

A Comprehensive Review of the Complete Primary Repair Technique for Bladder-Exstrophy-Epispadias Reconstruction: First Surgical Attempt Should Be the Best One

Parham Torabinaid, Abdol-Mohammad Kajbafzadeh*

Purpose: To evaluate the effectiveness of the Complete Primary Repair of Exstrophy (CPRE) technique for bladder exstrophy-epispadias complex (BEEC) reconstruction and its comparison with the Modern Staged Repair of Exstrophy (MSRE) technique.

Materials and Methods: A comprehensive literature review of CPRE and MSRE was conducted, focusing on factors such as continence rates, postoperative outcomes, and complications. Various studies on pelvic biometry, surgical approaches, and long-term evaluations of renal function and continence were analyzed.

Results: CPRE demonstrates promising outcomes, particularly in resource-limited settings, by reducing the number of surgeries and associated risks compared to MSRE. Success rates for continence post-CPRE were higher when performed correctly in the first attempt, with fewer complications such as vesicoureteral reflux and hydro-nephrosis. Pelvic biometry assessments, including bladder neck placement and levator ani angle, were significant predictors of successful continence outcomes.

Conclusion: CPRE offers a viable alternative to MSRE, particularly in low-resource environments, with favorable continence and renal outcomes. Proper surgical execution in the first attempt is critical for long-term success, emphasizing the importance of surgeon expertise and postoperative care. Further long-term studies are necessary to solidify CPRE's role as the primary surgical approach for BEEC.

Keywords: exstrophy; epispadias; review; reconstruction

INTRODUCTION

Bladder exstrophy is a rare congenital condition characterized by pelvic, urologic, and abdominal structural defects resulting from migration failure during embryonic development. This condition involves the fusion of the evaginated urinary bladder to the skin of the abdominal wall, originating from the inner surface of the bladder. Diagnosis typically occurs through prenatal ultrasound or after birth. This malformation may manifest as an isolated occurrence or as part of a more extensive condition known as bladder exstrophy epispadias complex (BEEC), with the most severe form being cloacal exstrophy (CE), which represents the most severe subtype in the BEEC spectrum⁽¹⁾. **Figure 1** illustrates two patients with BEEC.

In classic bladder exstrophy (CBE), several anatomical differences are notable, including a more vertically positioned vagina and a more distally located cervix in females⁽²⁾. Moreover, BEEC patients exhibit a more posteriorly positioned levator ani with a shorter anterior part, as well as an anteriorly located anus, compared to healthy individuals^(3,4). In CBE, there is also a 30% shortage of bone in the anterior pelvis. Surgical reconstruction aims to align the reconstructed structures more

closely with natural anatomy by deeply positioning the bladder, bladder neck (BN), and posterior urethra within the pelvic diaphragm⁽⁵⁾. The surgical objectives encompass reconstructing the bladder, repairing the epispadias urethra, and achieving continence⁽⁶⁾. However, patients may experience ongoing psychological and social challenges post-surgery, such as social withdrawal, isolation, and low self-esteem, necessitating regular psychiatric sessions⁽⁷⁾.

Various surgical techniques and approaches are utilized worldwide, each yielding different results. The goal of repairing BEEC is to effectively close the bladder, creating a functional reservoir with low pressure, resulting in a normal appearance of the genitalia, preservation of kidney function, and achievement of continence⁽⁶⁾. In the spectrum of BEEC, males present with a completely exposed penile urethra, while females have a narrow vaginal opening and a split clitoris⁽⁸⁾. Urethroplasty is a critical component of the complex reconstruction process. Over the past few decades, extensive research has led to ongoing discussions on the most effective surgical approach. It is crucial to customize the decision-making process, considering the surgeon's expertise, comprehensive risk assessment, and the resources available at the patient-care center to determine the op-

Pediatric Urology and Regenerative Medicine Research Center, Gene, Cell and Tissue Research Institute, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran.

* Correspondence: Pediatric Urology and Regenerative Medicine Research Center, Pediatric Center of Excellence, Children's Medical Center, No. 62, Dr. Qarib's St, Keshavarz Blvd, Tehran 14194 33151, Iran (IRI)
Tel/Fax: + 98 21 66565400 E mail: kajbafzd@sina.tums.ac.ir.

Received October 2024 & Accepted December 2024

Table 1. Studies performed CPRE technique

Study	Author (year)	Technique (number of case)	Indication	Gender	Age at surgery	Objective	Follow-up rate	Success time	Operation	LOS	FBC
1	Merguerian(2023) 85	CPRE (36)	CBE	M: 26 F: 10	0.1	Long-term renal function and hypertension	120.12	-	-	-	-
2	Hammouda (2023) 51	CPRE (142)	CBE	M: 123 F: 19	2.21	Long-term continence status	145.2	88%	-	-	-
3	Joushi (2023) 40	CPRE (72)	BEEC	M: 31 F: 11	20.4	Kidney function	48	-	-	-	17
5	Kajbafzadeh (2022) 73	CPRE (37)	BEEC	F: 37	86.88	Long-term outcomes of females undergone CPRE	112.56	-	15.8	297	26
6	Bueno-Jiménez (2020)50	CPRE (13: early) CPRE (6: late)	CBE	Male	0.03 1.9	Comparison between early and late CPRE	108 12	85% 100%	-	-	-
7	Ebert (2020) 37	CPRE (prospective): 11 MSRE (prospective): 23 CPRE (cross-sectional): 53 MSRE (cross-sectional): 60	CBE	M: 24 F: 10 M: 74 F: 39	3 144	Outcomes of CURE-Net German BEEC database	- -	- -	39.5 21 28.5 27	- -	- -
8	Kajbafzadeh (2020)39	CPRE (49)	BEEC	Male	62.76	Long-term outcomes of CPRE without osteotomy	127.25	65.3%	17.2	321	38
9	Chua (2019)46	CPRE-BUR (10) SRBE-BUR(11)	BEEC	Male	0.15 0.067	Comparison of outcomes between a modified MSRE and CPRE	116.4 48	- -	20 18	580 664	0 0
10	Kajbafzadeh (2018)30	CPRE (9) Uretero-urethral engraftment (7) CPRE (44)	BEEC	Female	37.8 44.16	Comparing the outcomes between uretero-urethral engraftment and CPRE	72	55.55% 71.42%	35	- -	- -
11	Berjeaut (2018)86	CPRE (44)	BEEC	-	-	Long-term outcomes of CPRE and groin flaps	123.6	97.70%	-	-	-
12	Arab (2018) 87	CPRE (60)	CBE	M: 45 F: 15	9	Long-term outcomes of CPRE	168	23%	-	-	39
13	Srougi (2017)32	CPRE (15)	CBE	Male	50.4	Long-term outcomes of CPRE among males	123.6 116.4	93.3% 37%	13.2	325	11
14	Merguerian (2017)36	CPRE (30)	CBE	M: 17 F: 13	0.12	Long-term outcomes of upper urinary tract after CPRE	-	-	-	-	-
15	Alsowayan (2016)31	CPRE (10) MSRE (6)	CBE	M: 4 F: 6 M: 3 F: 3	- -	Long-term comparison of outcomes between CPRE and MSRE	216	93.8%	-	-	-
16	Kureel (2011)88	CPRE (25)	CBE	Male	1.17	Evaluation on of outcomes following their novel CPRE	24	-	-	420	-
17	Kajbafzadeh (2011)58	CPRE (11)	CBE	M: 7 F: 4	49.56	Evaluation of outcomes using biodegradable material in CPRE	30.1	66.7%	13.4	-	6
18	Ebert (2009) 12	CPRE (12)	BEEC	-	51	Evaluation of postoperative biometry in CPRE	172.8	-	-	-	-
19	Ebert (2009) 24	CPRE (17)	CBE	-	31.3	Long-term psychologic, sexual, and continence status	232.8	-	-	-	12
20	Ebert (2008) 48	CPRE (17)	BEEC	Male	-	Long-term sexual and hormonal changes after CPRE	228	95%	-	-	-
21	Caione (2007) 47	CPRE (28)	BEEC	M: 18 F: 10	7.2 6.8	To evaluate the outcomes after CPRE regarding gender variety	32.4	42% 83.3%	- -	- -	- -
22	Youssif (2007) 89	CPRE (15)	CBE	M: 12 F: 3	8.6	CPRE outcomes in older children and those with FBC	24	-	-	390	8
23	Ebert (2005) 7	CPRE (100)	BEEC	M: 76 M: 24	174	Psychologic evaluation	133.2	-	-	-	-
24	Borer(2005) 45	CPRE (23)	CBE	M: 16 F: 7	-	Early outcomes after CPRE	8-96	80%	-	-	-
25	Borer (2005) 44	CPRE (23) MSRE (14)	CBE	M: 16 F: 7 44.4	0.04	UDS between CPRE and MSRE	-	-	-	-	-
26	Bharati (2004) 90	CPRE (10)	CBE	M: 4 F: 6	1.5-6	Anatomic evaluation of patients	-	-	-	-	-
27	Hammouda (2004) 38	CPRE (33)	CBE	M: 26 F: 7	2	Primary outcomes of CPRE	42	-	-	-	2
28	Riccabona (2003) 91	CPRE (21)	BEEC	M: 14 F: 7	7	Primary outcomes of CPRE	62	-	-	-	9
29	Khoury (2003) 59	CPRE (9)	CBE	Male	0.13	MRI findings after CPRE	36	-	-	-	-
30	Mitchell (2000) 22	CPRE (24)	CBE	-	0.03	Primary outcomes of CPRE	44	87.5%	-	-	-
31	Mildenberger (1996) 5	CPRE (15)	CBE	M: 9 F: 6	0.06-13	Primary outcomes of CPRE	-	53.33%	-	-	-
32	Montagnani (1988) 92	CPRE (8) MSRE (31)	CBE	- -	- -	Primary outcomes of CPRE	- -	- -	- -	- -	- -

