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ORIGINAL ARTICLE

Vesicoureteral reflux increases the risk of urinary tract infection prior to corrective surgery in newborn males with anorectal malformation

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Abstract

Purpose The ideal colostomy type indicated for patients with anorectal malformation (ARM) is disputed. The aim of this study was to analyze the clinical factors associated with urinary tract infection (UTI) prior to corrective surgery in male ARM without perineal fistula having undergone diverting enterostomy.

Methods A retrospective review of patients diagnosed with ARM and surgically managed at our center from January 2011 to December 2019 was performed. Logistic regression was used to analyze the association between clinical factors and UTI.

Results Eighty boys with ARM without perineal fistula underwent diverting enterostomy and subsequent corrective surgery via laparoscopic-assisted anorectal pull-through. A sigmoid loop colostomy was most often performed (70 patients, 87.5%). Twenty-nine patients (36.3%) were diagnosed with vesicoureteral reflux (VUR), including 14 (48.3%) with febrile UTIs. Six patients had other concomitant genitourinary anomalies excluding VUR. Multivariate logistic regression analysis revealed the presence of VUR as the only independent factor associated with the occurrence of febrile UTI (OR 17.3, 95% CI 3.51–85.26, $p < 0.001$).

Conclusion The development of UTI in newborn males with ARM is associated with the presence of VUR, regardless of stoma type. Voiding cystourethrography should be considered in patients with ARM for early diagnosis of VUR and subsequent antibiotic prophylaxis.

Keywords Anorectal malformation · Loop colostomy · Divided colostomy · Vesicoureteral reflux · Urinary tract infection · Voiding cystourethrography

Introduction

Vesicoureteral reflux (VUR) is a common anomaly of the urinary tract in childhood, which increases the risk of febrile urinary tract infection (UTI) with subsequent renal scarring and dysfunction [1]. Anorectal malformation (ARM) has a high incidence of associated genitourinary anomalies such as VUR, with a reported incidence ranging from 20 to 47% [2, 3]. The standard screening protocol for associated anomalies in ARM patients includes genitourinary ultrasonography and voiding cystourethrography (VCUG) for the diagnosis of urologic anomalies. A recent study reported genitourinary anomalies including VUR as risk factors for UTI in children with ARM [4].

Diverting colostomy is the initial surgical procedure generally performed in an ARM newborn without perineal fistula. Divided colostomy was the type of colostomy recommended by Pena et al. intended to avoid stool passage to the distal limb leading to UTI or fecal impaction [5]. Before stoma takedown and definitive anorectal corrective surgery are performed at 2–3 months of age, overflow of feces to the distal pouch may theoretically result in bacterial overgrowth in the distal pouch and recurrent UTIs via the recto-urinary tract fistula [6]. In terms of the surgical technique, divided colostomy entails an invasive initial procedure and stoma takedown with the consequent risk of intra-abdominal adhesion [7]. However, a loop colostomy is easier to create and subsequently take down [8]. Recent studies including a meta-analysis reported the overall incidence of UTI after

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stoma formation ranged 4–42% and no significant difference in the incidence of UTI between loop and divided colostomy [7, 9].

The aim of this study was to analyze the clinical factors associated with UTI prior to corrective surgery in male ARM patients without perineal fistula treated with diverting enterostomy.

Materials and methods

Between January 2011 and December 2019, ARM in 225 newborns was surgically managed at Samsung Medical Center (Seoul, South Korea). The retrospective review included medical records of 127 newborn males and 98 newborn females. The analysis included 80 boys with ARM without perineal fistula who underwent diverting enterostomy as initial surgery. This study was approved by the Institutional Review Board at Samsung Medical Center (IRB 2020-03-106).

