Posterior Urethral Valves

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23.1 Introduction

Posterior urethral valve (PUV) is a congenital condition which very often deals with bladder problems, not only due to neonatal bladder outlet obstruction but also because of a number of consequences on bladder function during infancy and childhood, often persisting through adolescence and long life. For the above reasons, PUV should be considered one of the main issues of clinical urodynamic in children. The condition is early detected prenatally by obstetric ultrasound but can be diagnosed later on.

Despite early relief of bladder outlet obstruction, remaining pathological changes in the bladder can cause significant bladder dysfunction resulting in incontinence and impaired upper tract drainage. A considerable quote of children (about 20%) suffer from urinary incontinence, and urodynamic bladder dysfunction was seen in many patients (55%, 0–72%) after primary treatment.

While a certain degree of bladder recovery will occur in most patients, some have long-term issues severe enough to result in compromise of the upper urinary tracts and renal function. The progressive slow deterioration that some of these patients present over years in renal function has been showed as a result of bladder dysfunction. Bladder function is often compromised since infancy as low compliant or overactive, with possible consequent delayed toilet training. Later in life the bladder tends to become oversized and empties poorly. Polyuria which is associated with renal failure as well as secondary changes in the bladder neck also has an effect on bladder function and emptying.

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23.2 Posterior Urethral Valves in Neonate

Demography. Posterior urethral valves (PUV) are the commonest etiology of urinary tract obstruction in the neonate. It is the commonest cause of chronic kidney disease secondary to urinary obstruction in children. A population-based study found the incidence to be 2.48 (2.14–2.81) per 10,000 live births [1].

Antenatal diagnosis. *Prenatal ultrasound* scanning has increased detection rate of PUV: in a population-based study, prenatal diagnosis rate was 46.9% [1]. Sonographic features of PUV include thick-walled bladder, bilateral hydronephrosis, scanty liquor, dilated bladder and posterior urethra, and echo-bright kidneys (Fig. 23.1a, b).

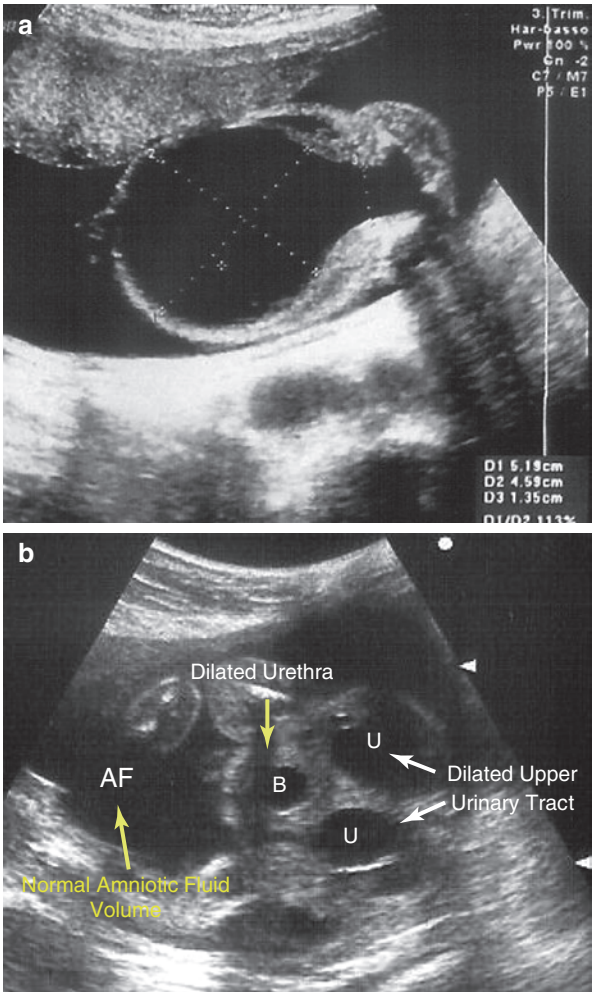

Fig. 23.1 Ultrasound antenatal diagnosis. (**a**) Antenatal US of a male fetus at 20 weeks of gestational age, showing an enormously dilated bladder and dilated posterior urethra with normal amniotic fluid volume. (**b**) Antenatal US (21 weeks g.a.) shows a dilated upper urinary tract and dilated posterior urethra (arrow), under a not severely dilated bladder (B) but dilated ureters (U), with normal amniotic fluid volume (yellow arrow)

