*Kristina D. Suson, MD and John P Gearhart, MD, FAAP**

Bladder Exstrophy: Long Term Outcomes of Bladder Reconstruction

**Director-Professor, Division of Paediatric Urology, The James Buchanan Brady Urological Institute, Johns Hopkins University School of Medicine, Baltimore, USA*

One hundred years ago, the outlook for patients with bladder exstrophy was bleak. With 50% of children dying by age ten,[1] clearly the health and function of the bladder was not the top priority. However, with the advent of concomitant osteotomies in 1958,[2] a successful bladder closure became more likely, thus attention shifted to improving the rates of eventual continence. Although some patients may still require intermittent catheterization through the urethra or through an abdominal stoma, most patients can expect continence.

Currently most pediatric urologists reconstruct the lower urinary tract with the modern staged repair of exstrophy (MSRE) or complete primary repair of exstrophy (CPRE), with radical soft-tissue mobilization (RSTM) as an alternative. MSRE is a progression of the staged repair. Originally, bladder closure was followed by bladder neck reconstruction at age two to three and later an epispadias repair. MSRE instead follows closure with epispadias repair at six to twelve months of age, with the hope of increasing bladder capacity by creating a more physiologic outlet resistance. Bladder neck reconstruction is ideally offered when the child demonstrates not only interest in becoming continent, but a willingness to actively to participate in the continence process.

Many patients who have their initially closure beyond three days old will have synchronous osteotomies , with some requiring additional osteotomies at the time of bladder neck reconstruction.[3] CPRE, which may also be accompanied by osteotomies, usually includes epispadias repair and bladder neck reconstruction at the time of closure.[4]

In 1995, Kelly described radical soft-tissue mobilization. This three-stage procedure relies upon the elevation of the ischial and pubic periosteum so that the attachments of the sphincter muscles can be mobilized, along with the pudendal neurovascular structures, and wrapped around a neourethra. With this technique, osteotomies are avoided.[5]

Important outcomes to consider when evaluating reconstructive options include success of closure, continence and voiding. While all of these procedures have certain attendant complications, a reconstructed lower urinary tract lends itself to long-term complications.

Bladder Closure

Success rates for bladder closure are presented in Table 1. Rates of 95% or greater are reported for staged closure.[6,7] CPRE rates range from 69%[8] to 100%.[9,10] In one cohort, although two patients dehisced their abdominal fascia and pubic symphysis, necessitating return to the operating room, the bladder closure remained secure, thus they were not considered failed closures.[10] The Oklahoma group included two patients with vesicostomies among their 100% successful closure rate.[9] In Kelly's report of RSTM, he describes closure success rates of 81%.[5] Reasons for failure were similar despite the technique employed for closure. The most commonly encountered cause was dehiscence, accounting for 20 of the 30 reported failures in Table 1.[4,5,6,7,8] Fistulae were also a common cause of failure, accounting for 7 of the 30 reported failures.[4,8] Bladder prolapse was the rarest reported cause of failure.[7]

Continence

Continence rates are shown in Table 2 and in Fig. 1 Regardless of initial approach, many children required multiple procedures to become continent.

Modern Staged Repair of Exstrophy

Overall continence rates quoted for staged repairs range from 79%–98%, by the authors' definitions. The Toronto group reviewed their experience with the staged repair in a retrospective study of 43 exstrophy patients, including 36 with classic bladder exstrophy, who presented for continence procedures. Overall, 79% of patients achieved good or acceptable continence, with 72% having three hour dry intervals and 7% having two hour dry intervals or stress incontinence requiring up to two pads per day.[11] The Johns Hopkins group has reviewed continence results in multiple populations. In a study of patients who underwent successful closure elsewhere

followed by modified Young-Dees-Leadbetter bladder neck reconstruction at their institution, 96% had dry intervals of three hours or greater.[12] When reviewing patients who completed all stages of MSRE at their institution, 91% of patients obtained three hour daytime dry intervals.[13] In Shaw's study of 48 classic exstrophy patients, 90% achieved three hour daytime dry intervals, as well as nighttime continence.[14]

