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Bladder capacity as a predictor of voided continence after failed exstrophy closure☆

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Abstract *Objective:* To evaluate potential predictors of voided continence among bladder exstrophy patients with a history of a failed closure.
Patients and methods: The authors reviewed all patients who underwent a bladder neck reconstruction (BNR) with a history of one or more failed exstrophy closures between 1979 and 2007. The following data were collected for each patient: number of failures, site of surgery, mode of failure, presence of osteotomy, bladder capacity, need for additional procedures, and continence status.
Results: Among patients who underwent successful reclosure following one or more failed closures, 52 patients underwent BNR, and 24 (46%) were continent at last follow-up. Bladder capacity was the only variable predictive of voided continence. The median bladder capacity at the time of BNR differed between those who achieved continence (100 mL) and those who did not (65 mL) ($p = 0.005$). ROC analysis showed an optimal pre-BNR bladder capacity cutoff for predicting future BNR success of between 80 and 100 mL.
Conclusion: As previously shown in patients with successful primary closure of exstrophy, these data suggest that bladder capacity also has predictive value in the success of BNR after failed exstrophy closure.

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Introduction

Regardless of which type of primary repair is used, successful closure of bladder exstrophy is a critical determinant of long-term urinary continence. When applying the techniques of the modern staged repair of exstrophy, bladder neck reconstruction (BNR) results in voided urinary continence in 70–75% of patients after successful primary closure [1,2]. Children with one or more failed closures represent an extremely challenging subset of patients with poorer outcomes. The consequences of failed initial closure include increased collagen and scar formation [3,4], decreased bladder growth [5], decreased capacity [6], and increased rates of urinary incontinence [7]. Dryness can be achieved in patients with failed initial closure, but often at the expense of intermittent urethral catheterization or continent urinary diversion [8].

Voided continence may be achieved in some patients by means of BNR. Determining which children are candidates for BNR can be difficult. Among children who have undergone successful primary closure with the modern staged repair of exstrophy, capacity represents the best way to determine which bladders are suitable for repair [9]. Despite this, a significant number of children who undergo BNR after failed closure remain incontinent and require further major surgical procedures to attain dryness. The authors aimed to identify variables that can reliably predict the success of BNR following prior failed exstrophy closure.

Materials and methods

After approval by the institutional review board, all patients with classical bladder exstrophy born between 1979 and 2007 who underwent a BNR with a history of one or more failed closures were identified from an institutionally approved weekly updated exstrophy database. Criteria for inclusion were diagnosis of classical bladder exstrophy, a history of one or more failed closures, and a BNR performed with the purpose of achieving voided continence. At the authors' institution, all patients underwent a Modified Young–Dees–Leadbetter BNR [10]. Patients with cloacal exstrophy, exstrophy variants, continence procedures (i.e. augmentation cystoplasty, artificial urinary sphincter, etc.) performed prior to BNR, or a BNR performed in conjunction with another continence procedure were excluded from the analysis. The medical records of all patients were retrospectively reviewed for the following information: gender, age at each surgery, duration of time between surgeries, site of surgery, number of failures, mode of failure, whether or not an osteotomy was performed with initial and successful reclosures, bladder capacity at the time of BNR, and continence status at last follow-up. Only patients with a minimum follow-up of 6 months were included in this study.

At our institution, bladder capacity was obtained prior to BNR by gravity cystogram under anesthesia by instillation of normal saline at 30 cm of water pressure into the bladder using a catheter with an overinflated balloon to prevent leakage. All patients undergo a plain film cystogram when the bladder is determined to be at maximum capacity. If vesicoureteral reflux is demonstrated on cystogram, 1 mL for each grade of reflux is subtracted from the total capacity (i.e. 6 mL subtracted in patients with bilateral grade 3 reflux). If reflux was noted to be dilating or high grade, a second radiograph is performed after the bladder is drained. No patient in this study had evidence of upper tract obstruction.

Continence was defined as volitional voiding through the urethra, night-time dryness, and a >3-h interval of dryness during the day. At the time of follow-up, patients were evaluated for continence and length of dry interval.

Subjects were placed into one of two groups for comparison. Based on data from last follow-up, patients either had a successful BNR (voiding and continent) or an unsuccessful BNR (incontinent, requires intermittent urethral catheterization, or underwent subsequent continent urinary diversion). Univariate analyses of categorical and continuous variables were obtained by the Fisher exact test and the Student t test, respectively. Multivariate logistic regression analysis was also performed. Sensitivities and specificities were calculated for statistically relevant predictors of BNR success found through variate analysis and the values were plotted on a receiver operating characteristics (ROC) curve. All statistical analyses were performed with Microsoft Excel 2007 and Stata IC 12. A p value < 0.05 was considered statistically significant.