Prenatal interventions. Interventions on the fetuses, like vesico-amniotic shunt/vesicocentesis, have been done for many years. The rationale was that early drainage of obstructed system would allow improvement in renal function and survival with prevention of lung damage [2], but among survivors, prenatal drainage did not alter renal function status. An extensive randomized trial (PLUTO) did not answer questions on benefit of prenatal intervention in bladder outflow obstruction [3]. Nowadays, oligohydramnios should be considered the main prognostic factor in terms of kidney function and survival, but prenatal diagnosis has not globally improved long-term outcomes.

23.2.1 Neonatal Management

After delivery, bladder is catheterized, and it is no longer a surgical emergency. By this way, babies with urosepsis, dehydration, and acidosis can be managed. Rarely, it may not be possible to catheterize the urethra, and some newborns require suprapubic catheter. If kidneys fail to drain despite adequate bladder drainage, upper tract drainage can be required, especially if the kidney is infected.

Diagnosis. The first imaging needed is *ultrasound* scan, which may demonstrate enlarged/thick-walled bladder, dilated urethra, dilated kidneys and ureters, and bladder diverticula. Urinary ascites and/or urinoma may also be seen on US, presumably due to high-pressure systems with rupture of the upper urinary tract. *Voiding cystourethrogram* (VCUG) is the mainstay of diagnosis for PUV: it shows dilated/small bladder, reflux, trabeculations of bladder, dilatation of posterior urethra, and bladder neck hypertrophy (Fig. 23.2a–c). At this stage, *isotope scans* are not necessary.

23.2.2 Endoscopic Interventions in Neonate

Endoscopic valve ablation remains the definitive intervention in PUV. Earlier, cutting loops were used, while these days, bugbee electrode is preferred, and some surgeons prefer to use cold knife. Valves are incised at 5 o'clock and 7 o'clock position (Fig. 23.3). The role of bladder neck incision is controversial (see paragraph): even if it is supposed to represent a further aid to remove obstruction, little information are available regarding subsequent late retrograde ejaculation in adolescence/adulthood.

Complications with valve ablation/fulguration can occur with significant morbidity in the neonate: strong current, excessive destruction of tissue can lead to stricture formation. Other complications, as urinary extravasation and bladder injury, are rare. Urethral stricture occurring in a long term can be successfully treated endoscopically [4].

Minimal invasive laser ablation. To prevent complications, an alternative approach is to ablate the obstructive tissue by laser energy, with minimal invasive procedure. Few series are published, the largest on 40 children aged average 2 years [5] and a more recent one on 17 neonates [6]. Both used the holmium:YAG laser,