Table 2. Studies performed osteotomy with the CPRE technique

Study	Author (year)	Approach	Osteotomy type	Type of immobilization	Duration of immobilization	Fixation	Diastasis
1	Gearhart (2023) 62	Multi-stage: 65 Single-stage: 16	Combined: 36 Posterior: 16 Anterior: 14	Buck: 35 Bryant: 17 Spica: 16	-	External: 43 None: 39	6 (3.25-16) cm
2	Hammouda (2023) 51	Single-stage	Bilateral ATIO	Spica: 142	4 weeks	-	-
3	Gearhart (2023) 42	Multi-stage: 42	Combined: 39 Posterior: 1 Anterior: 2	Modified Buck	4-6 weeks	External	6.55 (5.7-7.7) cm 5.9 (5.1-7.2) cm
4	Sack (2015) 93	Single-stage: 17	Anterior innominate	Spica: 17	4-6 weeks	-	-
5	Youssif (2007) 89	Single-stage: 15	Anterior: 15	Spica: 15	4 weeks	-	5.4 (4-6) cm
6	Hammouda (2004) 38	Single-stage: 33	Bilateral ATIO: 33	<1 year old: Spica >1 year old: External	<1 year old: 2-3 week >1 year old: 3-4 week	-	-

timal method^(9,10).

The surgical reconstruction for patients can be performed shortly after birth (early) or later in infancy (delayed). Surgeons typically use three main surgical approaches: Complete primary repair of extrophy (CPRE), modern staged repair (MSRE), and Kelly's procedure. When choosing the surgical approach, it's crucial to consider factors such as the timing of primary closure, associated risks, complications, and the necessity of pelvic osteotomy⁽¹¹⁾. While extensive research has focused on MSRE and efforts have been made to assess its superiority over CPRE, limitations in providing long-term follow-up and resources for extended hospital stays have led us to prioritize CPRE as our method of choice. Despite recognizing the potential advantages of MSRE, a comprehensive analysis of CPRE is necessary to optimize outcomes within our resources and capabilities. **Table 1** summarizes the details of studies conducted CPRE for BEEC reconstruction.

Pelvic biometry

Various imaging modalities have been utilized for better elucidation of the pelvic floor structures, providing essential data for clinicians and advanced surgical techniques. Magnetic resonance imaging (MRI) revealed that patients who underwent BEEC reconstruction had significantly higher intersymphyseal distance and levator ani diversion angle than healthy individuals 3. Those with smaller pubic diastasis, deeper placement of the BN, and higher levator ani angle showed better continence after surgery⁽¹²⁾. Postoperative computed tomography (CT) scans revealed that an increase in the anteroposterior diameter of the pelvis was linked to

improved continence⁽¹³⁾. Furthermore, the cardinal ligaments of the pelvic floor play a role in pelvic organ prolapse in adult females after BEEC reconstruction. This underscores the significance of routinely assessing pelvic dimensions and biometry for surgeons before reconstructive surgeries to enhance postoperative outcomes. Gearhart found that the intersymphyseal gap and levator angle were significant predictors of continence status after BEEC reconstruction⁽¹⁴⁾. Ebert was among the first to use transperineal 3D ultrasonography to evaluate pelvic structures, highlighting the importance of this method for long-term assessment of female pelvic structures to prevent postoperative pelvic organ prolapse^(12,15). Following BEEC reconstruction, patients showed a more flattened pelvic floor and a larger transverse diameter of the hiatus^(16,17). The transverse diameter of the levator hiatus and levator angle were notably greater in BEEC patients than in nulligravid women, leading to less support of the muscle to the bladder, BN, and urethra. The levator hiatus's anteroposterior diameter, thickness, and area were similar between the two groups. Additionally, the maximum levator thickness was observed on both sides dorsal to the vagina, indicating significant muscle divergence towards the anterior region⁽¹²⁾.

CPRE versus MSRE

Prior to the late 1950s, urinary diversion was the preferred surgical approach 18. The first attempt at repairing bladder exstrophy dates back nearly 150 years⁽¹⁹⁾. The modern staged repair of bladder exstrophy, developed in the 1970s, entails closing the abdominal wall, bladder, and posterior urethra, as well as approximating the pubic bones. This is followed by neo-urethroplasty

Table 3. Various definitions for continence in literature

	Definition
1	Complete continence Partial continence Incontinent
2	Grade 0 (social/total continence) Grade 1 (occasionally wet) Grade 2 (frequently wet) Grade 3 (Incontinent)
3	Continent Incontinent
4	Excellent Good Fair Poor

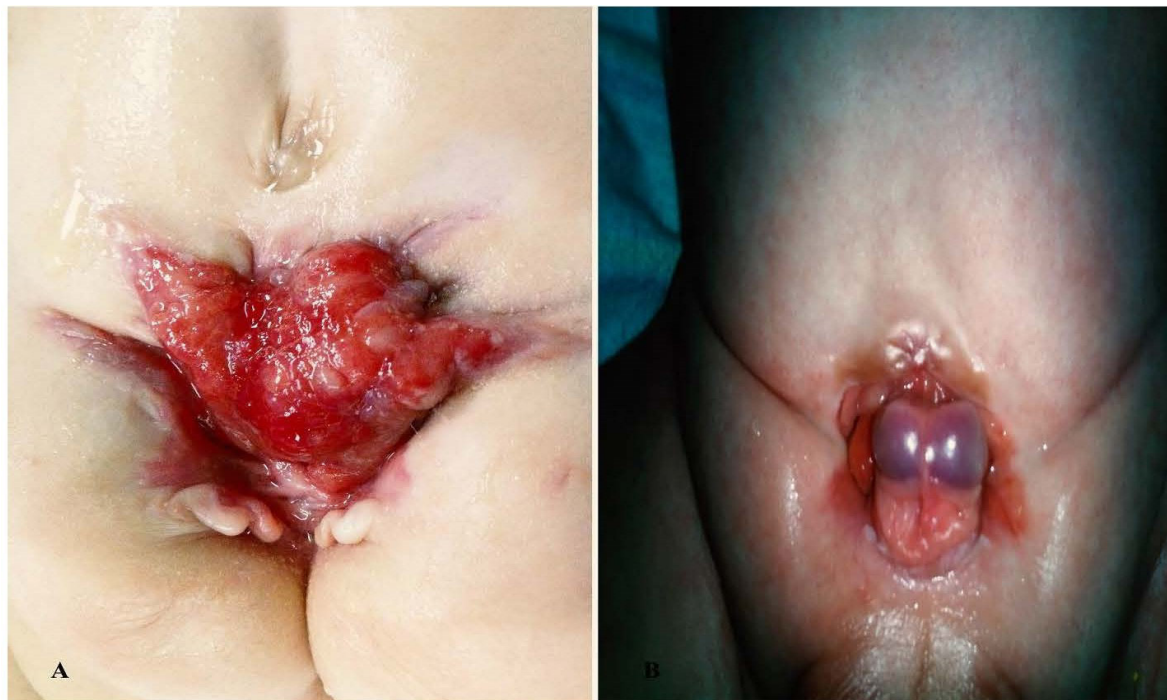


Figure 1. (A) Bladder exstrophy-epispadias complex in a female patient, highlighting the exposed bladder tissue. The severe defect in the abdominal wall and the anterior wall of the bladder emphasizes the need for surgical intervention to repair and protect the exposed bladder tissue. (B) The image depicts the bladder exstrophy-epispadias complex in a male patient, showing the protrusion of bladder tissue and abnormal development of the penile structures associated with epispadias that underscores the requirement for comprehensive surgical management to address both functional and cosmetic concerns.

ty for epispadias repair and bladder neck reconstruction (BNR)⁽¹⁸⁾. The technique of CPRE was initially described in 1960⁽²⁰⁾, and a modified version was introduced in the 1990s to reduce the total number of surgeries and enhance BN resistance^(21,22). While there is an ongoing debate between CPRE and MSRE, both methods yield similar outcomes when performed by their respective advocates⁽²³⁾. The potential advantage of employing one-stage reconstruction methods is the seamless integration of major reconstruction steps, al-

lowing unobstructed access to the BN. Consequently, this approach may result in fewer bladder scars and contribute to the efficient development of bladder capacity through cycling and addressing bladder outlet resistance (BOR)⁽²⁴⁾.