TABLE 1. Closure success

Reconstruction	Author	Number (%) Successfully Closed	Number (%) Dehisced/Fistula/ other
Staged	Aadalen *et al*[6]	95/100 (95%)	5 (5%)/0 (0%)/0 (0%)
	Sponseller *et al*[7]	76/78 (97%) 47/49 (96%) primary closure 29/29 (100%) repeat closure	1 (1.3%)/0 (0%)/1 (1.3%)
CPRE	Borer *et al*[4]	21/23 (91%)	1 (4%)/1 (4%)/0 (0%)
	Shnorhavorian *et al*[10]	39/39 (100%)*	0 (0%)/0 (0%)/0 (0%)
	Kibar *et al*[9]	16/16 (100%)†	0 (0%)/0 (0%)/0 (0%)
	Ebert *et al*[18]§	17/17 (100%)	0 (0%)/0 (0%)/0 (0%)
	Shoukry *et al*[8]	35/51 (69%)	8 (16%)/6 (12%)/2 (4%)
RSTM	Kelly[5]	22/27 (81%)	5 (19%)/0 (0%)/0 (0%)

* Two patients dehisced their fascial closure and symphysis pubis, necessitating return to operating room.
† Two patients had vesicostomies at the time of analysis.
§ Functional single-stage reconstruction, classified with CPRE for technique comparison.

TABLE 2. Continence

Recons-truction	Author	Overall Continence	Initial Surgery	Continence Procedure	Augment	Diver-sion
Staged	Capolicchio *et al*[11]	79%(72%^{3}/7%^{2s})	n/a	12% BNR	23%	44%
	Surer *et al*[12]	96%^{3}	n/a	83% BNR	3%	10%
	Chan *et al*[13]	94%(80%$^{3d°}$/14%^{3})	n/a	91% BNR	0	3%
	Shaw *et al*[14]	98%(90%^{3d}/8%^{1ns})	8%	15% BNR	62%	n/a
CPRE	Gargollo *et al*[17]	67%(19%^{3}/19%^{2s}/ 29%^{1ns})	19%^{3}	19%(5%^{3}/ 14%^{2}) BNR	n/a	n/a
	Shnorhav-orian *et al*[10]	74%^{2}*	22%	18% BNI 13% BNR 22% BNR+ BNI	n/a	n/a
	Kibar *et al*[9]	78%^{4}	11%	22% BNR	33%	11%
RSTM	Kelly[5]	74%(37%^{4d}/37%^{nsf})	n/a	74% SPH(s)	0	0
	Jarzebowski *et al*[19]	71%(35%^{3d}/35%^{2ns})	n/a	68% SPH†	unknown	3%

BNR = bladder neck reconstruction, BNI = bladder neck injection, SPH = sphincteroplasty
Superscript key for continence definition: number = dry interval, d = dry nights, n = occasional enuresis, s = mild stress incontinence, f = frequency
* Includes only volitional voiding.
† Number may include some patients who underwent augmentation.

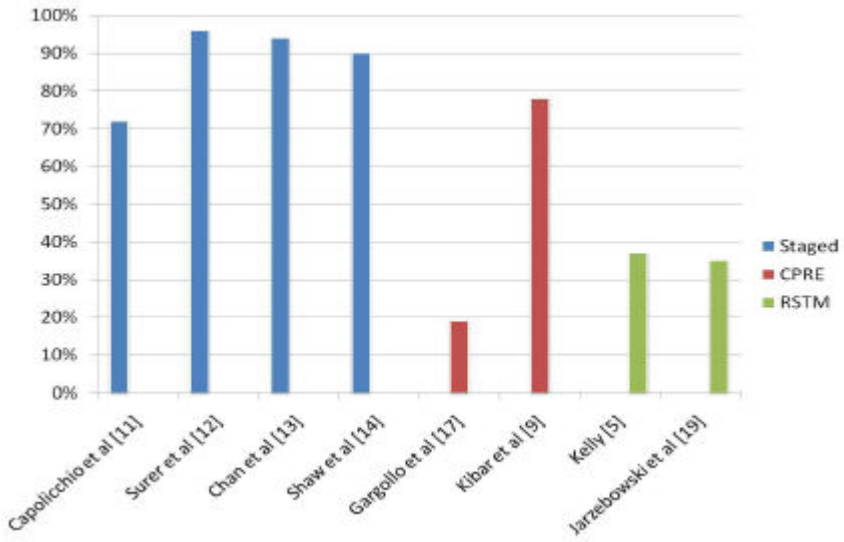

Fig. 1. Continence rates in children with bladder exstrophy

Several factors have emerged as influencing eventual continence. Pre-operative factors include successful initial closure and establishment of a good bladder capacity before bladder neck reconstruction. Early successful closure enables more normal bladder development, ultimately resulting in better capacity and compliance.[12] Chan *et al* found that patients with a bladder capacity at time of bladder neck reconstruction greater than 85 mL were more likely to achieve continence.[13] Similarly, Shaw *et al* found a trend towards improved continence with larger bladder capacity.[14] Age at the time of bladder neck reconstruction does not appear to influence continence.[13]