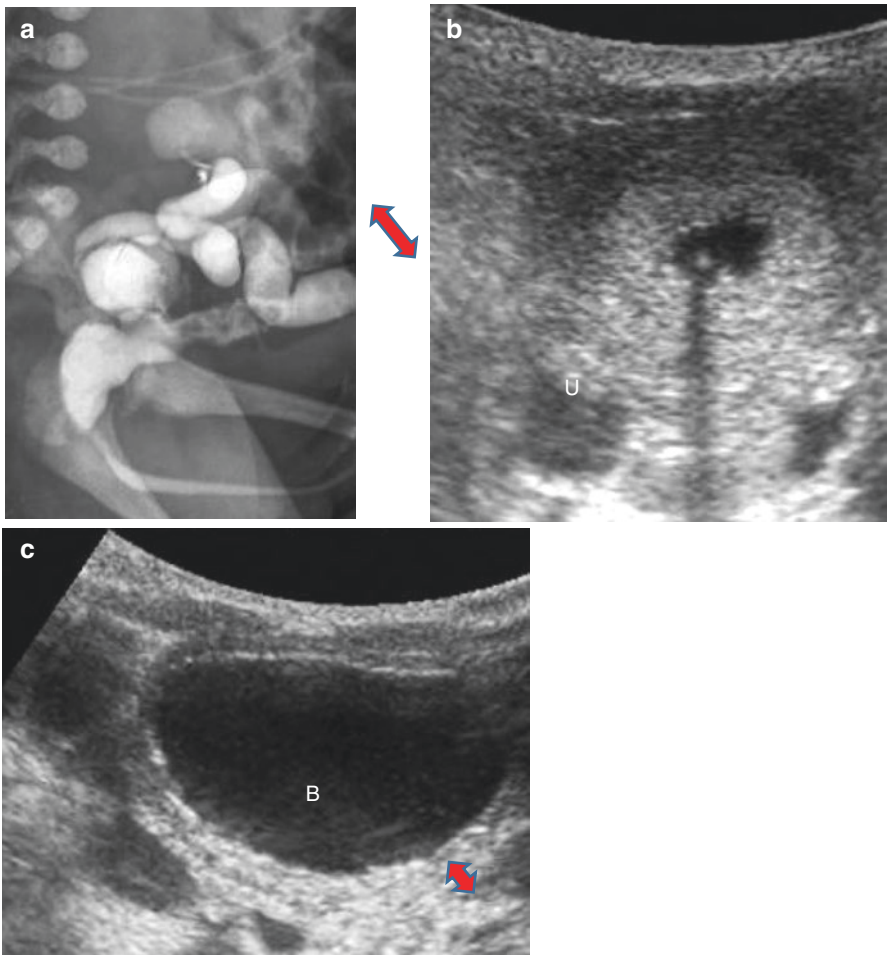

Fig. 23.2 Newborn with PUV: voiding cystourethrography and ultrasound. (**a**) VCUG of a newborn (2 days) with severe PUV, diagnosed prenatally. Evidence of posterior urethra dilatation and narrowing under the sphincteric area; severe bilateral redundant ureteral reflux. (**b**) US at 2 days: very small bladder, with severe thickened bladder walls and widely dilated ureters (U). (**c**) US at 15 days, after endoscopic valve section: the bladder is wide (B) and dilated, bladder wall is thickened (red arrow), but much less than prior to valves resection and only one ureter is still dilated

which is recommended for soft tissues. We currently use this technique, with apparent good immediate results on voiding after removal of catheter and no hematuria. We are confident that minimal invasive ablation is a preventive tool also in terms of late bladder dysfunction.

Fig. 23.3 Endoscopy for posterior urethral valves ablation by classical fulguration

23.2.3 Early Diversion in PUV?

In preterm babies, small neonates may not be suitable for endoscopic valve ablation. These babies can be managed with indwelling bladder catheter till they are able to undergo cystoscopic ablation. Failing this, supravesical diversion (i.e., cutaneous vesicostomy) provides for adequate low-pressure bladder drainage, and patients can undergo valve ablation and diversion closure at a later date. Vesicostomy can be closed whenever conditions are favorable. It is a procedure of choice in developing countries, and mini-vesicostomy facilitates clean intermittent catheterization (CIC) and overnight bladder drainage [7]. Some patients with enormously dilated ureters and poor drainage may benefit by ureterostomy: a high ureterostomy provides better drainage of kidney, but low "loop ureterostomy" provides kidney drainage while some urine drains into the bladder allowing cycling, which is good for late bladder function.

Nephrostomy is an alternative in very small/sick children, but it is associated with chronic infection and difficult subsequent reconstruction.