The perioperative management scheme for male ARM without perineal fistula is outlined in Fig. 1. When a newborn male is diagnosed with ARM, the patient is admitted to the neonatal intensive care unit (NICU). In the NICU, a full physical examination is performed by the pediatric surgeon to determine the type of ARM and set up a therapeutic plan. When no fistula opening is identified around the perineal skin, the newborn undergoes fecal diversion, via sigmoid loop colostomy. Further radiological work-up is conducted to identify concomitant congenital anomalies: echocardiography (done preoperatively), infantogram, VCUG, abdominal ultrasonography, spinal ultrasonography, and brain ultrasonography. A high-pressure contrast study through the distal loop of the colostomy is also done. The rectum is thoroughly irrigated through the distal opening of the colostomy to remove all residual meconium prior to discharge. The baby is discharged at 7–10 days postoperatively when full oral feeding is attained. Regular clinic visits are scheduled at 3- to 4-week intervals until the baby is admitted for corrective surgery via laparoscopic-assisted anorectal pull-through (LAARP) at 3 months of age. A contrast study via the distal loop of the colostomy is repeated on the day before LAARP. Cystoscopy is performed under general anesthesia at the time of LAARP to identify the precise location of the fistula.

LAARP was performed as corrective surgery in all patients based on the description by Georgeson et al. with minor modifications [10]. In all cases, stoma closure was performed with corrective surgery concurrently. This two-stage operation has the advantage of reducing the risks of additional operation/anesthesia and the overall hospitalization costs. Previous studies reported that the two-stage operation is feasible and safe [11, 12]. Details of the procedure have been described previously [12].

All statistical analyses were performed using SPSS software (version 25.0 for Windows, SPSS Inc., Chicago, IL, USA). Results are expressed as mean ± standard deviation for continuous data and as numbers with percentages for categorical data. Logistic univariate regression analysis was conducted to assess the effects of variables on the occurrence of UTI. Clinically significant factors and variables with p-values smaller than 0.05 in univariate analysis were further subjected to a multivariate logistic regression analysis with backward selection method to identify independent factors predicting UTI occurrence.

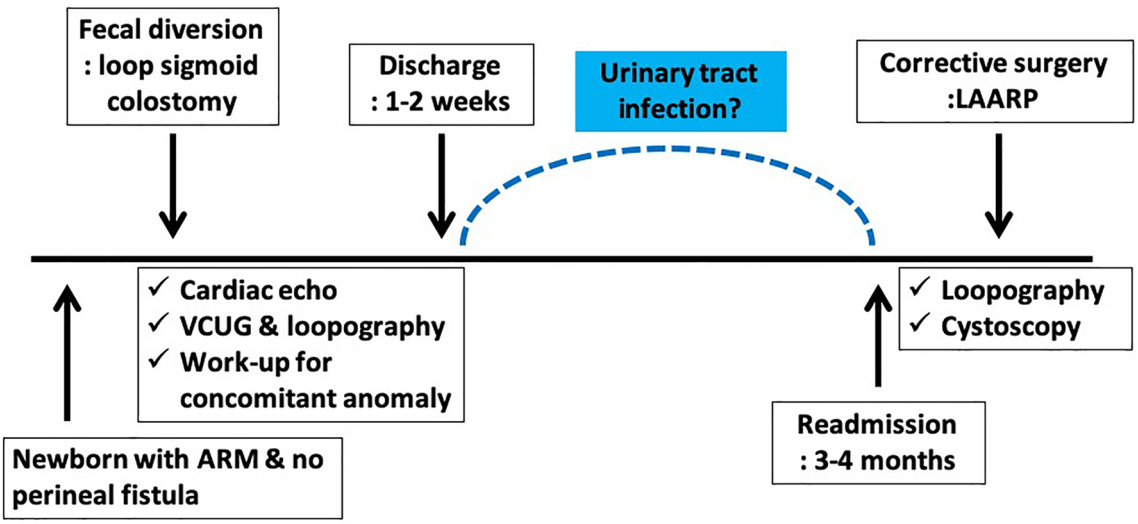

Fig. 1 Flowchart outlining the evaluation and treatment protocol for ARM patients without perineal fistula

Results

Eighty male newborns were included in the analysis. The mean gestational age was 38.1 weeks and the mean birth weight was 2912 g. The fistula type was rectovesical fistula in 11 cases, rectourethral fistula in 65 cases, and no fistula in 4 cases. All 80 patients underwent a VCUG, including 29 (36.3%) newborns diagnosed with VUR of varying degrees. Sixteen patients had concomitant genitourinary tract anomalies: hydronephrosis, renal dysplasia, single kidney, duplication of kidney, horseshoe kidney, and ectopic kidney. Among these 16 patients, six had genitourinary anomaly except VUR. Fifteen patients (18.8%) had spinal anomalies including tethered cord, sacrococcygeal deformity, spinal lipoma, caudal regression, spina bifida. Four patients confirmed to have no fistula all underwent loop sigmoid colostomy and had no VUR and UTI. The clinical characteristics of the patients are outlined in Table 1.