The continence procedure performed also impacts on continence. Capolicchio *et al* stratified 43 exstrophy patients into three groups by continence procedure: bladder neck reconstruction alone (group 1), bladder neck reconstruction and augmentation with or without appendicovesicostomy (group 2) and bladder neck closure with appendicovesicostomy. They found that 56% of group one, 67% of group two, and 100% of group three achieved some degree of continence. Of note, group three included all patients with cloacal exstrophy, and most patients referred from outside centers, from the older cohort, or with a small bladder plate.[11]

Shaw *et al* also reviewed the procedures necessary to obtain continence in a study of 48 classic exstrophy patients. 90% of patients were dry for three hour intervals and at night, 8% of patients were dry for one to three hours, had minor stress incontinence, or occasional nocturnal enuresis. Four patients were dry from bladder closure, seven patients were dry from bladder neck reconstruction alone, and thirty patients were dry from augmentation with or without bladder neck reconstruction. Only 34% of patients became continent with bladder neck reconstruction. In their series, patients who failed initial attempts at bladder neck reconstruction alone always failed a second time, unless combined with augmentation cystoplasty.[14] Mouriquand *et al* also found in their population few patients achieved continence after undergoing one bladder neck reconstruction. Their retrospective study included 80 patients with classic bladder exstrophy who underwent staged reconstruction with modified Young-Dees-Leadbetter bladder neck repair. 45% of patients became continent for at least three hour daytime intervals following one bladder neck reconstruction. The age at bladder closure was older in this cohort than in most current patients, with a mean age at bladder closure of 200 days. Bladder capacity before bladder neck reconstruction is not mentioned.[15]

Time from surgery appears to influence continence as well. In the short term, daytime and nighttime continence improves in the one to two years following bladder neck reconstruction.[13] Over the long term, the influence is less clear. Shaw's study included six patients who were initially dry from from bladder neck reconstruction but ultimately required augmentation to remain continent.[14] However, the QUALEX (Quality of Life of Bladder Exstrophy) study, published in 2010, concluded that for its cohort, continence is achieved mostly in adolescence. This study was comprised of self-administered, validated quality of life questionnaires, as well as general functional and socioeconomic surveys. All patients were reconstructed in infancy. They were divided

into three groups: adults (34), adolescents (18), and children (17). Of adults, the initial surgery was simple bladder closure in 67%, MSRE in 11%, ureterosigmoidostomy in 4.2% and no CPRE, with 82% undergoing a later continence procedure. 77% had no or little daytime incontinence, and 76% had no or little nighttime incontinence. 31% ultimately underwent continent urinary diversion, and 12% underwent incontinent diversion. Of adolescents, the initial surgery was simple bladder closure in 56%, CPRE in 17% and MSRE in 6%, with 67% undergoing a later continence procedure. 65% reported no or little daytime leakage, while 67% reported no or little nighttime leakage. 22% underwent continent urinary diversion, with no patients requiring incontinent diversion. Children had the worst continence scores, with only 12% reporting no or little daytime leakage.[16]

Complete Primary Repair of Exstrophy

The Boston group evaluated outcomes in 32 patients who underwent CPRE. They assessed dry intervals in the 21 patients who were over 4 years old: seven patients were dry for less than 1 hour, six for 1 to 2 hours, four for 2 to 3 hours, and only four patients were dry for greater than 3 hours. Of patients over four who only underwent CPRE, 19% were continent for three hours or greater. All patients more than six months from bladder neck reconstruction were dry for at least two hours. Including endoscopic procedures, a total of 193 procedures were performed on the 32 patients studied.[17]

In a report from Seattle of 39 patients with a median follow-up of 58 months, 23 children were old enough to be evaluated for continence, defined as two hour daytime dry intervals. 74% were continent, with 29% continent with CPRE alone., 18% became continent after bladder neck injection, 24% requiring bladder neck reconstruction, and 29% requiring bladder neck reconstruction and subsequent injection.[10]

In the University of Oklahoma experience, sixteen patients were available for long-term follow-up, with nine children considered to be of continence age. 78% were dry at night and had a 4 hour dry interval by day. Additional surgeries required to obtain continence included bladder neck reconstruction, bladder neck injection with a bulking agent, augmentation, and diversion with bladder neck transection. 15 continence procedures had been performed on these nine patients, for an average of 1.66 procedures in addition to the initial complete repair.[9]