Long-term outcome of early diversion. Supravesical drainage has not been conclusively shown to improve outcomes and is at best a temporizing measure in those babies with fragile kidneys. In a prospective study over 6 years, vesicostomy and fulguration were compared in 45 neonates with PUV: patients did not have significant difference of renal function and somatic growth [8]. In summary, very few cases of valve bladder actually have obstructed ureters, dictating that upper tract diversions are rarely necessary. On the contrary, studies showed that, compared to valve ablation alone, temporary vesicostomy or supravesical diversion led to less bladder instability and better compliance and capacity on urodynamics, later on [9].

23.2.4 Postneonatal Follow-Up

All patients are followed for improvement of renal function. *Urodynamic* evaluation is performed when the child is older, while a check *VCUG* or *cystoscopy* may be required 3–6 months following initial cystoscopy.

23.3 Bladder Dysfunction

Despite early relief of bladder outlet obstruction, remaining pathological changes in the bladder can cause significant bladder dysfunction resulting in incontinence and impaired upper tract drainage. While a certain degree of bladder recovery will occur in most patients, some have long-term issues severe enough to result in compromise of the upper tracts. Different studies have indicated that the progressive slow deterioration that some of these patients present over years in RF is a result of bladder dysfunction [10, 11]. Over time, one or a combination of three abnormal urodynamic patterns of myogenic failure, detrusor hyperreflexia, and decreased compliance/small capacity may develop [12]. In addition, bladder function has been shown to change with time from poor compliance in newborns to instability from hypercontractility in older children to myogenic failure in postpubertal patients. Myogenic failure, in conjunction with increasing capacity and poor emptying, is primarily a later phenomenon and is most likely to be secondary to increased urine production and decreased frequency of voiding with advancing age [13].

Despite early and correct valve ablation, a large proportion of boys treated for PUV have gradual detrusor 'decompensation' and/or secondary bladder neck outlet obstruction leading to obstructive voiding and finally underactive detrusor [14].

The bladder neck was once recognized as the major cause of bladder outlet obstruction in patients with PUV. It may be evident since newborn age, at postoperative bladder ablation cystogram (Fig. 23.4), and/or may occur later on, at videourodynamic studies carried out because of persistence urinary incontinence and signs of outlet obstruction, where it isn't easy to differentiate between bladder neck and residual urethral obstructions. The concept was largely disputed by Glassberg [15], and many pediatric urologists suspect that ongoing bladder neck dysfunction is responsible of obstruction subsequent to valves ablation. Various treatments have been directed at the bladder neck, including alpha blockers, bladder neck incision (BNI), and clean intermittent catheterization (CIC) which is difficult to establish in boys with PUVs. In 2007, Kajbafzadeh evaluated the effects of simultaneous BNI and valve ablation on urodynamic abnormalities in 46 patients with posterior urethral valves: he concluded that simultaneous valve ablation and BNI effectively reduces bladder hypercontractility and prevents development of myogenic failure [16]. The concept is attractive, thinking in terms of late outcome of possible bladder decompensation due to residual obstruction. But, in the absence of clear long-term data on continence and regular ejaculation, this procedure should be avoided or reserved to peculiar patients with persisting poor bladder compliance or high residuals demonstrating anatomical obstruction or nonobstructive retention. In fact, several patients ameliorate spontaneously, thus conservative management should be preferred or a temporary measure as Botox injection can be considered.