Results

A total of 52 patients (44 male/8 female) with a history of failed primary closure who underwent a BNR with intention of voided urethral continence were identified and were included in the analysis. Follow-up data were available on all 52 patients with a median follow-up of 13 years (range 6 months–26 years) after time of BNR. Forty-five (87%) were referred after one or more failed primary closures, and seven (13%) represented failed primary closures from the authors' institution.

The median age at the time of initial failed closure was 2 days (range 0 days–12 months). Prior to successful reclosure, 39 (75%) patients had one, 11 (21%) patients had two, and two (4%) patients had three prior failed closures. Mode of initial failure included dehiscence in 28 (54%) and prolapse in 24 (46%) subjects. Eight patients (15%) at a median age of 3 days (range 0 days–4 months) had an osteotomy with initial failed closure. The remaining 44 (85%) were closed without osteotomy at a median age of 2 days (range 0 days–12 months). At the time of initial failed closure, 29 patients were immobilized with spica casts or mummy wraps, 15 patients were placed into modified Bryant's traction, four patients had external fixation with modified Buck's traction (after osteotomy), and four patients had no postoperative immobilization or traction.

All patients underwent successful reclosure at a median age of 17 months (range 7 days–70 months). Forty (77%) patients underwent successful reclosure at the authors' institution, and 12 (23%) patients underwent successful reclosure at an outside institution before they were referred. Median time between initial failed closure and successful reclosure was 16 months (range 6 days–59 months). Osteotomy was not performed in eight (15%) patients at the time of successful reclosure (5 of these

Table 1 Comparison of successful vs. unsuccessful bladder neck reconstruction (BNR).

	Successful BNR (n = 24)	Unsuccessful BNR (n = 28)	p value
No. male (%)	21 (88)	23 (82)	0.264[a]
Median age at (range)			
Initial closure in days	2 (0–49)	2 (0–368)	0.389[b]
Successful closure in months	16 (0–60)	18 (4–70)	0.979[b]
Epispadias repair in months	29 (6–60)	27 (4–173)	0.473[b]
BNR in months	59 (36–201)	58 (20–148)	0.948[b]
Median time between (range)			
Initial and successful closure in months	15 (0–59)	17 (3–57)	0.901[b]
Successful closure and BNR in months	36 (12–153)	38 (0–129)	0.931[b]
Epispadias repair[c] and BNR in months	33 (8–157)	35 (11–76)	0.686[b]
Surgery at outside institution (%)			
Initial closure	20 (83)	25 (89)	0.260[a]
Successful closure	5 (21)	7 (25)	0.244[a]
BNR	2 (8)	9 (32)	0.208[a]
No. of prior failed closures (%)			
One	18 (75)	21 (75)	0.251[a]
Two	4 (17)	7 (25)	0.208[a]
Three	2 (8)	0 (0)	0.208[a]
Mode of failure (%)			
Prolapse	9 (37)	15 (54)	0.115[a]
Dehiscence	15 (63)	13 (46)	0.115[a]
No. with osteotomy at (%)			
Initial closure	6 (25)	2 (7)	0.068[a]
Successful closure	18 (75)	26 (93)	0.068[a]
Median bladder capacity (range)	100 (60–180)	65 (35–165)	0.005[b]

[a] Fisher exact test.
[b] Student t test.
[c] Only includes patients that had epispadias repair prior to the time of BNR.

patients were closed at outside institutions). Among those who underwent osteotomy at the time of successful closure, 22 patients were immobilized with external fixation and placed into modified Buck's traction, 19 were immobilized with Bryant's traction, and three were placed into a spica cast or mummy wrap. Among those who were closed without osteotomy, four were placed into a spica casts or mummy wrap, three had no postoperative immobilization or traction, and data regarding immobilization were unknown in one patient.

Epispadias repair was performed in 44 (100%) of the 44 male patients at a median age of 28 months (range 4–173 months). Epispadias repair occurred prior to the time of BNR in 39 (89%) patients at a median of 35 months (range 8–189 months) prior to BNR. Five (11%) patients underwent epispadias repair at the time of or after BNR at median time of 1 month (range 0–115 months) between procedures.