Ebert *et al* studied long-term outcomes in seventeen males over the age of 16, including 16 classic exstrophy patients and one complete epispadias patient, who underwent functional single-stage reconstruction. In five of the patients it was a primary attempt, while in 12 patients it was a secondary attempt. Subjective and objective continence were evaluated, complete continence being defined as dry intervals of greater than three hours with dry nights. While 16 patients considered themselves continent, only 10 patients (59%) met the objective criteria; those patients were not stratified by the need for additional procedures. Four patients experienced stress incontinence, and seven were wet more than one night per month.[18]

Shoukry *et al* reviewed their experience with 51 patients who underwent CPRE. Early outcomes suggested that as many as 82% of patients had a dry interval, however, as the patients aged, the percentage of patients with a dry interval declined to 38%. All continent older patients required augmentation cystoplasty, with many patients also undergoing bladder neck reconstruction. They attribute the low continence rate to not performing osteotomies at the time of repair in patients older than 72 hours.[8]

Radical Soft-Tissue Mobilization

In Kelly's original description of RSTM, continence was assessed in 19 patients who were at least one year from the second stage procedure. 74% were considered physiologically or socially continent, in that there was a demonstrated ability to store urine and void spontaneously, with about half of those patients experiencing frequency, occasional daytime or nighttime incontinence, or the need to wear one pad.[5]

Limited long-term data has accrued on RSTM outcomes. Jarzebowski *et al* examined continence, cosmesis, and pelvic organ prolapse in 31 classic exstrophy patients who had undergone RSTM and 13 classic exstrophy patients who had undergone other staged procedures with questionnaires. The median age at follow-up from the first procedure was 13 years. Complete continence was defined as being dry three or more hours per day and having no more than two wet nights per month. Partial continence was defined as being dry two or more hours per day and having no more than three wet nights per month. They quote an overall continence rate of 71%, with around 35% achieving complete, and 35% achieving partial continence, Some patients required multiple procedures, including repeat sphincteroplasty, augmentation or diversion, then requiring to self catheterise (CIC).[19]

Voiding and Diversion

In addition to continence, voiding is an important long-term outcome to consider; Table 3. Rates of patients who solely relied upon voiding per urethra ranged from 9% to 97%, while rates of those solely dependent upon clean intermittent catheterization (CIC) ranged from 3% to 91%.[5,9,10,11,12,13,14,17,18,19] Clearly the patient population impacts on bladder emptying, as patients with small bladder capacities, failed closures, or cloacal exstrophy are more likely to require diversion to obtain continence.[11]

TABLE 3. Voiding in patients of continence age

Reconstruction	Author	Spontaneous Voiding	Voiding+CIC	CIC
Staged	Capolicchio *et al*[11]	9%[c]	0-36%[c]	55-91%[c]
	Surer *et al*[12]	86%[c]	3%[c]	11%[c]
	Chan *et al*[13]	82-97%[c]	0-15%[c]	3%[c]
	Shaw *et al*[14]	24%[c]	19%[c]	57%[c]
CPRE	Gargollo *et al*[17]	94%[a]	3%[a]	3%[a]
	Shnorhavorian *et al*[10]	71%[c]	24%[c]	6%[c]
	Ebert *et al*[18]	71%[a]	6%[a]	24%[a]
	Kibar *et al*[9]	33%[a]	55%[a]	11%[a]
RSTM	Kelly[5]	95%[a]	0%[a]	5%[a]
	Jarzebowski *et al*[19]	55%[a]	23%[a]	23%[a]

c = percentage of continent patients
a = percentage of all patients of continence age

Rates of voiding and diversion are highly variable among patients undergoing staged repair. At one end of the spectrum, Surer *et al* and Chan *et al* found that 82 to 97% of continent patients can void per urethra.[12,13] At the other end of the spectrum, Capolicchio *et al* and Shaw *et al* found only 9 to 24% of continent patients could void volitionally per urethra.[11,14] In the population studied by Capolicchio *et al*, 19 of 43 (44%) required bladder neck transection and diversion. All patients with cloacal exstrophy and most patients referred with failed closures, from an older cohort, or with small bladder plates required this procedure.