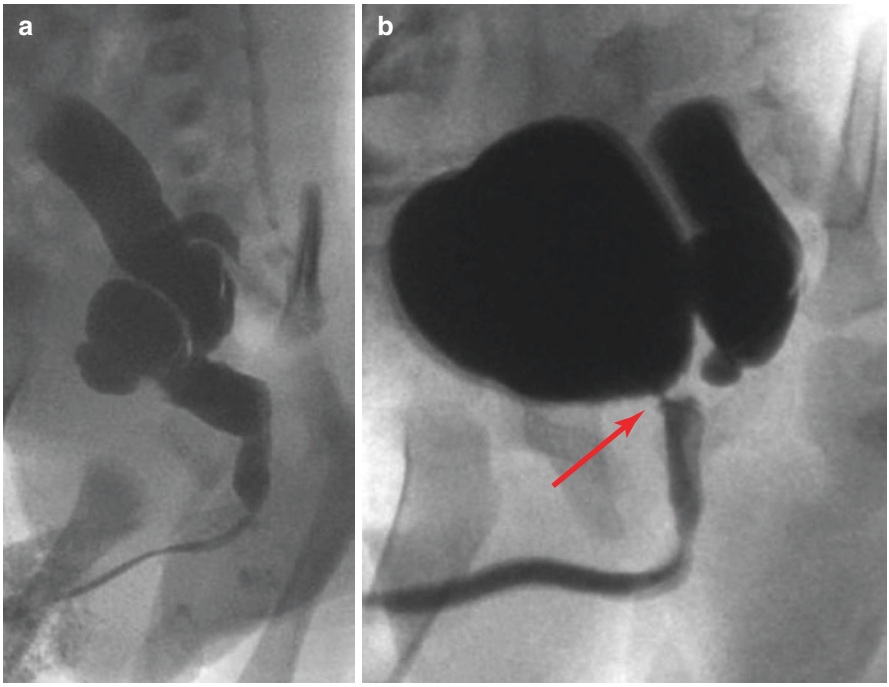

Fig. 23.4 (**a**) Cystogram of a newborn with severe valves: dilated posterior urethra, small bladder and regularly opening bladder neck, and gross reflux. (**b**) The same boy 1 year following successful endoscopic valves ablation. The VCUG shows a very narrow bladder neck (red arrow) at voiding, and the urethra shows a nice caliber with resolution of valves obstruction, with persistence of gross reflux

23.3.1 Bladder Dysfunction and Renal Failure

Several studies have shown the predictability of the development of renal failure based on specific detrusor patterns seen on urodynamic evaluation. Persistent poor compliance, high detrusor pressures, bladder outlet obstruction (BOO), and or chronic failure of the detrusor to adequately contract during voiding with increased post-voiding residual (PVR) are the most likely causes of deterioration [12]. Consequently, bladder dysfunction will be a determinant of the development of long-term renal dysfunction in some patients with treated PUV.

23.3.2 Urodynamics in PUV

Since lower urinary tract dysfunction is long established and possibly related to deterioration of upper urinary tract function, long-term urodynamic follow-up is widely recommended in boys with PUV. The clinical challenge is to identify those individuals at risk for long-term bladder dysfunction and its deleterious side effects [17]. Timing of urodynamic follow-up, however, are still undefined. Some literature

argues that the use of a urethral catheter in urodynamics falsely increases voiding pressure. But there are findings which support voiding pressure as a valid independent urodynamic parameter in this population that can be objectively measured before and after therapeutic intervention [18]. All children with PUV are different and do not necessarily follow any schedule in terms of deteriorating bladder function, but it is clear that different patterns of bladder pathology are seen specifically in children with PUV.

Noninvasive urodynamic. Due to catheterization of a sensate urethra, boys with PUV usually experience strong discomfort during urodynamic study so that many decline further invasive studies. Noninvasive urodynamic evaluation is considered effective in detecting non-neurogenic LUTD. Noninvasive urodynamic evaluation, which is widely recommended as a first-line assessment, avoids some of the pitfalls of invasive urodynamics, including the complex methodology and the lack of cooperation of children undergoing a painful examination [19]. Additionally, it was recently reported that invasive urodynamics did not correlate better than noninvasive techniques in terms of clinical diagnosis and outcome in children with OAB and dysfunctional voiding [20]. Findings in a longitudinal series of 28 children, half monitored conservatively by noninvasive urodynamics, support the safety and effectiveness of this strategy in detecting LUTD and preventing late-onset renal failure in boys with PUVs. Moreover, noninvasive studies promote the reassessment and involvement of patients in diagnostic evaluation and treatment; regular contacts with patients promote also awareness of lower and upper urinary tract, encouraging repeated evaluations and appropriate rehabilitative and pharmacological treatments. Based on these findings, it may be possible to limit invasive urodynamic testing to cases of progressively deteriorating LUTD or worsening upper urinary tract function [21].

