% of patients had pseudomonas aeruginosa. Treatment of UTIs included Cotrimoxazole (38%), Aminopenicillins (18%), Cephalosporines (9%), Nitrofurantoin (9%), and Trimethoprim (5%). In 21% of cases, the antibiotic used was not documented. In these patients, prophylaxis was commonly used and comprised of Cotrimoxazole (56.6% at last follow-up) and Nitrofurantoin (38.1% at last follow-up).

Other studies confirm a high prevalence of UTIs in these children [32]. Moreover, even with regular CIC, febrile infections are common, secondary to the high incidence of bacteriuria that CIC induces and the associated predisposing factor of constipation. The diagnosis of UTI is particularly difficult in these patients. Relying on a culture is very unreliable in the absence of symptoms. Up to 70% of these patients will present with asymptomatic bacteriuria that does not require treatment [33], whereas only 5% of these patients will be symptomatic and will receive needed treatment [34]. We recommend being very vigilant regarding rUTI's but also ensuring that we do not over-treat these children and induce antibiotic resistance by following stringent diagnostic criteria to prove a UTI. Symptomatic UTIs or positive cultures associated with high CRP/inflammatory markers are positive markers of a true UTI in children on CIC [35].

Development of secondary VUR as marker of renal risk

A recent study found that 30–40% of children with myelomeningoceles developed some degree of renal dysfunction [36]. More specifically, previous studies have demonstrated that the presence or new onset of vesicoureteric reflux is particularly associated with

chronic kidney disease (CKD). This is probably related to the strong correlation between VUR, DSD, and the high voiding pressures. Also, secondary VUR as this can be especially dangerous in the presence of bacteriuria induced by CIC. In a recent study from Taiwan, 15% of patients with spina bifida progressed into end-stage renal failure after 20 years [3]. In that study, the prevalence of end-stage CKD increased from about 2.5 to almost 10/1000 dialysis patients over the last decade, and the incidence of VUR in those patients increased significantly from 2.5 to 6/1000 [4]. In a similar study, the mechanism of VUR was analyzed more in depth. It was found that lack of coordination between the detrusor contraction and external sphincter relaxation (detrusor sphincter dyssynergia) is the most important predictor of urinary tract deterioration. DSD promotes vesicoureteric reflux, and in fact, most children with spina bifida who have VUR can be assumed to have DSD, even though that is a urodynamic diagnosis [37]. In a series of 36 infants with myelomeningocele, 50% of infants had discoordination of the detrusor and external urethral sphincter, 25% had synergic activity of the sphincter, and 25% had absent sphincter activity. Thirteen of the 18 infants with DSD developed hydroureteronephrosis (72%) and reflux [38].

Using the same cohort of 159 spina bifida patients named above, we analyzed the prevalence of VUR and compared this with ultrasound imaging. Seven hundred and twelve ultrasounds were performed altogether on the 159 patients at a rate of one ultrasound for every patient yearly. During the first years of life, 22% had an abnormally shaped bladder, thickened bladder wall or post-void residual urine; 26% showed signs of VUR, such as dilatation of the retrovesical ureter, urinary tract or the renal pelvis, while 5% had anatomical pathologies, such as rotation anomaly, renal cysts or abnormalities in kidney size and shape. Almost all (90%) of the 159 patients underwent a VCUG, which were repeated on an average every 2.5 years. Pathological findings were found in 87% of patients, including abnormal bladder shape, evidence of DSD, residual urine or a wide-open bladder neck and external sphincter. Furthermore, 50% of these patients developed VUR by the age of nine (Fig. 2). More specifically, 22% were found with grade I/II reflux, 33% with grade III, and 33% with grade IV/V, while the remainder 12% was not determined. In 16 of those patients that had

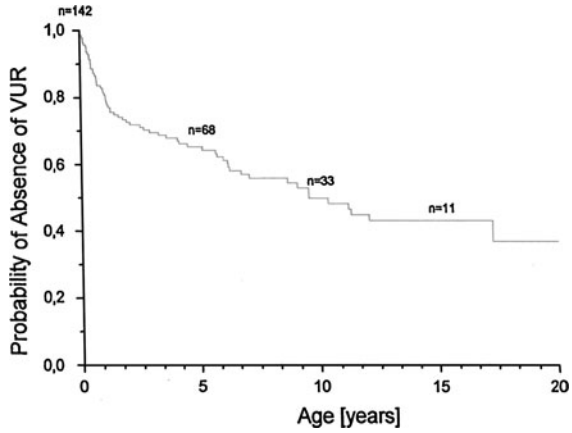

Fig. 2 Life-table analysis of the probability of absence of vesicoureteric reflux in 159 children with spina bifida, followed between 1972 and 1992

subsequent 4 VCUG's, VUR improved in seven patients, worsened in six, and remained unchanged in three.