Diverting enterostomy was performed in all patients. A sigmoid loop colostomy was most often performed (70 patients, 87.5%). Of the 29 patients with VUR, UTI prophylaxis was carried out in 16 patients (55.2%), including eight patients with grade III or greater VUR. Clinically significant UTI was diagnosed in 14 patients when pyuria and fever requiring hospital admission for intravenous antibiotics were present. Eight of these 16 patients using UTI prophylaxis went on to develop febrile UTI (50%).

Table 1 Baseline characteristics

	$N=80$ (%)
Gestational age (weeks), mean ± SD[a]	38.1 ± 2.1
Birth weight (g), mean ± SD[a]	2912 ± 610
Fistula type	
Rectovesical fistula	11 (13.8)
Rectourethral fistula	65 (81.3)
No fistula	4 (5.0)
Vesicoureteral reflux	
No	51 (63.7)
Grade 1	4 (5.0)
Grade 2	10 (12.5)
Grade 3	9 (11.3)
Grade 4	4 (5.0)
Grade 5	2 (2.5)
Genitourinary anomalies[b]	
Present	6 (7.5)
Absent	74 (92.5)
Spinal anomalies	15 (18.8)

[a]SD standard deviation

[b]Excluding vesicoureteral reflux

All patients underwent LAARP with concomitant enterostomy closure for correction of ARM. The mean time from stoma formation to corrective surgery was 4.0 months and mean postoperative follow-up period was 44.7 months. Fistula tracts were visible in the contrast study via the distal enterostomy loop in 58 cases (72.5%). Fistula openings were found upon cystoscopic evaluation at the time of corrective surgery in 39 cases (48.8%). Twenty-nine patients obtained a result of urine culture before stoma closure, and almost all (28, 96.6%) underwent loop colostomy. Nineteen of these 29 (65.5%) showed bacteriuria and all were with a loop colostomy. Among 14 patients with bacteriuria and VUR, 7 (50%) had a febrile UTI; however, among five patients with bacteriuria without VUR, one patient who diagnosed with severe bilateral hydronephrosis (20%) had a febrile UTI. There were febrile UTI in seven patients after stoma closure/corrective surgery and they all had VUR postoperatively. Four of these 7 patients had UTI even before surgery and the other three were newly occurred patients. All three patients with newly occurred febrile UTI after surgery had urologic anomaly such as single kidney or dysplastic kidney (Table 2).

Univariate analysis showed that the presence of VUR, VUR grade ≥ III, and use of oral antibiotics prophylaxis were significantly associated with clinically significant UTI ($p < 0.05$). Multivariate analysis was carried out including these significant factors and other parameters associated with the occurrence of UTI. Presence of VUR was the only independent factor associated with the occurrence of clinically significant UTI (Table 3).

Discussion

VUR is a common urological anomaly in children, which increases the risk of developing febrile UTI and subsequent renal scarring and renal dysfunction [13]. The use of prophylactic antibiotics has been shown to be effective in reducing the number of children developing new or progressive renal damage, but not the frequency of recurrent febrile UTIs [14]. VUR has been reported in 20–47% of children with ARMs [2, 3]. The European consortium on anorectal malformations (ARM-NET) has recently published a clinical analysis of the representative dataset of European ARM patients [15]. The findings suggested that the majority of study patients were investigated for bladder anomalies or VUR on the basis of clinical symptoms instead of routine screening. Furthermore, ARM-NET recommended routine ultrasonography of the urinary tract and kidneys in every newborn with ARM; however, VCUG was included in case of specific conditions such as dilated upper urinary tracts. In addition, Sanchez et al. reported that the presence of genitourinary malformations as well as VUR were associated with a UTI in ARM