23.3.3 Pharmacotherapy

Oxybutynin. The beneficial effects of anticholinergics on bladder wall compliance in patients with PUVs have been documented [22]. Theoretically if one acts early to improve the bladder dynamics associated with hypertrophic muscle in the bladder wall, then more rapid remodeling of bladder muscle will occur. A study demonstrates that the early use of anticholinergic therapy in infants with high voiding pressures and/or small bladder capacity after primary PUV ablation has beneficial effects on bladder and compliance [23].

Alpha-blockers. Accumulating data have shown the efficacy of alpha-blockers in improving voiding dysfunction and upper tract dilatation in patients with PUV, presumably through decreasing intravesical pressure and outlet resistance [24]. Terazosin has recently proved to be safe and results in significant improvement in bladder emptying in patients with posterior urethral valves [25].

Botox. The use of Botox to treat bladder neck obstruction would be effective and present an alternative to other more aggressive bladder neck procedures. An interesting study on children with VUPs and persistent BOO looked at this difficult group of

patients and randomized 20 patients to receive a bladder neck injection of 100 units of Botox at the time of their check cystoscopy and followed them for a further 6 months: both the Botox and control groups improved during the follow-up period, but there was no additional benefit demonstrated by the Botox injection [26].

23.4 Reflux in PUV Boys

Vesicoureteral reflux (VUR) secondary to PUV is known to affect the ultimate outcome of treatment and renal function status after correction of PUV [27] and is present in up to 72% of cases. The relationship between PUV and VUR should be considered taking into account the urodynamic phenomena which occur into the lower and upper urinary tracts. It seems that bladder function is a key determinant of renal outcome in children with VUR secondary to PUV [28]. Increased storage and/or voiding pressures caused by lower urinary tract symptoms may lead to a spectrum of intravesical anatomic disorders possibly predisposing the patient to VUR. Contrary to the results in primary VUR cases, no difference in the resolution of VUR was observed among different grades of secondary reflux, and moreover, even high-grade secondary VURs can resolve with conservative therapy in some cases [29]. Accordingly, attempts should be focused on correction of bladder function rather than performing invasive procedures for the correction of the radiologic findings regarding VUR.

Overall, conservative therapy can be regarded as the mainstay of reflux treatment after successful valve correction as it is associated with a 66% success rate [30].

The best option is an observation with management of bladder/bowel dysfunction (BBD), in addition to treatment of urinary tract infections (UTI), as they occur [31]. In children with PUVs, bladder surgery should be in general avoided, to prevent deterioration of bladder function, which may lead with the necessity of bladder augmentation.

23.5 Urinary Continence

The natural evolution of urinary continence in boys following posterior urethral valves ablation is difficult to investigate, due to the various conditions present in the single patient. Due to early treatment of valves and bladder dysfunction, nowadays children with have better outcome in terms of continence achievement. No doubt that recent groups of patients, who receive an accurate toilet training program and strict follow-up, achieve continence earlier compared with older series of boys who are now adults and didn't receive that treatment.

Anyway, continence achievement is delayed in PUV children, compared to normal population, especially in those who have chronic renal failure (high creatinine level at 5 years). There are no data regarding significant difference in boys with/without initial reflux or who underwent temporary ureteral diversion.

The impression is that a conservative management after valve ablation, limiting surgery on the bladder, is a big help to avoid urinary incontinence. Boys with PUVs can achieve regular voiding and continence, if early but conservatively treated, if they don't have initial renal impairment with consequent polyuria, and if receiving adequate toilet training and subsequent close follow-up with urotherapy and noninvasive urodynamic assessment.