Ultimately, all patients should achieve continence, proceeding in a stepwise fashion from bladder neck reconstruction to augmentation to diversion if necessary. Some patients, such as those with a small capacity or with cloacal exstrophy, undergo diversion as the first option.[11]

Shaw *et al* noted that some patients who initially require only bladder neck reconstruction may later require augmentation and likely CIC (74% in their own series).[14]

Currently, patients are unlikely to undergo incontinent diversion. In the QUALEX study, 31% of adult patients underwent continent urinary diversion and 12% underwent incontinent diversion, while 22% of adolescents underwent continent urinary diversion with no patients undergoing incontinent diversion.[16]

Voiding rates for patients undergoing CPRE are also highly variable, with 33%-94% of children of continence age voiding per urethra.[9,10,17,18] The Boston group found only 3% of patients relied completely upon intermittent catheterization[17], and the Seattle group found 6% of patients relied completely upon catheterization.[10] Of note, these populations included only patients with classic exstrophy. An additional 3% to 18% of patients used CIC to improve bladder emptying.[10,17] However, in the experience of the Oklahoma group, 66% of patients performed CIC, including one patient with a bladder neck transection.[9] In Ebert's study, 12% required continent urinary diversion.[18]

Of patients undergoing RSTM, 55% to 95% of patients volitionally void, with an additional 24% performing CIC and voiding, with 3% to 5% undergoing continent urinary diversion.[5,19]

Long-Term Complications

Neoplasm

Traditionally, patients treated with ureterosigmoidostomy or other procedures with concomitant storage of urine and feces are considered high risk for malignancy. Smeulders and Woodhouse confirmed this risk, but also demonstrated an increased risk of malignancy in patients who underwent early bladder closure or undiversion of urine from a colorectal reservoir. When compared to the normal population, they found an increase relative risk of all primaries of 47 (42-52 95% CI) and a relative risk of bladder cancer of 694 (660–727 95% CI). Furthermore, the relative risk of death from cancer was 65 times that of the general population (57-72 95% CI). Three patients in their cohort with bladder cancer had undergone cystectomy before 5 years of age, demonstrating that early cystectomy did not prevent its development. After the introduction of screening patients at high risk of colorectal neoplasia with annual colonoscopy, no deaths from colorectal carcinoma were noted. A similar strategy to prevent bladder cancer deaths is not in practice.[20]

In an attempt to elucidate the malignancy potential of the closed exstrophy bladder, Novak *et al* studied polyps removed at the time of closure (Fig. 2). Two basic types of polyp were observed: fibrotic and edematous. No overt dysplasia was identified, however reactive lesions such as squamous metaplasia, von Brunn's nests, cystitis cystic, and cystitis glandularis were noted. Cystitis glandularis, which is associated with adenocarcinoma, was identified in significantly more secondary closures (71.4%, p=0.0014) than primary closures. The authors recommend surveillance of adult patients with a history of secondary closures.[21]