Many surgeons favor utilizing MSRE (58.1%) and CPRE (38.7%) for BEEC reconstruction (96.8%), with CPRE being particularly performed in North America. MSRE demands more resources due to the increased requirement for prolonged hospital stays and surgeries.

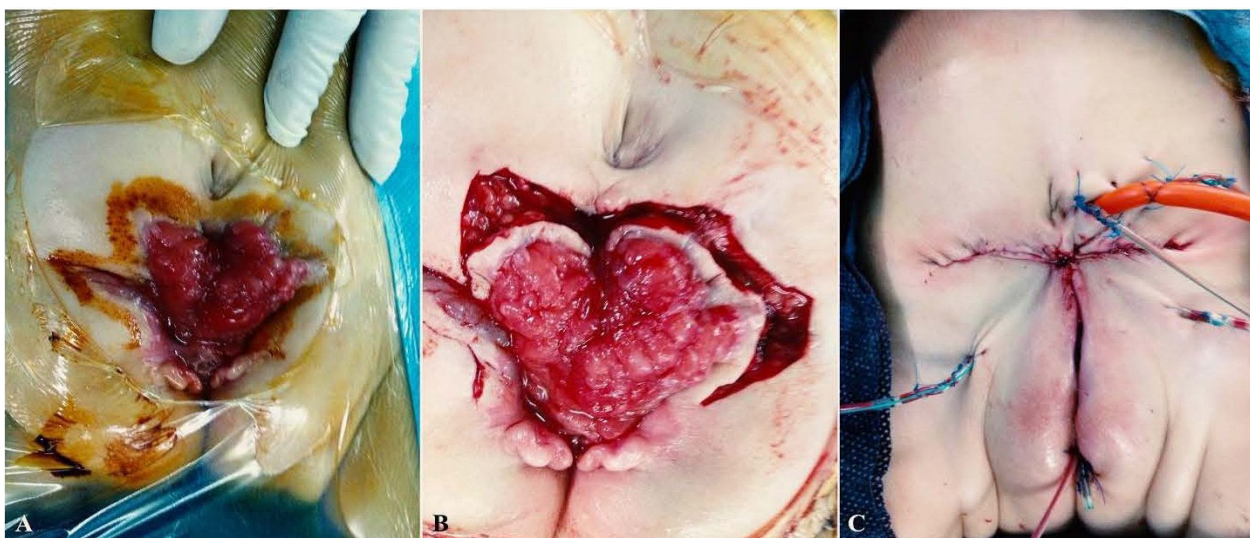


Figure 2. (A) Intraoperative image showing bladder exstrophy-epispadias complex in a female patient with exposed bladder mucosa meticulously prepped for CPRE technique. (B) Careful dissection of the bladder mucosa and surrounding tissues to enable anatomical reconstruction of the bladder and urethra. (C) Postoperative status, showing a well-approximated midline closure of the bladder and abdominal wall. Urinary diversion is maintained via suprapubic and urethral catheters to ensure drainage, with the suture lines visible at the site of bladder and pelvic floor reconstruction. Successful reapproximation of the pubic symphysis, genitalia, and abdominal wall musculature are critical for long-term continence and normal anatomical development.



Figure 3. (A) A male patient immobilized in a supine position after osteotomy, with the legs secured in a spica cast to stabilize the pelvis. (B) The immobilization setup ensures that the osteotomy site remains aligned, promoting optimal healing in the context of bladder exstrophy repair. (C) Postoperative care includes careful monitoring of the cast and limb positioning to prevent complications and support effective recovery.

Meanwhile, CPRE may offer a promising approach for low-income countries or healthcare facilities with limited medical resources. Despite MSRE being the traditional reconstruction method, newer techniques such as CPRE have yet to demonstrate significant advantages over this approach 10. In CPRE, bladder reconstruction, and epispadias repair are performed concurrently, reducing the total number of surgeries and associated risks⁽²⁴⁾. Failure in the initial bladder reconstruction diminishes the likelihood of achieving continence and bladder capacity, with the probability decreasing further with repeated failures⁽²⁵⁾.

The MSRE procedure involves closing the bladder, posterior urethra, and abdominal wall in newborns. Additionally, auxiliary techniques include epispadias

repair and BNR performed at different age groups⁽²⁶⁾. Ideal candidates for CPRE are individuals with fresh bladder closure or primary closure in late infancy⁽²⁷⁾. On the other hand, for cases involving the closure of the posterior urethra, single-stage reconstruction involving BNR and epispadias repair has yielded better results in continence achievement in CPRE than MSRE⁽²⁸⁾. Long-term assessment of CPRE has revealed that glomerular filtration rate (GFR), kidney length, and ureteral reimplantation (UR) are associated with a reduced risk of subsequent hypertension. Conversely, BNR and continence status showed no significant association with hypertension. Patients demonstrating normal kidney length and upper tract construction are less likely to develop future hypertension. However, patients under-



Figure 4. (A) Postoperatively, the bladder mucosa is no longer exposed, and the abdominal wall has been successfully closed, achieving a more natural appearance at the midline. The penis is surgically reconstructed to restore a more typical length and shape, correcting the dorsal curvature and creating a functional urethra, improving both the aesthetic and urinary outcomes. (B) The umbilicus and surrounding skin are realigned to enhance the overall cosmetic result, with scarring minimized through careful surgical technique, ultimately leading to a more normal abdominal contour. (C) A well-reconstructed penis following surgery with a restored straight penile shaft and closure of the previously open urethral groove, improving both functional and cosmetic outcomes. The scrotum appears symmetrically aligned, and the penile skin is smooth with minimal scarring, indicating successful healing and attention to aesthetic detail during the CPRE process. The surgical outcome demonstrates a significant improvement in the overall appearance of the genitalia, with a nearly normal anatomical structure, which will further support psychological well-being and future functional use.

going MSRE may experience hypertension as a result of osteotomy and subsequent traction, which can be resolved after the removal of traction⁽²⁹⁾.

Current research emphasizes the importance of achieving optimal BOR to facilitate urine flow without causing damage to the upper urinary tract (UUT)⁽³⁰⁾. Some studies suggest that additional surgeries after bladder closure can improve continence rates^(31,32). However, histopathologic assessments have revealed that repeated surgeries for BEEC result in decreased muscle fibers and a significant presence of fibrous tissue around the bladder⁽³³⁾. It has been highlighted that the initial BEEC reconstruction attempt is crucial for achieving continence, with a 75% success rate for first surgeries compared to an 18% success rate for subsequent attempts. Moreover, the present review underscores the significance of the initial procedure in achieving continence post-bladder closure, with continence being achieved in all patients following the closure. Hence, prioritizing the success of the first surgery is paramount^(34,35). Another study showed that after CPRE, all patients achieved social continence except those who had two failed bladder closures, indicating the importance of the first attempt⁽³⁰⁾. Concerns have also been raised about the potential adverse effects of CPRE on the UUT, including increased hydronephrosis and its impact on kidney function. Additionally, studies have identified the risks of vesicoureteral reflux (VUR), hydronephrosis, cortical defects, and urinary tract infections (UTIs) in patients undergoing CPRE^(32,36,37). The prophylactic administration of antibiotics before surgery has been found to reduce the incidence of UTIs 38. Furthermore, it has been observed that despite frequent occurrences of hydronephrosis, a small number of patients develop kidney impairment, with specific risk factors such as recurrent UTIs, severe hydronephrosis, impaired renal function, and male gender⁽³⁶⁾. On the other hand, time of closure, osteotomy, gestational age, and the surgeon's speciality were also found to correlate with successful closure⁽²³⁾. Additionally, the dimensions of the urethral plate, quality of the bladder plate, intersymphseal distance, and phallus size were identified as important factors affecting closure outcomes⁽³⁹⁾.