Table 2 Clinical outcomes of patients

	N = 80 (%)
Time from stoma to corrective surgery (months), mean ± SD[a]	4.0 ± 1.3
Postoperative follow-up period (months), mean ± SD[a]	44.7 ± 25.0
Enterostomy type	
Loop sigmoid colostomy	70 (87.5)
Divided sigmoid colostomy	6 (7.5)
Loop transverse colostomy	2 (2.5)
Loop ileostomy	2 (2.5)
UTI[b] prophylaxis (oral antibiotics)	
Yes	16 (20.0)
No	64 (80.0)
Clinically significant ("febrile") UTI[b]	
Yes	14 (17.5)
No	66 (82.5)
Febrile UTI[b] after stoma closure/repair surgery	7 (8.8)
Both before and after surgery	4
Newly occurred after surgery	3
Bacteriuria before stoma closure	
Yes	19 (23.8)
No	10 (12.5)
Urine culture not done	51 (63.8)
Visible fistula tract on contrast study[c]	
Yes	58 (72.5)
No	22 (27.5)
Visible fistula opening on cystoscopy[c]	
Yes	39 (48.8)
No	21 (26.3)
Cystoscopy not done	20 (25.0)

[a]SD, standard deviation

[b]UTI, urinary tract infection

[c]Performed at the time of corrective surgery

patients, thus suggesting the need for VCUG evaluation in all children diagnosed with ARM [16]. Similarly, multivariable logistic regression analysis revealed that the presence of VUR in patients with ARM was significantly associated with the development of UTI. Our finding also supports the importance of performing VCUG for the investigation of VUR in all children with ARM during initial hospitalization after birth. Finally, the prophylactic use of antibiotics in ARM patients with early diagnosed VUR may help prevent renal scarring and damage, as reported in previous studies. The American Urological Association (AUA) recommends antibiotic prophylaxis for children with grade III–V VUR even in the absence of UTI [1]. However, no formal recommendations for the management of febrile UTIs in children with ARM and VUR are established to date. Our hospital protocol provides prophylactic antibiotics (e.g., amoxicillin) for ARM patients manifesting VUR grade ≥ III or recurrent UTIs. In view of low prophylactic antibiotics use (55.2%) in our study, extended use of prophylactic antibiotics to all grades of VUR patients is worth consideration. In addition, even with the use of prophylactic antibiotics in patients with ARM and VUR, the incidence of febrile UTI was high (50%) in our study. Further study is needed to find out the reason for the high incidence of febrile UTI in patients with ARM and VUR who underwent stoma formation.

To alleviate intestinal obstruction in a newborn with ARM, diverting colostomy is often the initial surgical procedure performed. Traditionally, divided colostomy created at the junction of the descending and the sigmoid colon has been recommended [17]. Since the proximal stoma and distal mucous fistula are situated far apart, no downstream spillage can occur in this approach. In our center, we prefer sigmoid loop colostomy for our ARM newborns for its simplicity and minimal procedural time. The sigmoid loop colostomy is also more suited to our management protocol of concomitant colostomy takedown during the corrective surgery (LAARP), since a shorter distal limb does not increase the tension on the anastomosis between the rectum and neoanus. A common belief among pediatric surgeons is that spillage of fecal contents into the distal limb of a colostomy and into the urinary tract through the recto-urinary fistula can lead to the development of UTI [8]. However, our results suggest that the sigmoid loop colostomy does not increase the risk of UTI compared with other types of diverting enterostomy in ARM newborns, which is consistent with the findings of a recently published meta-analysis [7]. There were febrile UTI in seven patients after stoma closure/corrective surgery in our study. Nine out of 12 patients with preoperative VUR and UTI were successfully treated by VUR repair surgery (75%) after stoma closure/corrective surgery. The reason why the prevalence of febrile UTI appears to decrease after repair surgery is thought to be mainly due to surgical treatment of VUR. In ARM patients accompanied by VUR, the analysis for protective effect of divided stoma on the occurrence of UTI was not conducted due to a relatively small number of divided stoma in our study (26 vs. 3 cases). The revision from an already created loop colostomy to divided stoma is considered unnecessary, given the risk of additional anesthesia.