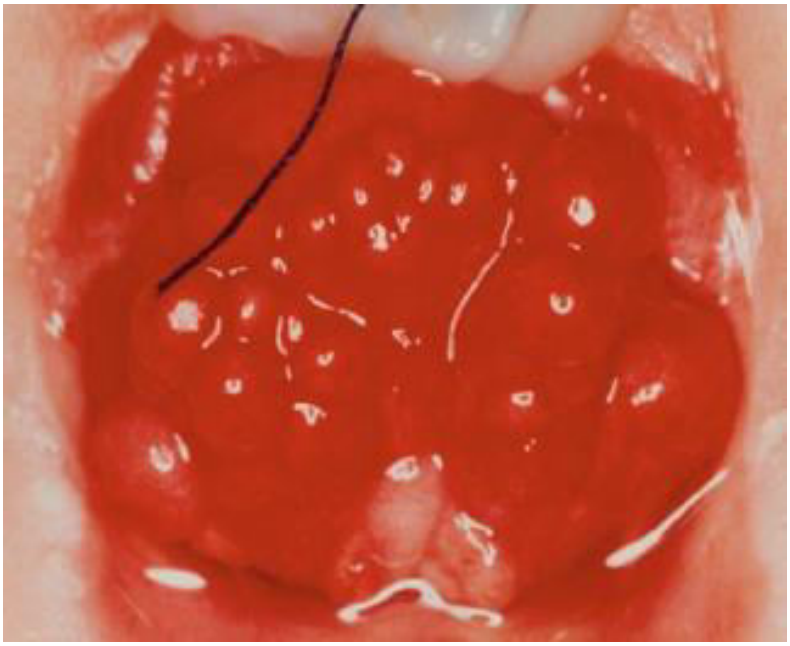

Fig. 2. Bladder Exstrophy

Whether bladder augmentation is an independent risk factor for malignancy is debated. Higuchi *et al* examined patients with congenital bladder malformation and a history of augmentation cystoplasty, including patients with neurogenic bladder, exstrophy/epispadias, or posterior urethral valves. This group was age and gender matched to patients with the same underlying bladder pathology who perform intermittent catheterization. They found no difference in incidence (4.6% in augmented patients, 2.6% in controls, p=0.54), age at diagnosis (51 years in augmented patients, 49.5 years in controls, $p > 0.7$), stage (3.4 in augmented patients, 3.8 in controls, $p > 0.5$), mortality rate (71% in augmented patients, 100% in controls, $p > 0.4$), or median survival (18 months in augmented patients, 17 months in controls, $p > 0.8$). Patients on immunosuppression did have an increased risk of bladder cancer, regardless of augmentation status.[22] In another analysis of this patient set, Husmann and Rathbun concluded that post-augmenation bladder cancer was associated with known carcinogens, such as tobacco, or the increased risk secondary to immunosuppression or bladder exstrophy.[23]

Urolithiasis

Patients with exstrophy are at risk of urolithiasis. Silver *et al* found that bladder augmentation ($p < 0.001$) and bladder neck reconstruction ($p < 0.001$) increased the risk of stones. Urolithiasis most commonly occurred in the bladder. Additional risk factors, including urinary tract infection, foreign bodies, and urinary stasis, are similar to the general population. Vesicoureteral reflux was also associated with stones. Recurrence, which occurred in 39% of patients, was associated with urinary tract infection and struvite stone composition. Stones occurred more commonly in patients with cloacal exstrophy (25%) than classic exstrophy (16%). The contribution of underlying metabolic disorders has not been elucidated, but in this study, metabolic acidosis was not a risk factor.[24]

Especially in patients with recurrent calculi, prevention, rather than treatment, would be ideal. Hensle *et al* evaluated the utility of an irrigation protocol consisting of irrigation with 240 mL normal saline twice a week and 120 mL - 240 mL gentamicin sulfate solution (240-480 mg gentamicin/L saline) in once a week in preventing reservoir calculi. Their cohort included patients with neurogenic bladder, exstrophy, posterior urethral valves, and rhabdomyosarcoma. Around 55% catheterized per stoma, while 45% used their native urethra. The overall incidence of reservoir calculi in patients placed on the irrigation protocol was 7%, compared to 43% in those treated in the standard fashion ($p=0.001$). Patients with an abdominal stoma had a greater risk than those using the native urethra (66% versus 15%, $p < 0.05$).[25]

Metabolic Consequences

Patients who undergo bladder augmentation or replacement with bowel have the additional risk of metabolic abnormalities. A literature review by Gilbert and Hensle focusing on long-term complications of enterocystoplasty included metabolic consequences. Both ileal and colonic bladder augmentation/replacement have been linked to metabolic acidosis, with symptoms that include fatigue, anorexia, weight loss, polydipsia, and lethargy. Treatment typically consists of oral alkalinization with sodium bicarbonate, sodium citrate, or citric acid solutions. Chronic acidosis can also lead to bone demineralization, with calcium and phosphate loss, ultimately resulting in osteomalacia. In addition to correcting the acidosis, these patients also benefit from calcium and vitamin D. There may also be an impact on linear growth, although this conclusion is debatable. Metabolic acidosis can cause hypokalemia, but this risk is mitigated by potassium resorption in patients with ileal augmentation or replacement.

Patients with gastric segment reconstruction may experience dehydration and metabolic alkalosis. Hyperammonemia syndrome, which occurs in the setting of hepatic dysfunction or infection, can lead to encephalopathy and coma. Excessive removal of terminal ileum from gastrointestinal continuity results in vitamin B12 deficiency, which when unrecognized may cause megaloblastic anemia and neurologic damage. Vitamin B12 injections are given intramuscularly on a monthly basis in patients at risk of deficiency.[26]

Penile Ischemia

While penile ischemia is a complication in the short term, it has long-term ramifications. This complication has been reported with RSTM and CPRE penile disassembly. Purves and Gearhart reviewed four patients with complications from RSTM procedures, two of whom suffered penile ischemia.[27] Berrettini *et al* also report penile ischemia resulting in glans loss in a series of nine patients who underwent RSTM.[28] Similar ischemia has also been reported in CPRE patients. Potential mechanisms of penile ischemia to be recognized and avoided include direct damage to pudendal or accessory vessels, or compression of these vessels by pubic apposition. When undue pressure is placed upon the vascular structures, impaired venous outflow can lead to congestion and ultimately compromise blood flow to the capillaries. It is important to note this can happen even with adequate arterial doppler signals.[29]