Several factors may contribute to the severity of renal scarring. While some studies suggest that the severity of VUR affects the likelihood of scarring with an 18-fold increase in the scarring in patients with high-grade reflux [39], other studies did not demonstrate a direct relationship between the severity of VUR and scarring [40].

Finding the ideal renal function marker in children with spina bifida

As previously discussed, patients with spina bifida are at a significantly increased risk of developing renal damage directly related to the functional and structural abnormalities of their urinary tract, specifically their urinary bladder [41]. For this reason, it is vital to be able to monitor their renal function using an accurate glomerular filtration rate (GFR) [35]. In standard practices, the GFR is equal to the sum of the filtration rates in all of the functioning nephrons [31]. The gold standard in GFR measurement is inulin clearance because it is freely filtered at the glomerulus, nontoxic, neither secreted nor reabsorbed by the renal tubules, and not changed during its excretion by the kidney [42]. However, this molecule is not used in modern practice because it is not easily measured [43]. Over the years, other methods have been used, such as endogenous creatinine clearance; however,

creatinine secretion in the tubules falsely elevates the GFR [44]. In North America, common methods to estimate the GFR are the serum creatinine concentration or the creatinine clearance [45], and more reliably, using a height creatinine ratio [46]. A dilemma with the current GFR measurements is that it depends on age, sex, and body size with considerable variation among healthy individuals [47]. In those with CKD, the creatinine excretion is much greater than the filtered load; therefore, there will be a large overestimation of GFR [48–51]. For obvious reasons, this is fallacious, and caution is recommended in clinical practice because renal function of these patients will be more severely deteriorated than that depicted by the GFR calculation. Specific for our considerations, monitoring renal function in spina bifida patients is particularly challenging because of the abnormal body muscle mass and the degree of immobility imposed by the anomaly. In spina bifida associated with paraplegia, the reduced muscle mass, and therefore creatinine, which is dependent on muscle mass, is no longer an accurate measurement [52].

Cystatin C (CysC) is a low molecular weight protein that is produced by all human nucleated cells and almost completely filtered in the glomeruli [53]. Formation of CysC is independent of muscle mass, height, size, and body mass index, but thyroid dysfunction and medium doses of glucocorticoids may slightly alter production [47]. Small molecular weight proteins such as CysC may serve as ideal endogenous markers of GFR because their small molecular weight allows them to be freely filtered through the normal glomerular membrane; they are subject to protein degradation in the proximal tubule and do not undergo tubular secretion/non-renal elimination [54]. Studies using human CysC in rat subjects have shown that renal clearance is 94% of the renal clearance of the generally used GFR marker [55]. The most beneficial factor regarding CysC in spina bifida patients is the fact that it remains constant from around 1 to 50 years of age [56–60] and is independent of body composition [61–63]. Therefore, CysC forms the only reliable marker in patients with spina bifida or spinal cord injuries [46, 64]. However, Abrahamson et al. [65] recently demonstrate that even though CysC serves as a good tool for estimation of GFR in spina bifida patients, it fails to predict the extent of renal damage and scarring.

Unilateral damage precedes global renal damage

As outlined by Abrahamson et al. [53], even measurements with CysC fail to recognize a number of patients at risk. Specifically, unilateral renal damage cannot be identified with a marker that measures global renal function. Functional imaging with nuclear medicine techniques will therefore have to be employed. The collective 159 patients in our study mentioned previously were subject to repeated ^{123}Iodine hippurate scans ($n = 157$) in 47% of the patients and studied by life-table analysis (Fig. 3). The frequency of scans was one scan per patient every 5 years. It was found that mild and severe unilateral renal function loss was evident in 50% of patients by the age of 15.