All patients underwent BNR at a median age of 58 months (range 20–201 months). Forty-one patients (79%) underwent BNR at the authors' institution, and 11 (21%) had a BNR at an outside institution prior to referral. Median time between successful reclosure and BNR was 36 months (range 0–153 months). Median bladder capacity at the time of BNR was 90 mL (range 35–180 mL). At last follow-up, 24 (46%) patients were continent and voiding through the urethra, three (6%) required intermittent urethral catheterization, 17 (33%) underwent continent urinary diversion, and eight (15%) were incontinent and awaiting a definitive continence procedure. Thus, 24 patients had a successful BNR, and 34 (54%) patients had an unsuccessful BNR.

All patients were evaluated with renal ultrasonography following BNR. Two patients (1 male and 1 female) who underwent BNR at an outside institution developed worsening hydronephrosis secondary to elevated storage pressures and ultimately underwent continent urinary diversion with augmentation cystoplasty. Bladder capacities at the time of BNR were 50 and 60 mL. The remaining 50 patients had no evidence of hydronephrosis or upper tract changes on postoperative ultrasonography.

Table 1 summarizes and compares the demographical and clinical characteristics of patients with successful and unsuccessful BNR. Gender, age of surgery, site of surgery, number of prior failed closures, mode of failure, and presence of osteotomy were not significantly associated with success of BNR on univariate analysis (Table 1) or multivariate analysis (Table 2). Bladder capacity at the time of BNR was the only variable associated with success of BNR and found to be statistically significant on both univariate (p = 0.005) and multivariate analyses (p = 0.042).

Fig. 1 shows a ROC curve with varying preoperative bladder capacity thresholds for which BNR success can be predicted. Based on this curve, all patients who became continent had a bladder capacity of at least 60 mL (true positive 100%; false positive 60%). Similarly, all patients who were incontinent at last follow-up had capacity of under 170 mL (true positive 19%; false positive 0%).

Table 2 Multivariate analysis.

	Coefficient	95% CI	*p* value
Gender	4.64	0.05–112.63	0.664
Age at BNR	0.18	0.54–1.26	0.387
Site of BNR surgery	2.46	0.13–25.67	0.658
No. of prior failures	2.10	0.40–13.59	0.343
Mode of failure	2.35	0.54–14.44	0.544
Osteotomy at initial closure	1.93	0.17–16.08	0.656
Bladder capacity	0.01	1.00–1.06	0.042

BNR = bladder neck reconstruction.

Discussion

In addition to preservation of renal function, voided continence is a primary goal of bladder exstrophy repair. Children with failed exstrophy closures have a lower rate of bladder growth and smaller capacity than children with successful primary closures [6]. Furthermore, the likelihood of voided continence is significantly less among children with failed primary closures [4,5]. Failure of the bladder to reach an adequate capacity secondary to failed primary closure may preclude the child from undergoing BNR and ultimate voided continence. Among patients with failed primary closure that require reclosure(s), the rate of voided continence after BNR is substantially lower than children who have a successful primary closure. Novak et al. [7] revealed that only 18% of 122 patients with a history of failed closure achieved continence by way of BNR. The remaining patients were incontinent or underwent continent urinary diversion. The study presented here within aimed to examine only patients who underwent BNR, including patients who ultimately underwent continent urinary diversion. In this series, only 46% of patients who were felt to be a candidate for BNR achieved voided continence. These results may lead some pediatric urologists to abandon BNR altogether in children with a history of failed primary closure. However, our data also suggest that a successful outcome can be achieved in select patients with adequate bladder capacity.

Among patients who undergo successful primary closure, bladder capacity remains a useful tool to determine which children are candidates for BNR. Several years ago, a threshold of 60 mL was used as the minimum capacity desired prior to performing a BNR in this population [11]. More recently, Chan et al. [2] have shown that children with a capacity of >85 mL have better outcomes than children with capacities <85 mL. As the modern staged repair of bladder exstrophy has evolved over time, children are undergoing continence procedures at older ages when they are motivated be dry and have larger capacities.

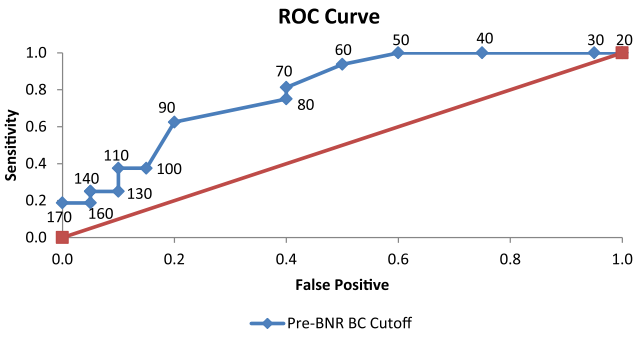

Figure 1 Bladder capacity receiver operating characteristic curve. BNR = bladder neck reconstruction.