Late Failure

Some studies have suggested that patients with initial successful continence outcomes ultimately result in failures.[14] Woodhouse and Redgrave reviewed late failures in 57 patients with bladder exstrophy born between 1965 and 1974. They found only 13 patients retained their native bladders in adolescence. Of those, 8 patients required further reconstruction, mostly secondary poorly compliant, low capacity bladders. The authors speculate that bladder outlet obstruction or urethral failure may compromise the reconstructed bladder and underline the importance of continued follow-up throughout adulthood.[30] Since 1974, tremendous progress has been made into reconstructive techniques. It will be important to evaluate the durability of the repairs into adulthood.

Conclusion

While all of the currently employed techniques offer patients the hope of continence, rates vary by patient population, technique and institution. Furthermore, continence may only be achieved after augmentation, typically necessitating clean intermittent catheterization, or diversion in some patients. In addition to clinical data such as success of initial closure and bladder capacity, research into the exstrophic smooth muscle may enhance our ability to counsel patients and prognosticate bladder growth and continence potential. This may prove particularly helpful in determining which patients are appropriate for staged bladder neck reconstruction or further continence procedures for patients who undergo CPRE. Further understanding may also reveal treatment options that increase bladder capacity or augment to urethral mechanism, ultimately resulting in improved continence. Patients must be followed into adulthood; as more exstrophy patients enter adulthood with reconstructed bladders, adult urologists may encounter complicated patients and should familiarize themselves with current management strategies.

Reference:

1. Mayo CH, Hendricks WA. Exstrophy of the bladder. *Surg Gynecol Obstet.,* 43: 129–134, 1926.
2. Shultz WG.Plastic repair of exstrophy of bladder combined with bilateral osteotomy of ilia. *J Urol.,* 79(3): 453-458, 1958.
3. Mathews R, Gearhart JP. Modern staged reconstruction of bladder exstrophy—still the gold standard. *Urology,* 65(1): 2-4, Januarny, 2005.
4. Borer JG, Gargollo PC, Hendren WH, Diamond DA, Peters CA, Atala A, Grant R, Retik AB. Early outcome following complete primary repair of bladder exstrophy in the newborn. *J Urol.,* 174(4 Pt 2): 1674-1678, discussion 1678-1679, October, 2005.
5. Kelly JH. Vesical exstrophy: repair using radical mobilisation of soft tissues. *Pediatr Surg Int.,* 10: 298-304, 1995.
6 Aadalen RJ, O'Phelan EH, Chisholm TC, McParland FA Jr, Sweetser TH Jr. Exstrophy of the bladder: long-term results of bilateral posterior iliac osteotomies and two-stage anatomic repair. *Clin Orthop Relat Res.,* (151): 193-200, 1980.
7. Sponseller PD, Jani MM, Jeffs RD, Gearhart JP. Anterior innominate osteotomy in repair of bladder exstrophy. *J Bone Joint Surg Am.,* 83-A(2): 184-193, 2001.
8. Shoukry AI, Ziada AM, Morsi HA, Habib EI, Aref A, Badawy HA, Eissa M, Daw M. Outcome of complete primary bladder exstrophy repair: single-center experience. *J Pediatr Urol.,* 5(6): 496-499, December, 2009.
9. Kibar Y, Roth CC, Frimberger D, Kropp BP. Our initial experience with the technique of complete primary repair for bladder exstrophy. *J Pediatr Urol.,* 5(3): 186-189, Epub 2009 March 28, June, 2009.
10. Shnorhavorian M, Grady RW, Andersen A, Joyner BD, Mitchell ME. Long-term followup of complete primary repair of exstrophy: the Seattle experience. *J Urol.,* 180(4 Suppl): 1615-1619, discussion 1619-1620, October, 2008.
11. Capolicchio G, McLorie GA, Farhat W, Merguerian PA, Bägli DJ, Khoury AE. A population based analysis of continence outcomes and bladder exstrophy. *J Urol.,* 165(6 Pt 2): 2418-2421, June, 2001.
12. Surer I, Baker LA, Jeffs RD, Gearhart JP. Modified Young-Dees-Leadbetter bladder neck reconstruction in patients with successful primary bladder closure elsewhere: a single institution experience. *J Urol.,* 165(6 Pt 2): 2438-2440, June, 2001.
13. Chan DY, Jeffs RD, Gearhart JP. Determinants of continence in the bladder exstrophy population: predictors of success? *Urology,* 57(4): 774-777, April, 2001.
14. Shaw MB, Rink RC, Kaefer M, Cain MP, Casale AJ. Continence and classic bladder exstrophy treated with staged repair. *J Urol.,* 172(4 Pt 1): 1450-1453, discussion 1453, October, 2004.
15. Mouriquand PD, Bubanj T, Feyaerts A, Jandric M, Timsit M, Mollard P, Mure PY, Basset T. Long-term results of bladder neck reconstruction for incontinence in children with classical bladder exstrophy or incontinent epispadias. *BJU Int.,* 92(9): 997-1001, discussion 1002, December, 2003.