Vesicoureteral reflux and kidney scarring did not appear to be indicative of impaired GFR but may suggest the necessity for thorough monitoring⁽⁴⁰⁾. Research has found a prevalence of chronic kidney disease (CKD) stage 2 or higher in adults who had undergone reconstruction for BEEC during childhood. Despite concerns about the potential impact of bladder reconstructive procedures on the UUT, some studies have indicated that these procedures do not significantly affect renal function or the risk of proteinuria^(40,41). Overall, comprehensive large-scale studies with long-term follow-up are still required to assess the relationship between urodynamic parameters, lower urinary tract reconstruction, and the outcomes of bladder reconstructive procedures. During long-term evaluations of patients, it was found that renal outcomes were comparable to other techniques and were not significantly affected by BUR or lower urinary tract conditions⁽⁴⁰⁻⁴²⁾. Additionally, modern CPRE has not been shown to have a negative impact on renal function 43. This underscores the importance of regular and thorough monitoring of children undergoing CPRE over an extended period⁽⁴⁰⁾. Some studies showed that CPRE appears to have a deleterious impact

on genital outcomes (e.g., glans necrosis, hypospadias, appearance) and UUT preservation⁽⁴⁴⁾. However, a 19-year follow-up study revealed no renal scarring or upper urinary tract injury among the CPRE group with normal renal function for their age 43. However, CPRE is not recommended in cases of prematurity, small tissue size of the urethral plate, and subjective small appearance of the bladder⁽⁴⁵⁾. A comparison between CPRE and MSRE regarding bladder capacity progression after repair showed a substantial difference in bladder capacities. However, no significant differences were found between the two surgical approaches when comparing the percent predicted bladder capacity. CPRE is beneficial for bladder development and the establishment of BOR. Additionally, CPRE resulted in lower detrusor overactivity and higher EMG normality, with comparable bladder compliance to the MSRE group⁽⁴⁴⁾.

MSRE has been found to offer advantages over CPRE, such as avoiding vascular damage from penile disassembly and reducing external compression from pubic approximation⁽⁴⁶⁾. A study comparing males and females undergoing CPRE has revealed differing complication rates and continence statuses between the genders, with females demonstrating better outcomes in continence and bladder function⁽⁴⁷⁾. As for male sexual function and fertility, early surgical reconstruction and BNR have been found to not correlate with impairment of sperm function and fertility^(43,48). The timing and number of attempted BNRs were significantly associated with fertility success among males⁽⁴³⁾.

In summary, irrespective of the advantages and disadvantages of each surgical technique, it is considered crucial that the first surgery should be the best and optimal surgery. The number of subsequent surgeries is associated with a decreased likelihood of achieving continence. The first surgery is the leading predictive determinant factor of successful closure. It was also observed that hospital charges for patients with successful primary closure were significantly lower than those requiring more procedures⁽²³⁾. Finally, we believe that while both techniques bear some merits and drawbacks compared to the other, the decision on the surgical technique must be individualized due to both patient and healthcare specifications.

Timing of the surgery

The optimal timing for bladder closure surgery in newborns is also a matter of debate within the medical community. Some studies suggest that early closure, typically within 72 hours after birth, causes less damage and inflammation to the bladder mucosa⁽⁴⁹⁾. However, histopathologic examinations have shown no microscopic difference between early and delayed closure approaches 48. On the other hand, some experts argue that early surgery is associated with higher failure rates⁽²³⁾. A comparison of outcomes between early and delayed treatment groups demonstrated promising results in the delayed group. Specifically, the delayed approach does not require general anesthesia and further respiratory support, which can adversely affect immature newborns. Additionally, prolonged hospital stays can deprive the child of crucial emotional support provided by physical contact with the mother⁽⁵⁰⁾.

While there was no significant difference in dehiscence rates between the early and delayed approaches 50, the repair is optimal at two months old, as kidney function stabilizes after six weeks. Immature kidney function is

susceptible to injury from anesthesia or antibiotics, further supporting the case for delayed closure⁽⁵¹⁾. Some experts argue that delayed closure may be beneficial due to a lack of expertise in neonatal reconstruction or inadequate urethral plate length⁽⁵²⁾. Moreover, the hemodynamic status of newborns is crucial, and most ischemic changes occur during this period, which supports the rationale for delaying the surgery^(53,54). According to research by Dickson and colleagues, the success rate for the delayed approach for bladder closure surgery was 100%, compared to 87% for the early approach⁽⁵⁵⁾.

Description of the technique

The preoperative management of children with BEEC involves specific care of the extrophied structures. This includes daily saline wash during diaper changes or using hydrogel dressings to keep the surface of the structures hydrated⁽⁵⁾. According to the published method 39, the bladder plate was meticulously delineated, and the boundaries of the urethra were precisely defined to ensure that the verumontanum was not positioned inside the bladder (**Figure 2: A-B**). Any inaccuracy in locating the verumontanum could lead to the urinary sphincter's fibers extending into the bladder, potentially impacting continence. An approximately 0.5–1 cm margin of skin was intentionally preserved within the boundaries to provide a secure anchoring point for the subsequent stay sutures. The silk stays sutures carefully navigate the bladder plate, which was meticulously separated from the underlying rectus fascia and peritoneum down to the central vascular pedicle. At the same time, the fibers of the urogenital diaphragm were meticulously separated from the pubic arches down to the corpora cavernosa. The bladder plate was liberally freed before pubic approximation, allowing it to be closed in two layers without any tension. According to the Cantwell-Ransley approach, the urethral plate was detached from the corpora, and the corpora were separated up to the glans while leaving 1 cm intact distally, followed by tubularization of the urethral plate (**Figure 2: C**). The corpora are then rotated medially and anastomosed proximally during caverno-cavernostomy to achieve a dangling position for the penis in the flaccid state and to keep the neourethra in the ventral position. When performed before closure, this procedure allows for a deeper bladder positioning, suggesting the potential for improved continence.

The cystorrhaphy procedure involved removing a portion of the surrounding skin and then suturing the bladder wall in two layers. During cystorrhaphy, the bladder is closed in two planes and positioned deep in the pelvic floor to achieve a tension-free state. This involves separating the bladder from the pelvis and installing the deep urethra and bladder into the deep surface of the pelvis. To support continence attainment, the bladder, BN, and proximal urethra are placed deep in the pelvic floor, minimizing pressure on the pubic bones and providing an appropriate environment for support by pelvic muscles. In the next step, a cystostomy tube of the proper size was inserted into the bladder. Catheters were placed in the ureters and secured to the bladder lining using absorbable sutures. The pubic bones were gradually brought together using a Bailey rib retractor, an absorbable C-plate, and strong sutures. The fibers of the muscles around the BN were meticulously shaped to create a circular sphincter, with the strongest fibers placed at the top. Careful control was exercised using

rotating sutures on the corpora cavernosa to prevent excessive central cavernosal fine arteries from twisting. The application of urogenital diaphragm flaps around the bladder neck was carried out without undue tightness. Following the procedure, patients did not need postoperative leg plaster or leg traction but utilized a frog leg bandage for 1–3 weeks.

According to another study, abdominal closure involves rotating the flaps toward the midline using muscle aponeurosis of the rectus, external oblique, and hypogastric muscles⁽³²⁾. A specific technique, known as cutting the inter-symphyseal band before penile disassembly, facilitates posterior vesicourethral release from the pelvic floor, enhances visibility during urethral plate separation, and decreases the risk of bleeding⁽⁴⁵⁾. The rotational skin flap performs the penile skin closure. Besides, for female patients, the reconstruction involves mobilization of BN and urethra from the midline of the pelvic floor, symmetrical reassembly of the muscular complex using a bipolar stimulator, tabularization and elongation of BN and urethra, and genitoplasty⁽⁴⁷⁾.

After surgery, it's important to carefully monitor the patient's BOR, conduct ultrasound examinations to detect VUR and hydronephrosis, assess for residual urine, and collect monthly urine samples for analysis and culture to prevent UTI and subsequent kidney infections. Long-term, thorough follow-up is crucial to evaluate various factors, including the patient's psychosocial well-being, achievement of continence, voiding patterns, sexual activity, urinary system function, fertility, hormonal changes, and organ prolapse risk. Ongoing discussions will also center on each individual's best surgical techniques and personalized approaches⁽³⁰⁾.

Osteotomy

Previous challenges regarding BEEC management were surrounding choosing the type of closure; however, the current debate is about the need to perform the osteotomy. In 1958, Schultz introduced an innovation for managing BEEC patients, marking a significant advancement in surgical correction 56. This technique affects the closing of the abdominal wall, which promotes wound healing and reduces bladder tension^(42,57). Osteotomy, an essential step in BEEC reconstruction, offers numerous advantages, particularly for failed bladder closure (FBC) and delayed closures 11. However, there are drawbacks to osteotomy, including increased operation time, risk of dehiscence, blood loss, wound infection, prolonged hospitalization, and the need for immobilization for 4–6 weeks⁽⁵⁸⁾. Despite ongoing debate around the necessity of osteotomy for BEEC management, it has been found that osteotomy provides more space by enhancing levator length for better support of the bladder, urethra, and adjunct structures⁽⁵⁹⁾. Furthermore, it significantly increases the success rate of bladder closure in female bladder extrophy cases⁽¹¹⁾. Studies have also revealed that osteotomy reduces the risk of inguinal hernias through pelvic dimension reconstruction⁽³⁷⁾. **Table 2** summarizes the specifications of studies that performed osteotomy with CPRE for BEEC repair.