Based on our ROC curve, the optimal bladder capacity threshold to predict voided continence following BNR in patients who have a history of failed primary closure should be between 80 and 100 mL. At a threshold of 80 mL, 81% of the patients who will benefit from a BNR will undergo the surgery. However at that threshold, 40% of the patients who will not benefit still undergo BNR and will likely require additional continence procedures in the future. At a threshold of 100 mL, only 20% of patients who will not benefit from BNR undergo this procedure and 37% who may have a successful outcome will not be considered for surgery. In trying to identify what is the optimal bladder capacity threshold among this subset of exstrophy patients, one must consider which is the lesser of two evils: patients who undergo BNR with unsuccessful outcomes or patients who undergo continent urinary diversion that may have benefited from a BNR. In deciding which patients are suitable candidates for BNR after failed primary closure, these findings should be shared with parents as they are counseled through the decision-making process.

The authors also believe that in addition to capacity, bladder function must also be assessed. Given that patients with bladder exstrophy may have bladders with poor detrusor activity, it is possible that BNR may cause upper urinary tract damage or lead to need for intermittent urethral catheterization among patients who have poorly functioning bladders [12]. Previous research has demonstrated that the majority of patients with bladder exstrophy that remain incontinent following BNR have either detrusor overactivity or underactivity [13]. Therefore, the authors have recently begun obtaining urodynamics in addition to cystogram under anesthesia in all patients who are being evaluated for possible BNR. Before this practice was adopted, urodynamics data were scant in most children included for analysis.

This study was limited by its retrospective design and selection bias. Only patients who were judged to be candidates for BNR were included in this study. The fact remains most patients with failed primary closures will never achieve a bladder capacity suitable for BNR. Inherent to most retrospective studies in rare conditions such as exstrophy, patient selection is a limitation in this study: patients with a failed primary bladder closure are often not considered for BNR and this may have skewed our interpretations. Furthermore, the characteristics of the bladder templates at birth are unknown. Urodynamic studies may have provided valuable information about the functional status of the bladder and probably elucidated other reasons for urinary incontinence, but until recently, it was not routinely performed at the author's institution on children with bladder exstrophy. The non-randomized selection of our patient population is another limitation of the study. Despite our best efforts to unify the definition of failure across our patient population, most of the cases were referrals from different institutions with different approaches to exstrophy

closure. Additionally, a minority of patients underwent measurement of bladder capacity and BNR at an outside institution. While no significant differences were found among patients who underwent procedures at an outside institution, it is possible techniques vary significantly between institutions and may have influenced the results.

To our knowledge, this is the first study to evaluate the success of BNR among patients with bladder exstrophy who have a history of one or more failed closures. Given the dire consequences of failed closure on the fate of urinary continence, it is not surprising that many pediatric urologists proceed straight to continent urinary diversion among patients in this subset. This study examined several variables that have been known to affect urinary continence among patients with bladder exstrophy, and the only variable found to be significant was absolute bladder capacity at the time of BNR.

The authors are hopeful that success of BNR in this population can improve with proper education of patients and their caregivers regarding potential outcomes along with careful evaluation to determine which patients are candidates for BNR. Determining which patients are candidates for BNR after failed primary closure is difficult. Given the results reported in this study, the authors recommend considering only patients with a capacity of at least 100 mL for a BNR following failed primary closure. Once a patient is judged to have an adequate bladder capacity and motivated to be dry, the authors also recommend using urodynamics to evaluate patients for adequate compliance and detrusor activity. Similarly, at the time of surgery, the bladder must also be carefully evaluated for collagen deposition. Only patients who are motivated to be dry, have a bladder capacity of at least 100 mL, and have a bladder that is compliant and functional should undergo BNR with the intention of voided continence. Other patients are best suited for continent urinary diversion and augmentation cystoplasty. It remains to be seen whether or not the success rate of BNR in this particularly challenging subset of exstrophy patients will improve as we gain further insight into which patients are the best candidates for BNR.

Conclusions

Failed primary closure of bladder exstrophy remains a challenge to the pediatric urologist. The expectation of voided continence is substantially lower in this group of patients. In select cases, BNR can be performed with reasonable success. This study demonstrates that absolute bladder capacity is currently the best way to evaluate which patients are candidates for BNR after failed closure and is the only variable predictive of successful outcome.

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Conflict of interest

None.

Ethical approval

Approval from our institution's internal review board was received for this manuscript.

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