In children aged 2–5, mild functional loss was seen in 13%. This increased over time in the children to 80% by the 10th–13th year of life. Only 3% of children between 2 and 5 years of age appeared with severe functional loss, while 23% showed aggravation of unilateral loss of function. In a sub-analysis of children with severe unilateral loss, 50% worsened by the time they reached 10 years of age. Moreover, it was found that unilateral dysfunction during the first 5 years of life was more common in those children with VUR than in children without VUR (Fig. 4). Not unexpectedly, patients with VUR were affected more severely than patients without VUR.

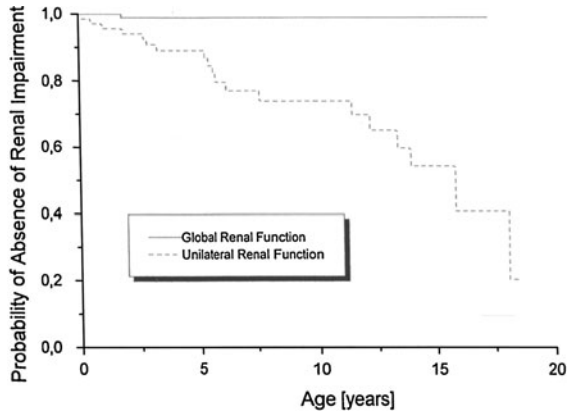

Fig. 3 Life-table analysis of the probability of absence of unilateral renal damage and globally impaired GFR estimated by creatinine in 75 children with spina bifida, followed between 1972 and 1992. There was a statistically significant difference between both curves ($P < 0.05$, log-rank test, equivalent to Mantel–Haenszel test)

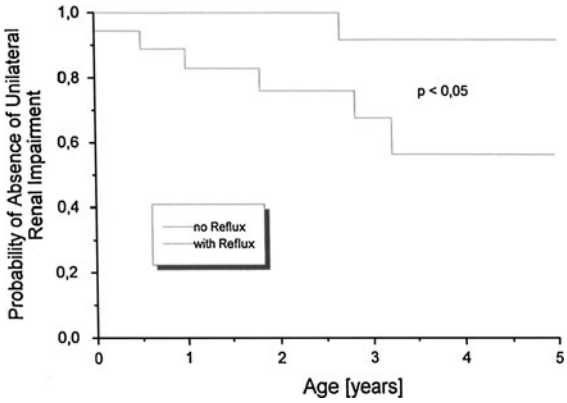

Fig. 4 Life-table analysis of the probability of absence of unilateral renal damage and globally impaired GFR estimated by creatinine in 75 children with spina bifida, followed between 1972 and 1992, stratified by the presence of absence of VUR. There was a statistically significant difference between both curves ($P < 0.05$, log-rank test, equivalent to Mantel–Haenszel test)

The high proportion of patients with unilateral renal damage was surprising, and questions arose as to whether this old cohort of spina bifida patients was managed according to Lapides' seminal work on intermittent bladder catheterization [3]. However, almost all patients were on clean intermittent bladder catheterization and on prophylaxis as well.

There are multiple other factors that influence the likelihood of renal scarring. A study specific to spina bifida patients identified late referral, female gender, overactive detrusor, and detrusor sphincter dyssynergia as having detrimental effects on renal parenchymal function in these patients [66]. Certainly, early initiation of treatment of pyelonephritis in spina bifida patients with effective antibiotics reduces the likelihood of renal scarring [67, 68]. Similarly, treatment of reflux, more recently with endoscopic therapy, may reduce renal scarring [69]. The role of prophylactic antibiotics for the prevention of renal scarring remains controversial [70], and appropriate technology for the assessment needs to be used to differentiate between dysplasia in patients with congenital VUR and acquired scarring [71]. The results of the American RIVUR study (randomized Intervention for Children with Vesicoureteral Reflux) will not be available for a while. However, a recent Swedish study with a three-randomization of children with VUR to placebo, deflux therapy and prophylaxis clearly demonstrates a benefit of prophylaxis for the reduction in renal scarring [72]. It is important to point out that these studies were not all performed in spina bifida patients. The study presented here in the current publication had almost all patients on Septra or Nitrofurantoin prophylaxis.