For BEEC patients, pelvic bone length diminishes by almost 30%, leading to a waddling gait, increased hip spacing, and outward rotation of the lower limbs due to substantial diastasis between the pubic rami^(1,60). There is a 2.6-fold increase in closure failure for every additional centimeter increase in diastasis size before

surgery⁽⁶¹⁾. Consequently, regardless of the diastasis width, osteotomy is recommended for patients with CE⁽⁶²⁾. The methods of immobilization following osteotomy are varied, including spica casting, Bryant's traction, Buck's traction, external fixation, Montgomery straps, Velcro binders, internal pins, Russell traction, leg wraps, and Kling dressing with adduction splints⁽⁶³⁻⁶⁵⁾. Some methods, such as spica cast and mummy wrap, have shown more side effects and less effectiveness^(23,65). **Figure 3** shows immobilization of a patient undergone osteotomy. While posterior iliac osteotomy with repositioning adjustments was the initial approach, it has evolved to anterior ramotomy, anterior diagonal iliac osteotomy, and anterior pubic ramotomy. The later introduction of anterior innominate osteotomy combined with posterior vertical iliac osteotomy led to reduced surgical blood loss, improved visibility, and enhanced access to the anterior and posterior structures of the pelvis⁽⁵⁷⁾.

In summary, despite its drawbacks, osteotomy remains vital in reconstructing BEEC and offers significant advancements in treating BEEC. According to the Gearhart approach to osteotomy, the standard procedure involves a combined technique of anterior innominate osteotomy and posterior vertical iliac osteotomy, followed by installing an external fixator. After 2-3 weeks, the abdominal wall is closed, and the pubic tubercle is positioned using metal screws and plates⁽⁶²⁾. While studies also used metal screws and plates for pubic fixation, this method necessitated additional surgery to remove them. In contrast, one study utilized biodegradable devices to avoid further surgery, resulting in promising outcomes with a minimal diastasis recurrence rate and shorter hospital stays⁵⁸. Gearhart's findings indicate a growing trend towards the combined technique and a decrease in the use of the posterior approach over time^(23,62).

Additionally, there were significant increases in immobilization, Buck's traction, and external fixation⁽²³⁾. In a recent study by Gearhart et al., improved outcomes with multiple-stage osteotomy in the context of closure success were showcased. The research found no significant variances in closure outcomes based on the surgical center locations and emphasized the importance of osteotomy in successful closure. The combined technique is the gold standard approach at Gearhart Institute. It has high success rates for patients, regardless of whether they had previous closure failures. The results in their cohort were 100% for the combined technique, 71% for the posterior approach, and 60% for the anterior approach⁽⁶²⁾.

Not performing osteotomy is thought to be a contributing factor to the development of degenerative joint disease⁽⁶⁶⁾. Srougi used groin flaps after osteotomy, stating that most patients were referred cases with FBC and couldn't collaborate for long-term traction. However, the main disadvantage of this method is the need to repair the bladder exstrophy defect between 45 and 60 days after birth, along with a potential risk of inadequate blood supply and flap loss⁽³²⁾. It was observed that patients who did not undergo osteotomy in the CPRE groups were more likely to develop further granular necrosis⁵⁴. Typically, osteotomy is performed on the same day that the bladder is closed. Gearhart suggests that in cases with diastasis greater than 4 cm, a forceful pubic approximation is needed⁽⁵⁴⁾. If the diastasis

is more than 6 cm, the osteotomy is better performed two weeks earlier than primary closure using external fixators, with daily adjustment using the Mountaineer hardware device⁶⁷. However, in patients younger than three days old with less than 4 cm diastasis, an osteotomy may not be necessary, and an approximation of the pubic tubercles might be adequate⁽⁶⁸⁾. However, Gearhart supports osteotomy for CE patients, irrespective of diastasis⁽⁶²⁾.

Gearhart has developed a novel staged osteotomy method that gradually adjusts diastasis externally over 2-3 weeks, followed by 4-6 weeks of immobilization⁽⁶⁹⁾. This method is based on a study that suggests a direct association between diastasis and failure rate, showing a 2.6-fold increase in failure risk with each 1 cm increase in diastasis⁶¹. Several studies have evaluated the effectiveness of staged osteotomy for successful closure. In a recent publication, Gearhart argued in favor of the staged approach, citing a lower rate of orthopedic complications than the single-stage approach. Gearhart's research indicates a growing preference for using multi-stage over single-stage osteotomy, citing higher success rates. This reinforces their earlier claims that performing osteotomy followed by delayed closure yields promising results^(11,62). They advocate that the external fixator can minimize diastasis through gradual repositioning, creating a more favorable environment for future abdominopelvic reconstructions. However, the difference was not statistically significant, and there was no significant association between staged osteotomy and the overall success of closure⁽⁶²⁾. However, it's important to note that the number of cases analyzed was insufficient to draw a statistically significant conclusion, highlighting the need for further large-scale studies. Despite the numerous advantages highlighted by Gearhart and colleagues, it's worth considering that implementing a staged approach may pose challenges in healthcare centers with limited facilities and staff resources.

Continence attainment

The literature presents a wide range of continence rates for the CPRE technique, ranging from 12% to 88%, and a similar pattern is observed for MSRE^(51,70). It is noteworthy that only 68% of articles provided clear definitions of continence, and nearly half of the reported cases achieved continence, irrespective of factors such as the type of surgery, osteotomy, or gender⁷¹. Mitchell's study revealed a continence rate of 74%, with only 20% achieving continence without any procedures⁽⁷²⁾. Similarly, Srouge's findings showed a 60% continence rate, with only 13% not requiring more than one procedure, suggesting that CPRE alone may not be sufficient for complete continence attainment⁽³²⁾.

Numerous definitions of continence were discovered in the literature under review, summarized in **Table 3**. One set of definitions categorized continence as complete (more than 3 hours without leakage during day and night), partial (1-3 hours or stress incontinence), or incontinent (less than 1 hour). Another classification included grades from socially continent/totally continent to incontinent, based on dry intervals during the day and night. Assessing continence in children is challenging, as bladder function and capacity fully develop at 4-5 years. Kajbafzadeh's study emphasized pelvic floor stimulation, toilet training, and innovative surgical techniques to enhance continence achievement, with all

patients without previous surgery achieving social continence⁽⁷³⁾. Long-term follow-up of patients is essential, as continence status may change over time, as demonstrated by Woodhouse's study, which showed a gradual decrease in continence rates among repaired children⁽⁷⁴⁾. Additionally, bladder volume, capacity, and deep pelvic positioning were identified as factors associated with continence status^(5,38). In summary, the literature indicates that an early evaluation of continence status may not accurately predict the ultimate continence status 45, and long-term monitoring is crucial. Furthermore, it was noted that continence rates did not significantly differ between CPRE and MSRE techniques⁽²⁴⁾.

Complication control

The literature encompasses detailed medical information regarding various procedures and techniques related to urological repair secondary to BEEC reconstruction, and each of them requires a specific literature review. It includes managing complications of urethral stricture, bladder outlet obstruction, febrile UTIs, and conservative management of specific symptoms. Additionally, it addresses the criteria for successful surgery, lowering complications in BEEC repairs, and recommendations for regular urodynamic studies and renal ultrasonography. The literature also focuses on auxiliary surgical techniques, such as augmentation procedures to increase bladder capacity, continence procedures like BNR, bulking agent injections (BNI), and innovative approaches to enhance bladder capacity. It discusses success rates and predictive factors associated with BNR surgeries, emphasizing the importance of bladder capacity in achieving continence^(45,51). Success rates for BNR are reported in a broad spectrum from 43.8% to 94%^{31,70}. Hence, regular UDS and renal ultrasonography are recommended, especially when a great amount of urine residues or urinary symptoms are present⁽²⁴⁾.

A recent study discusses the effectiveness of the surgical approach in auto-augmenting (by bladder plate herniation) bladder capacity for patients with small bladder plates without causing harm to the upper urinary tract⁽⁷⁵⁾. Their technique can be used prior to primary reconstruction or other bladder reconstructions to increase bladder capacity. As mentioned before, bladder capacity is paramount in BEEC reconstruction, making the bladder ready for further surgeries and increasing the likelihood of continence attainment⁽⁷⁶⁾. Another study proposed conducting BNR for incontinent children based on specific bladder capacity and bladder urethral ratio measurements. Studies also outlined the management of penile ischemia, covering surgical techniques and causes. In cases of penile ischemia, the recommended approach involves releasing pubic approximation sutures and performing an osteotomy if necessary. Gearhart suggests using an anterior innominate and vertical approach, along with an external fixator if indicated, and employing rectus abdominis sheet flaps. Mitchell has highlighted two distinct causes for penile ischemia during CPRE. The first cause is a stitch placed around or through the blood supply to the corpora during the closure of the symphyseal diastasis. The second cause is excessive pressure between the pubic bones when the symphysis is brought together^(46,54,77).