23.6 Bladder and Renal Function Relationship

Posterior urethral valves (PUV) account for almost 17% of children with end-stage renal failure [32]. A pathophysiological relationship has been suggested between lower urinary tract dysfunction and late-onset renal failure. Furthermore, the polyuria occurring for CRF determines high volumes into the (dysfunctional) bladder, not only leading with urinary incontinence but also deteriorating the upper tract itself.

23.6.1 Polyuria and Bladder Volume-Dependent Obstruction

The urinary concentrating capacity is impaired in about 75% of PUV children, and tubular damage worsens with age, despite early relief of obstruction in many patients [33]. An increased daily urine volume can exacerbate bladder dysfunction, increasing the hydrostatic pressure transmitted to the kidneys in the presence of the decreased bladder capacity and compliance, and lead to progressive renal injury. For patients with salvageable RF, it is essential to control bladder pressure. Overnight catheter drainage in patients with persistent hydronephrosis and polyuria will allow bladder and UUT decompression for at least a third of each day and relieve a possible negative effect on renal function [34, 35].

23.6.2 Renal Transplant

It is unclear whether the initial valve intervention in children with PUVs has an effect on the development renal graft failure. One hypothesis is that primary valve ablation alone would lead to higher graft success, perhaps by resulting in less bladder dysfunction compared to that in patients with a non-functionalized bladder due to diversion. The impact on transplant kidney survival of valve treatment approaches and the impact of bladder dysfunction and its treatments have been studied. Graft survival at 5 years was 50% in those children with PUVs, while a control group with ESRD due to non-genitourinary causes had 75% graft survival, and it would be argued that the effect of the valve bladder may explain these findings [36]. Children with PUVs who received transplants have a significantly increased incidence of ureteral obstruction. Furthermore, pyelonephritis graft loss seems to be more frequent in PUV patients who underwent augmentation cystoplasty. Thus, provided that adequate surveillance of BD and high PVR is obtained, avoiding augmentation may be protective. Preemptive augmentation is not a first option, and it should be constructed only if

there is great risk associated with increased bladder pressures, higher than the risk associated with augmentation. Moreover, since a considerable number of PUV patients with high-pressure bladders eventually develop myogenic failure, it seems logical to postpone surgical options. On the contrary, an adequate management of BD is essential to improve bladder function and to minimize UTIs [37].

23.7 Transitional Care

23.7.1 Hyperfiltration Injury

Another factor that can contribute to the late onset of renal failure in PUV patients is the hyperfiltration injury due to the increased metabolic demands of puberty. Over the long term, and with time, hyperfiltration would produce proteinuria and focal segmentary glomerulosclerosis and result in renal failure. Proteinuria has been demonstrated to be a good indicator of the hyperfiltration. Early use of angiotensin-converting enzyme inhibitors or antagonists in patients who present proteinuria during follow-up may attenuate these hemodynamic alterations and delay or even avoid CRF [38].

23.7.2 Sexual Function and Fertility

Nowadays, more PUV boys reach adolescence and adulthood, and their sexual function and fertility have become relevant. However, information on these issues is still scant. In adolescents with treated PUV, the posterior urethra can remain widely dilated and the bladder neck open, despite adequate valve ablation, which will result in ejaculatory dysfunction. Furthermore, reflux into the vasa deferentia may be present, affecting testicular or prostatic components of semen. In a series of 21 men (mean age 24.6 years), 48% complained of slow or dry ejaculation, even if erections and orgasm were normal [39]. In another series of 16 patients (mean age 24 years), all experienced erections and orgasm, but 2 ones (1 on dialysis) had mild and 2 patients medium erectile dysfunction. Ejaculation was normal in all patients, except in the patient on dialysis [40]. The analysis of semen may show abnormally viscous semen, high pH, and increased liquefaction time, as possible reduction in prostatic or seminal vesicle fluid. Sexual function and fertility remain a matter of speculation owing to the scarcity of studies and the discrepancies in results. However, it would seem that these patients have normal sexual function (some with slow ejaculation).The ability to father children appears to be more dependent on RF than on PUV dysfunction.

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