A recent study by Shiroyanagi et al. from Japan described the significance of ^{99m}technetium dimercapto-succinic acid (^{99m}Tc DMSA) renal scans used in children with spina bifida. Similar to our study, Shiroyanagi et al. considered scans with a differential function of less than 40% as abnormal, concordant with our study criteria [73]. Precautions were taken in order to ensure that mean patient age, male-to-female ratio, leak point pressure, bladder compliance, and timing of CIC initiation did not vary among the groups (normal vs. abnormal scans). Of the 64 patients studied, 16 (25%) were found to be abnormal, while 48 (75%) were of normal function. Eleven (69%) patients with abnormal scans and 9 (19%) with normal scans had previous rUTIs, while 16 (100%) of children with abnormal scans and 15 (31%) of those with normal scans presented with VUR. They concluded that positive VUR and febrile rUTI's were associated with an abnormal DMSA scan. The authors suggested that ^{99m}Tc DMSA renal scans are useful in determining the loss of renal function in children with febrile UTI and reflux complications [64]. A positive DMSA scan also correlates with bladder wall thickness which is a surrogate marker for poor bladder compliance further highlighting the role of the bladder in upper tract damage [74]. We agree with the above conclusion and recommend performing ^{99m}Tc DMSA renal scans as a means of accurately assessing differential renal function and monitoring the status of current scarring or new/evolving scars.

Urodynamics

Routine early and repeated urodynamics (UDS) forms the basis of urological management of spina bifida–associated neurogenic bladder. It has been conclusively proven that urodynamics is the only definitive diagnostic modality to identify children at risk, which allows a window of opportunity to act before irreversible upper tract changes ensue [75]. Essentially, UDS evaluates bladder filling and emptying. Markers of poor bladder compliance include a

detrusor leak point pressure or end filling pressure >40 cm H_2O, low bladder volumes at 20–30 cm H_2O pressure, a rapid and early rise in detrusor bladder pressure, and an abnormally low compliance value [76]. Urodynamic studies have the ability to predict the risk of hydronephrosis and reflux by diagnosing those with DSD and can directly prognosticate progressive renal damage [38]. Bladder trabeculations suggest high filling pressures, and a smooth bladder is likely to be incontinent but safe for the upper tracts [77, 78]. DSD is a reliable marker for VUR and progressive upper tract damage [79]. Early and aggressive treatment is recommended based on pre/post UDS of the spina bifida patient with anticholinergics, CIC, and antibiotic prophylaxis when indicated [66]. Overnight catheter drainage [80], Botox [81], and eventually augmentation cystoplasty are required for the poorly compliant bladder with high filling pressures [82]. By contrast, a child with overwhelming incontinence is usually well protected against upper tract damage [83]. A continent child or one rendered continent following surgery is at a higher risk of renal damage [84]. The urologist has to weigh the advantage of a continent diversion against the risk of CKD owing to high bladder pressure. Again, UDS will help to assess for that risk.

Conclusion

The prevalence of progressive chronic kidney disease in children and adults with spina bifida is considerable, rising, and entirely preventable. This damage is secondary to renal scarring after febrile pyelonephritis and high bladder pressure causing ongoing damage. Patients with VUR, a surrogate marker for DSD, have inferior outcomes. Measurement of global renal function using creatinine is not reliable because of the altered muscle mass in these children. Cystatin C GFR performs better, but is insensitive in detecting unilateral renal damage. Repeated nuclear medicine scans using ^{99m}Tc DMSA for early detection of renal scarring are recommended. CKD in these patients is preventable, and despite primary prevention of spina bifida through folic acid programs, our current practices will continue to evaluate and treat these children. This article highlights the right tools for surveillance and emphasizes the role of proactive and early intervention to diagnose and treat the child with DSD and its correlation with VUR and rUTI. A multidisciplinary approach involving the urologists is paramount to address bladder pressure, VUR, and post-void residual. The onus lies on us to ensure that these children with a multitude of issues receive our best evidence-based care, and preventable issues are not thrust upon them and their families. This will require a concerted and coordinated effort from their nephrologists and urologists and ongoing recognition of changes in their bladder function and reevaluation of their risk of upper tract damage.

Acknowledgments The data for the retrospective chart review on the 159 children with spina bifida were gathered by Dr. Petra Lödige for her doctoral thesis at Hannover Medical School in 1996. She was supervised by GF and JHHE. The data were presented in 1995 at the conference of the International Pediatric Nephrology Association (IPNA) in Santiago de Chile, and published as abstract in Pediatr Nephrol 1995; 9(6): C41. This study was completed without any financial support.

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