Additionally, the literature explored the psychosexual and psychological aspects of patients undergoing reconstructive surgery, emphasizing their interests in individual sports, relationships with the opposite gen-

der, and the specific challenges they face. Regarding psychosexual and psychologic problems, Ebert and colleagues designed a questionnaire that has been specified for BEEC, reporting 61% and 58% with "Good" status for primary and referred cases, respectively. Moreover, most patients indicated a high interest in individual sports and reported that post-operation status rarely caused problems for them. Moreover, having a relationship with the same and opposite gender was frequent among 77% and 85%, respectively. However, doing group sports, group showering, and undressing in front of others were among the conditions that the patients mostly avoided. On the other hand, having intercourse with the opposite sex was reported among box genders with the dominance of females. Most males had successful erections (97%) and ejaculation (84%), while satisfaction with the appearance (22%) and size (6%) of their genitalia was not acceptable. Besides, all women reported normal menstruation; their main complaint was genital appearance⁽⁷⁾. According to a study, nearly 67% of male individuals exhibited penile deviation, with a greater prevalence of micropenis reported as a complication. **Figure 4** shows promising cosmetic outcomes after CPRE technique. Furthermore, a notable reduction in the incidence of penile deviations was achieved by modifying the surgical approach from the Young to the Cantwell-Ransley technique⁴⁸. Studies also addressed the impact of these surgeries on fertility and underscored the importance of providing psychological support to both patients and their parents^(24,48). Finally, the need for further surgeries after the primary one was not different between CPRE and MSRE. Moreover, despite higher short-term complication rates for the CPRE group, the long-term complications remain the same between CPRE and MSRE⁽³⁷⁾.

Prevention of complications

Since the male gender has lately been shown as a major risk factor for UUT deterioration, it is imperative to conduct serial UDS on all males after BEEC reconstruction for early detection of changes and prevention of complications of UUT^(36,47). An aggressive approach, including reimplantation, is necessary due to scarring of the kidneys in many patients. Some believe that reimplantation should be performed once pyelonephritis occurs, while others believe it should be considered as the primary step for all CPRE patients^(5,45). However, such an approach may lead to overtreatment⁽⁷⁸⁾. To decrease the blood transfusion rate, a modified Cantwell-Ransley and osteotomy may be beneficial, and complete penile disassembly is not negligible to prevent further blood loss⁽⁴⁵⁾. NVB injury, especially in the BNR area, may cause an immature bladder, compromised capacity, compliance, and detrusor activity⁽⁴⁴⁾. According to a study by Kufner and colleagues, optimal bladder capacity is recommended for epispadias repair around 12 months^(46,79). Long-term UDS are necessary to monitor bladder function and capacity changes over time.

It is recommended to be cautious in utilizing para-extrophy skin flaps and urethral tissue replacement to minimize the likelihood of additional strictures unless addressing inadequate strip length is essential⁽⁸⁰⁾. Furthermore, empirical evidence indicates suboptimal outcomes when administering para-exstrophy flaps to prevent fistula formation⁽⁸¹⁾. Utilizing interrupted sutures rather than running sutures may aid in preventing hypospadias more effectively⁽⁴⁵⁾. NG fixation can also

help reduce the risk of wound dehiscence and intra-abdominal pressure⁽⁵⁾. Ureteral reimplantation and closure techniques include cephalotrigonal, cross-trigonal, and Politano-Leadbetter techniques. For ureteral reimplantation, the cephalotrigonal technique is preferred over the cross-trigonal technique^(36,45). The Z-flap technique is used to prevent further dorsal tethering⁽⁴⁵⁾.

In cases involving simultaneous epispadias repair and CPRE, meticulous urethral calibration is imperative, and close postoperative monitoring is crucial⁽⁸²⁾. Attaining optimal continence may necessitate primary or secondary BNR⁽³²⁾. It may be advisable to leave the urethra attached to the glans during penile disassembly to minimize the risk of penile ischemia. Factors such as the low thickness of the urethral plate, small penis length, and epinephrine injection increase the chance of glans necrosis^(45,54,77). However, forceful pubic approximation or osteotomy, particularly without concurrent CPRE and epispadias repair, can lead to penile ischemia and catastrophic complications⁽⁸³⁾. Research has also indicated the potential benefits of using biodegradable screws and plates for fixation during CPRE to avoid penile ischemia, wound dehiscence, and bladder prolapse⁽⁵⁸⁾. Moreover, no clear evidence supports the superiority of MSRE over CPRE, emphasizing the importance of considering various factors in decision-making processes^(31,54). Furthermore, delaying epispadias repair and pretreatment with testosterone may contribute to better penile cosmesis and reduced risks of penile ischemia⁽⁴⁶⁾.

Absorbable sutures can be used for pubic approximation to prevent further urethral injury after pubis widening⁽⁴⁵⁾. Using biodegradable plates and screws for pubic appositioning also showed promising results as an alternative to current fixation methods⁽⁵⁸⁾. During the surgery, internal rotation of the lower extremities facilitates pubis approximation⁽⁴⁵⁾. Placing retropubic sutures in the upper half of the pubic bones can help prevent compression and injury to the pudendal neurovascular bundle, thus reducing the risk of impeding venous return⁽¹⁹⁾. A second suture can be placed in the lower rectus fascia at the fascia's junction with the pubis's upper aspect to facilitate further bony closure⁽⁸⁴⁾. Lastly, reports have shown much fewer hypospadias incidences among younger children, which can be justified by the difference in the elasticity of the urethral plate between different ages⁽⁴⁴⁾.

Moreover, to attain successful antegrade ejaculation, placement of seminal colliculus in the posterior urethra is necessary. Moreover, since BNR is known to be important for continence attainment, it has also been shown to play an important role in fertility⁴⁸. Several studies have demonstrated different factors influencing outcomes in genitourinary surgery. One study noted a significant association between the number of BNR attempts and better sperm quality. At the same time, another emphasized the need for careful separation during epispadias repair to avoid harmful effects on fertility outcomes⁽²⁴⁾. Additionally, infections after surgery and lower zinc levels were found to affect fertility, highlighting the importance of managing post-surgery infections and regularly evaluating semen for microbiological tests^(24,48).

CONCLUSIONS

In conclusion, the reviewed literature underscores

the challenges of implementing a staged approach in healthcare centers with limited resources and staff. The wide range of continence rates for CPRE and MSRE techniques highlights the complexity of achieving consistent outcomes in urological repair post-BEEC reconstruction. Clear definitions of continence and long-term monitoring are essential to assess and predict continence status, especially in children accurately. Managing complications and conducting serial UDS on all males after BEEC reconstruction is critical for preventing UUT deterioration. The psychological and psychosocial aspects of patients undergoing reconstructive surgery, as well as the impact of these surgeries on fertility, emphasize the need for comprehensive support for patients and their families. Overall, the literature emphasizes the multifaceted nature of urological repair post-BEEC reconstruction and the importance of tailored care and ongoing evaluation to achieve optimal patient outcomes.

CONFLICT OF INTEREST

The authors have no competing interests to declare relevant to this article's content.

AUTHORS' CONTRIBUTIONS

PT, AMK: conception of the study, project administration, development and supervision, critical review, data collection, investigation, methodology, critical review, manuscript drafting, and editing.

DATA AVAILABILITY

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

REFERENCES

1. Gearhart JP, Mathews R. Exstrophy-epispadias complex. *Campbell-Walsh Urology*. 2007;9:3547-3550.
2. Bujons A, Lopategui DM, Rodríguez N, Centeno C, Caffaratti J, Villavicencio H. Quality of life in female patients with bladder exstrophy-epispadias complex: long-term follow-up. *J Pediatr Urol*. 2016;12:210-e1.
3. Halachmi S, Farhat W, Konen O, et al. Pelvic floor magnetic resonance imaging after neonatal single stage reconstruction in male patients with classic bladder exstrophy. *J Urol*. 2003;170:1505-1509.
4. Stec AA, Pannu HK, Tadros YE, Sponseller PD, Fishman EK, Gearhart JP. Pelvic floor anatomy in classic bladder exstrophy using 3-dimensional computerized tomography: initial insights. *J Urol*. 2001;166:1444-1449.
5. Fuchs J, Glüer S, Mildenerberger H. One-stage reconstruction of bladder exstrophy. *European journal of pediatric surgery*. 1996;6:212-215.
6. Khemchandani SI. The long-term outcomes after staged repair of exstrophy-epispadias complex. *J Indian Assoc Pediatr Surg*. 2016;21:158-163.
7. Ebert A, Scheuering S, Schott G, Roesch WH. Psychosocial and psychosexual development in childhood and adolescence within the exstrophy-epispadias complex. *J Urol*.