In a study by Liechty et al. the subgroup analysis of ARM patients with recto-urinary fistula was controlled for other risk factors for UTI [4]. The findings showed that the risk of UTI was independent of the stoma type and only genitourinary anomalies were significantly associated with UTI. Similarly, in our study, factors that may be related to an increased risk of fecal spillage into the urinary tract including visible fistula tract in the contrast study and the visible fistula opening upon cystoscopy were not associated with higher UTI risk. We believe that this finding may be attributed to the bacteria entering the urinary tract,

Table 3 Univariable and multivariable logistic regression analyses for risk of UTI

	Univariable analysis		Multivariable analysis	
	p value	95% CI	*p* value	OR (95% CI)
Premature	0.464	0.44–6.04	–	
Low birth weight	0.883	0.27–4.57	–	
Genitourinary system anomaly[a]	0.955	0.10–8.72	–	
Spinal anomaly	0.083	0.86–11.23	0.158	2.99 (0.65–13.65)
Older age at corrective surgery	0.593	0.53–1.44	–	
Rectovesical fistula (vs. rectourethral fistula)	0.089	0.83–13.66	0.296	2.45 (0.46–13.08)
Presence of VUR[b]	< 0.001	3.51–85.26	< 0.001	17.29 (3.51–85.26)
VUR[b] grade ≥ III	0.002	2.01–26.13	–	
Oral antibiotics prophylaxis	0.001	2.66–35.15	0.206	2.71 (0.58–12.71)
Sigmoid loop colostomy (vs. all other types)	0.276	0.10–1.95	–	
Bacteriuria before stoma closure	0.244	0.48–17.55	–	
Visible fistula on contrast study[c]	0.092	0.74–49.49	0.448	2.47 (0.24–25.57)
Visible fistula on cystoscopy[c]	0.421	0.43–7.53	–	

[a]Excluding vesicoureteral reflux

[b]VUR, vesicoureteral reflux

[c]Performed at the time of corrective surgery

which were washed away by the urine flow from the bladder to the urinary meatus without colonizing the upper urinary tract and leading to febrile UTI. In patients who had VUR or other genitourinary anomaly with urinary retention, these normal voiding mechanisms were impaired and presumably resulted in UTI. Some patients in our study obtained a result of urine culture before stoma closure. Association among stoma type, bacteriuria, VUR may be useful to understand the occurrence process of febrile UTI. Interestingly, about 70% of patients with a loop colostomy had bacteriuria; bacteriuria without VUR caused relatively low febrile UTI rate in one patient who diagnosed with severe bilateral hydronephrosis (20%).

This study has several limitations. First, it was a retrospective study. Thus, results might be biased because some variables could not be obtained from all study patients due to insufficient medical records. Second, the timing of important diagnostic tests such as VCUG, urinalysis, urine culture varied among patients during the time from formation to closure of stoma. Thus, different timing of diagnostic study may have affected the results. Another drawback of our study was that the number of patients with other types of stoma is relatively small, probably resulting in low statistical power. Since we have performed a laparoscopic anorectoplasty with stoma closure concurrently, a sigmoid loop colostomy was the preferred choice of stoma in our center. A sigmoid loop colostomy was easier to close and provided better operative view at the time of laparoscopic corrective surgery. Therefore, this preference has resulted in discrepancy in number of patients between two stoma groups.

Conclusion

The development of UTI in children with ARM is associated with the presence of VUR, regardless of stoma type. Thus, VCUG should be considered in all children with ARM for early diagnosis of VUR and subsequent prophylactic use of antibiotics. A sigmoid loop colostomy is easy to perform and represents a sufficient diverting enterostomy for LAARP as a corrective surgery.

Compliance with ethical standards

Conflict of Interest The authors have no conflicts of interest to disclose.

Ethical approval Ethical approval was waived by the Institutional Review Board at Samsung Medical Center in view of the retrospective nature of the study (IRB no. 2020-03-106).

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