16. Jochault-Ritz S, Mercier M, Aubert D. Short and long-term quality of life after reconstruction of bladder exstrophy in infancy: preliminary results of the QUALEX (QUAlity of Life of bladder EXstrophy) study. *J Pediatr Surg.,* 45(8): 1693-1700, August, 2010.
17. Gargollo PC, Borer JG, Diamond DA, Hendren WH, Rosoklija I, Grant R, Retik AB. Prospective followup in patients after complete primary repair of bladder exstrophy. *J Urol.,* 180(4 Suppl): 1665-1670; discussion 1670, October, 2008.
18. Ebert AK, Schott G, Bals-Pratsch M, Seifert B, Rösch WH. Long-term follow-up of male patients after reconstruction of the bladder-exstrophy-epispadias complex: psychosocial status, continence, renal and genital function. *J Pediatr Urol.,* 6(1): 6-10, February, 2010.
19. Jarzebowski AC, McMullin ND, Grover SR, Southwell BR, Hutson JM. The Kelly technique of bladder exstrophy repair: continence, cosmesis and pelvic organ prolapse outcomes. *J Urol.,* 182(4 Suppl): 1802-1806, October, 2009.
20. Smeulders N, Woodhouse CR. Neoplasia in adult exstrophy patients. *BJU Int.,* 87(7): 623-628, May, 2001.
21. Novak TE, Lakshmanan Y, Frimberger D, Epstein JI, Gearhart JP. Polyps in the exstrophic bladder. A cause for concern? *J Urol.,* 174(4 Pt 2): 1522-1526, October, 2005.
22. Higuchi TT, Granberg CF, Fox JA, Husmann DA. Augmentation cystoplasty and risk of neoplasia: fact, fiction and controversy. *J Urol.,* 184(6): 2492-2496, December, 2010.
23. Husmann DA, Rathbun SR.Long-term follow up of enteric bladder augmentations: the risk for malignancy. *J Pediatr Urol.,* 4(5): 381-385, October, 2008.
24. Silver RI, Gros DA, Jeffs RD, Gearhart JP. Urolithiasis in the exstrophy-epispadias complex. *J Urol.,* 158(3 Pt 2): 1322-1326, September, 1997.
25. Hensle TW, Bingham J, Lam J, Shabsigh A. Preventing reservoir calculi after augmentation cystoplasty and continent urinary diversion: the influence of an irrigation protocol. *BJU Int.,* 93(4): 585-587, March, 2004.
26. Gilbert SM, Hensle TW. Metabolic consequences and long-term complications of enterocystoplasty in children: a review. *J Urol.,* 173(4): 1080-1086, April, 2005.
27. Purves JT, Gearhart JP. Complications of radical soft-tissue mobilization procedure as a primary closure of exstrophy. *J Pediatr Urol.,* 4(1): 65-69, 2008.
28. Berrettini A, Castagnetti M, Rigamonti W. Radical soft tissue mobilization and reconstruction (Kelly procedure) for bladder extrophy [correction of exstrophy] repair in males: initial experience with nine cases. *Pediatr Surg Int.,* 25(5): 427-431, 2009.
29. Cervellione RM, Husmann DA, Bivalacqua TJ, Sponseller PD, Gearhart JP. Penile ischemic injury in the exstrophy/epispadias spectrum: new insights and possible mechanisms. *J Pediatr Urol.,* 6(5): 450-456, Epub 2010 Jun 11, October, 2010.
30. Woodhouse CR, Redgrave NG. Late failure of the reconstructed exstrophy bladder. *Br J Urol.,* 77(4): 590-592, April, 1996.