- 2005;174:1094-1098.
8. Lowentritt BH, Van Zijl PS, Frimberger D, Baird A, Lakshmanan Y, Gearhart JP. Variants of the exstrophy complex: a single institution experience. *J Urol.* 2005;173:1732-1737.
 9. Cervellione RM, Mantovani A, Gearhart J, et al. Prospective study on the incidence of bladder/cloacal exstrophy and epispadias in Europe. *J Pediatr Urol.* 2015;11:337-e1.
 10. Zaman MH, Young EE, Maruf M, et al. Practice patterns in classic bladder exstrophy: A global perspective. *J Pediatr Urol.* 2020;16:425-432.
 11. Morrill CC, Haffar A, Harris TGW, Crigger C, Gearhart JP. Current management of classic bladder exstrophy in the modern era. *African Journal of Urology.* 2023;29:27.
 12. Ebert AK, Falkert A, Germer U, Rösch WH. Biometry of the pubovisceral muscle and levator hiatus assessed by three-dimensional ultrasound in females with bladder exstrophy-epispadias complex after functional reconstruction. *Ultrasound in Obstetrics and Gynecology.* 2009;34:98-103.
 13. Ait-Ameur A, Wakim A, Dubouset J, Kalifa G, Adamsbaum C. The AP diameter of the pelvis: a new criterion for continence in the exstrophy complex? *Pediatr Radiol.* 2001;31:640-645.
 14. Purves JT, Gearhart JP. The bladder exstrophy-epispadias-cloacal exstrophy complex. In: *Pediatric Urology: Expert Consult.* Elsevier; 2009:386-415.
 15. Woodhouse CRJ, Hirsch R. The anatomy and reconstruction of the adult female genitalia in classical exstrophy. *Br J Urol.* 1997;79:618-622.
 16. Stec AA, Pannu HK, Tadros YE, Sponseller PD, Fishman EK, Gearhart JP. Pelvic floor anatomy in classic bladder exstrophy using 3-dimensional computerized tomography: initial insights. *J Urol.* 2001;166:1444-1449.
 17. Stec AA, Pannu HK, Tadros YE, et al. Evaluation of the bony pelvis in classic bladder exstrophy by using 3D-CT: further insights. *Urology.* 2001;58:1030-1035.
 18. Jeffs RD. Functional closure of bladder exstrophy. *Birth Defects Orig Artic Ser.* 1977;13:171-173.
 19. Grady RW, Mitchell ME. Newborn exstrophy closure and epispadias repair. *World J Urol.* 1998;16:200-204.
 20. Lattimer JK, Dean AL, Dougherty LJ, Ju D, Ryder C, Uson A. Functional closure of the bladder in children with exstrophy: a report of twenty-eight cases. *J Urol.* 1960;83:647-655.
 21. Grady RW, Mitchell ME. Complete primary repair of exstrophy. *J Urol.* 1999;162:1415-1420.
 22. Grady RW, Mitchell ME. Complete primary repair of exstrophy: surgical technique. *Urologic Clinics of North America.* 2000;27:569-578.
 23. Inouye BM, Purves JT, Routh JC, et al. How to close classic bladder exstrophy: are subspecialty training and technique important? *J Pediatr Urol.* 2018;14:426-e1.
 24. 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.* 2010;6:6-10.
 25. Kasprenski M, Benz K, Maruf M, Jayman J, Di Carlo H, Gearhart J. Modern management of the failed bladder exstrophy closure: a 50-yr experience. *Eur Urol Focus.* 2020;6:383-389.
 26. SÜRER I, BAKER LA, JEFFS RD, GEARHART JP. Combined bladder neck reconstruction and epispadias repair for exstrophy-epispadias complex. *J Urol.* 2001;165:2425-2427.
 27. Gearhart JP, Mathews R. Penile reconstruction combined with bladder closure in the management of classic bladder exstrophy: illustration of technique. *Urology.* 2000;55:764-770.
 28. Gearhart JP, Baird A, Nelson CP. Results of bladder neck reconstruction after newborn complete primary repair of exstrophy. *J Urol.* 2007;178:1619-1622.
 29. Kanabolo D, Cain M, Brown M, et al. Long term renal outcome and risk of elevated blood pressure in children undergoing complete primary repair of bladder exstrophy (CPRE). *J Pediatr Urol.* 2023;19:370-e1.
 30. Kajbafzadeh AM, Sabetkish S, Sabetkish N. Ureteric-urethral engraftment as a new surgical technique for management of incontinence in bladder exstrophy complex: A retrospective cohort. *International Journal of Surgery.* 2017;46:158-163.
 31. Alsowayan O, Capolicchio JP, Jednak R, El-Sherbiny M. Long-term functional outcomes after bladder exstrophy repair: A single, low-volume centre experience. *Canadian Urological Association Journal.* 2016;10:E94.
 32. Giron AM, Mello MF, Carvalho PA, Moscardi PRM, Lopes RI, Srougi M. One-staged reconstruction of bladder exstrophy in male patients: long-term follow-up outcomes. *International braz j urol.* 2017;43:155-162.
 33. Peppas DS, Tchetchgen MB, Lee BR, Jeffs RD, Gearhart JP. A quantitative histological analysis of the bladder in classical bladder exstrophy in various stages of reconstruction utilizing color morphometry. *The Exstrophy—Epispadias Complex: Research Concepts and Clinical Applications.* Published online 1999:41-47.
 34. Novak TE, Costello JP, Orosco R, Sponseller PD, Mack E, Gearhart JP. Failed exstrophy closure: management and outcome. *J Pediatr Urol.* 2010;6:381-384.
 35. Husmann DA, McLorie GA, Churchill BM. Closure of the exstrophic bladder: an evaluation of the factors leading to its success and its importance on urinary continence. *J Urol.* 1989;142:522-524.
 36. Ellison JS, Ahn J, Shnorhavorian M, Grady R, Merguerian PA. Long-term fate of the upper tracts following complete primary repair of bladder exstrophy. *J Pediatr Urol.*

- 2017;13:394-e1.
37. Ebert AK, Zwink N, Reutter HM, et al. Treatment strategies and outcome of the exstrophy–epispadias complex in germany: data from the german CURE-Net. *Front Pediatr.* 2020;8:174.
 38. Hammouda HM, Kotb H. Complete primary repair of bladder exstrophy: initial experience with 33 cases. *J Urol.* 2004;172:1441-1444.
 39. Sabetkish S, Sabetkish N, Eftekhazadeh S, Kajbafzadeh AM. Single-staged male bladder exstrophy–epispadias complex reconstruction with pubic bone adaptation without osteotomy: 15-year single-center experience. *Int Urol Nephrol.* 2021;53:191-198.
 40. Joshi RS, Eftekhazadeh S, Shukla AR, et al. Kidney function outcomes in patients after complete primary repair of bladder exstrophy and penopubic epispadias: Results from the international bladder exstrophy consortium. *J Pediatr Urol.* 2023;19:34-e1.
 41. Handa N, Bowen DK, Guo J, Chu DI, Kielb SJ. Long-term kidney outcomes in exstrophy-epispadias complex: how patients present as adults. *Urology.* 2021;154:333-337.
 42. Haffar A, Hirsch AM, Crigger CB, et al. Multi-staged vs single-staged pelvic osteotomy in the modern treatment of cloacal exstrophy: bridging the gap. *J Pediatr Surg.* 2023;58:2308-2312.
 43. 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.* 2010;6:6-10.
 44. Borer JG, Gargollo PC, Kinnamon DD, et al. Bladder growth and development after complete primary repair of bladder exstrophy in the newborn with comparison to staged approach. *J Urol.* 2005;174:1553-1558.
 45. Borer JG, Gargollo PC, Hendren WH, et al. Early outcome following complete primary repair of bladder exstrophy in the newborn. *J Urol.* 2005;174:1674-1679.
 46. Chua ME, Ming JM, Fernandez N, et al. Modified staged repair of bladder exstrophy: a strategy to prevent penile ischemia while maintaining advantage of the complete primary repair of bladder exstrophy. *J Pediatr Urol.* 2019;15:63-e1.
 47. Caione P, Zavaglia D, Capozza N. Pelvic floor reconstruction in female exstrophic complex patients: different results from males? *Eur Urol.* 2007;52:1777-1783.
 48. Ebert AK, Bals-Pratsch M, Seifert B, Reutter H, Rösch WH. Genital and reproductive function in males after functional reconstruction of the exstrophy-epispadias complex—long-term results. *Urology.* 2008;72:566-569.
 49. Inouye BM, Massanyi EZ, Di Carlo H, Shah BB, Gearhart JP. Modern management of bladder exstrophy repair. *Curr Urol Rep.* 2013;14:359-365.
 50. Bueno-Jiménez A, Serradilla J, Nava B, et al. Preliminary results of complete delayed primary bladder exstrophy reconstruction in male patients. *Cir Pediatr.* 2020;33:75-78.
 51. Hammouda HM, Shahat AA, Oyoun NA, Safwat AS, Elderwy AA, Elgammal MA. Long term evaluation of continence after complete primary bladder exstrophy repair. *J Pediatr Urol.* 2023;19:696-e1.
 52. Baradaran N, Cervellione RM, Stec AA, Gearhart JP. Delayed primary repair of bladder exstrophy: ultimate effect on growth. *J Urol.* 2012;188:2336-2342.
 53. Cervellione RM, Fishwick J, Khan T. Routine delayed bladder exstrophy closure. In: 3rd International Bladder Exstrophy Symposium, Baltimore, Maryland. ; 2009.
 54. 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.* 2010;6:450-456.
 55. Dickson AP. The management of bladder exstrophy: the Manchester experience. *J Pediatr Surg.* 2014;49:244-250.
 56. Shultz WG. Plastic repair of exstrophy of bladder combined with bilateral osteotomy of ilia. *J Urol.* 1958;79:453-458.
 57. Wild AT, Sponseller PD, Stec AA, Gearhart JP. The role of osteotomy in surgical repair of bladder exstrophy. In: *Seminars in Pediatric Surgery.* Vol 20. Elsevier; 2011:71-78.
 58. Kajbafzadeh AM, Talab SS, Elmi A, Rad MV, Mazaheri T, Tanhaevash R. Use of biodegradable plates and screws for approximation of symphysis pubis in bladder exstrophy: applications and outcomes. *Urology.* 2011;77:1248-1253.
 59. Halachmi S, Farhat W, Konen O, et al. Pelvic floor magnetic resonance imaging after neonatal single stage reconstruction in male patients with classic bladder exstrophy. *J Urol.* 2003;170:1505-1509.
 60. Suson KD, Sponseller PD, Gearhart JP. Bony abnormalities in classic bladder exstrophy: the urologist’s perspective. *J Pediatr Urol.* 2013;9:112-122.
 61. Shah BB, Di Carlo H, Goldstein SD, et al. Initial bladder closure of the cloacal exstrophy complex: outcome related risk factors and keys to success. *J Pediatr Surg.* 2014;49:1036-1040.
 62. Haney NM, Crigger CB, Sholkapper T, et al. Pelvic osteotomy in cloacal exstrophy: A changing perspective. *J Pediatr Surg.* 2023;58:478-483.
 63. Shnorhavorian M, Song K, Zamilpa I, Wiater B, Mitchell MM, Grady RW. Spica casting compared to Bryant’s traction after complete primary repair of exstrophy: safe and effective in a longitudinal cohort study. *J Urol.* 2010;184:669-674.
 64. Sirisreetreerux P, Lue KM, Ingviya T, et al. Failed primary bladder exstrophy closure with osteotomy: multivariable analysis of a 25-year experience. *J Urol.* 2017;197:1138-1143.
 65. Meldrum KK, Baird AD, Gearhart JP. Pelvic and extremity immobilization after bladder

- extrophy closure: complications and impact on success. *Urology*. 2003;62:1109-1113.
66. Jani MM, Sponseller PD, Gearhart JP, Barrance PJ, Genda E, Chao EYS. The hip in adults with classic bladder exstrophy: a biomechanical analysis. *Journal of Pediatric Orthopaedics*. 2000;20:296-301.
 67. Mathews R, Gearhart JP, Bhatnagar R, Sponseller P. Staged pelvic closure of extreme pubic diastasis in the exstrophy-epispadias complex. *J Urol*. 2006;176:2196-2198.
 68. Inouye BM, Lue K, Abdelwahab M, et al. Newborn exstrophy closure without osteotomy: is there a role? *J Pediatr Urol*. 2016;12:51-e1.
 69. Silver RI, Sponseller PD, Gearhart JP. Staged closure of the pelvis in cloacal exstrophy: first description of a new approach. *J Urol*. 1999;161:263-266.
 70. CAPOLICCHIO G, MCLORIE GA, FARHAT W, MERGUERIAN PA, BÄGLI DJ, KHOURY AE. A population based analysis of continence outcomes and bladder exstrophy. *J Urol*. 2001;165:2418-2421.
 71. Lloyd JC, Spano SM, Ross SS, Wiener JS, Routh JC. How dry is dry? A review of definitions of continence in the contemporary exstrophy/epispadias literature. *J Urol*. 2012;188:1900-1904.
 72. Shnorhavorian M, Grady RW, Andersen A, Joyner BD, Mitchell ME. Long-term followup of complete primary repair of exstrophy: the Seattle experience. *J Urol*. 2008;180:1615-1620.
 73. Kajbafzadeh AM, Sabetkish S, Sabetkish N, Eftekhazadeh S, Daryabari SS. Insights and outcomes of single-staged repair of female bladder exstrophy-epispadias complex without osteotomy: 15 Years experience of a single institution. *J Pediatr Urol*. 2022;18:355-361.
 74. Woodhouse CRJ, North AC, Gearhart JP. Standing the test of time: long-term outcome of reconstruction of the exstrophy bladder. *World J Urol*. 2006;24:244-249.
 75. Sabetkish S, Kajbafzadeh AM. Bladder Herniation as an Auto-Augmentation Technique in Bladder Exstrophy: Initial Experience in Patients with Small Bladder Plate. *Urology*. 2020;139:151-155.
 76. Yonez MK, Atalan G, Karayigit MO, Alpman U. Use of fascia lata autograft for repair of urinary bladder defect in rabbits. *Acta Veterinaria Brno*. 2019;88:57-63.
 77. Husmann DA, Gearhart JP. Loss of the penile glans and/or corpora following primary repair of bladder exstrophy using the complete penile disassembly technique. *J Urol*. 2004;172:1696-1701.
 78. Braga LHP, Lorenzo AJ, Jreaz R, Bagli DJ, Salle JLP. Bilateral ureteral reimplantation at primary bladder exstrophy closure. *J Urol*. 2010;183:2337-2341.
 79. Kufner M, Gearhart JP, Mathews R. Impact of epispadias repair on bladder growth in boys with classic bladder exstrophy. *J Pediatr Urol*. 2010;6:578-581.
 80. Kouame BD, Kouame GSY, Sounkere M, et al. Aesthetic, urological, orthopaedic and functional outcomes in complex bladder exstrophy-epispadias's management. *African Journal of Paediatric Surgery*. 2015;12:56-60.
 81. Surer I, Baker LA, Jeffs RD, Gearhart JP. The modified Cantwell-Ransley repair for exstrophy and epispadias: 10-year experience. *J Urol*. 2000;164:1040-1043.
 82. Mathews R, Hubbard JS, Gearhart JP. Ureteral reimplantation before bladder neck plasty in the reconstruction of bladder exstrophy: indications and outcomes. *Urology*. 2003;61:820-824.
 83. Salle JLP. Commentary to "Penile ischemic injury in the exstrophy/epispadias spectrum: New insights and possible mechanisms." *J Pediatr Urol*. 2010;6:457-458.
 84. Hernandez DJ, Purves T, Gearhart JP. Complications of surgical reconstruction of the exstrophy-epispadias complex. *J Pediatr Urol*. 2008;4:460-466.
 85. Kanabolo D, Cain M, Brown M, et al. Long term renal outcome and risk of elevated blood pressure in children undergoing complete primary repair of bladder exstrophy (CPRE). *J Pediatr Urol*. 2023;19:370-e1.
 86. Giron AM, Mello MF, Berjeaut RH, et al. Single-stage abdominoplasty using groin flaps without Osteotomies: management of exstrophy-epispadias complex. *Urology*. 2018;120:266.
 87. Arab HO, Helmy TE, Abdelhalim A, Soltan M, Dawaba ME, Hafez AT. Complete primary repair of bladder exstrophy: critical analysis of the long-term outcome. *Urology*. 2018;117:131-136.
 88. Kureel SN, Gupta A, Kumar S, Singh V, Dalela D. A novel midline scroto-perineal approach facilitating innervation preserving sphincteroplasty and radical corporal detachment for reconstruction of exstrophy-epispadias. *Urology*. 2011;78:668-674.
 89. Youssif M, Badawy H, Saad A, Hanno A, Mokhless I. Single-stage repair of bladder exstrophy in older children and children with failed previous repair. *J Pediatr Urol*. 2007;3:391-394.
 90. Bharati K, Ashish J, Kumar T, Paras K. Anatomical repair of exstrophy bladder. *Pediatr Surg Int*. 2004;20:455-459.
 91. Riccabona M, Lusuuardi L, Beckers G, Koen M. Blasenekstrophie-Epispadiekomplex: Management und präliminare Ergebnisse. *Aktuelle Urol*. 2003;34:402-406.
 92. Montagnani CA. Functional reconstruction of exstrophied bladder. Timing and technique. Follow-up of 39 cases. *Zeitschrift für Kinderchirurgie*. 1988;43:322-330.
 93. Sack BS, Kryger J V, Mitchell ME, Durkee CT, Lyon R, Groth TW. Clinical pathway for early discharge after complete primary repair of exstrophy and epispadias by using a spica cast. *J Pediatr Urol*. 2015;11:212-e1.