available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Surgery in Motion

Long-term Follow-up of Detaenial Sigmoid Neobladder Reconstruction for Paediatric Patients with Bladder and Prostate Rhabdomyosarcoma: Technique and Results from a Single High-volume Centre

Peng Xu [a,1], *Chunxiao Chen* [a,1], *Binshen Chen* [a], *Enguang Bi* [a,b], *Wei Du* [a], *Ning Jiang* [a], *Zhe Liu* [a], *Hekui Lan* [c], *Manming Cao* [d], *Yazhen Liu* [a], *Jingwen Huang* [a], *Haiyan Shen* [a], *Cunrong Liu* [a], *Chunxiao Liu* [a,*], *Abai Xu* [a,*]

[a] *Department of Urology, Zhujiang Hospital, Southern Medical University, Guangzhou, China;* [b] *Department of Biochemistry and Molecular Biology, School of Basic Medical Science, Guangdong Provincial Key Laboratory of Single Cell Technology and Application, Southern Medical University, Guangzhou, China;* [c] *Department of Paediatrics, Zhujiang Hospital, Southern Medical University, Guangzhou, China;* [d] *Department of Oncology, Zhujiang Hospital, Southern Medical University, Guangzhou, China*

Article info

Article history:
Accepted August 14, 2022

Keywords:
Rhabdomyosarcoma
Paediatrics
Radical cystectomy
Neobladder

Abstract

Background: Rhabdomyosarcoma (RMS) is the most common paediatric soft-tissue sarcoma. Approximately 15–20% of RMS cases arise from the bladder and prostate (B/P). The optimal treatment strategy for B/P RMS remains unclear.
Objective: To retrospectively evaluate the applicability of our procedure performed to treat paediatric patients with B/P RMS.
Design, setting, and participants: This is a retrospective analysis from a single tertiary referral hospital. From August 2003 to March 2021, 62 children pathologically diagnosed with B/P RMS underwent radical cystectomy and orthotopic detaenial sigmoid neobladder reconstruction in our centre.
Surgical procedure: Surgical procedures included laparoscopic radical cystectomy and detaenial sigmoid neobladder reconstruction, which is demonstrated in the accompanying video.
Measurements: Demographic, clinical, and follow-up data were collected. Perioperative and long-term oncological and functional outcomes were reported. A logistic regression analysis was also performed.
Results and limitations: All surgeries, including three intracorporeal laparoscopic surgeries, were completed successfully. Of the 62 patients, 54 were alive without evidence of disease recurrence or metastasis at the last follow-up. Five of the 14 >12-yr-old boys reported that they experienced erections. Two female patients >12 yr old reported that

[1] These authors contributed equally to this work and are joint first authors.
* Corresponding authors. Department of Urology, Zhujiang Hospital, Southern Medical University, 253 Industrial Road, Haizhu District, Guangzhou, Guangdong, China. (Ch. Liu); Department of Urology, Zhujiang Hospital, Southern Medical University, 253 Industrial Road, Haizhu District, Guangzhou, Guangdong, China. Tel. +86 186 6562 6790; Fax: +86 20 616 432 56. (A. Xu).
E-mail addresses: liuchx888@163.com (C. Liu) lc96xab@163.com (A. Xu).

https://doi.org/10.1016/j.eururo.2022.08.015

they menstruated. However, this was a retrospective study conducted at a single centre with limited surgeon experience.

Conclusions: Our results confirmed the safety and feasibility of primary orthotopic sigmoid neobladder reconstruction after radical cystectomy for paediatric patients with B/P RMS. Good outcomes in terms of oncological control and functional recovery were achieved. The high histocompatibility and tissue adaptability of children are inspiring.

Patient summary: We describe our stepwise technique of radical cystectomy and detaenial sigmoid neobladder reconstruction for paediatric patients with bladder and prostate rhabdomyosarcoma. With this technique, we were able to achieve good functional recovery without compromising cancer control and significantly increasing complications.

1. Introduction

Rhabdomyosarcoma (RMS) accounts for 5% of all paediatric malignancies and is the most common paediatric soft-tissue sarcoma [1]. Approximately 15–20% of all RMS cases arise from the genitourinary tract, most commonly in the bladder and prostate (B/P) [2]. Multimodal therapy involving chemotherapy, extirpative surgery, and radiotherapy is commonly used in combination or sequentially [3–5]. The optimal treatment strategy remains unclear; however, extirpative surgery is considered to be an effective choice for tumour control, but postoperative functional outcomes vary [6].

By 2000, our centre had started performing orthotopic detaenial sigmoid neobladder reconstruction with good postoperative oncological and functional outcomes [7,8]. In 2003, we first applied this technique to a child with bladder RMS who had relapsed after chemotherapy. To date, we have successively treated 62 patients with neobladder surgery in our single centre. The study aim was to retrospectively evaluate the applicability of our procedure performed to treat paediatric patients with B/P RMS, and evaluate the 18-yr oncological and functional outcomes and prognostic factors.

2. Patients and methods

From August 2003 to March 2021, 62 children pathologically diagnosed with B/P RMS underwent open/laparoscopic radical cystectomy and orthotopic detaenial sigmoid neobladder reconstruction in our hospital (two patients underwent ureterocutaneostomy in other hospitals before admission). Patients were staged according to the Children's Oncology Group (COG; formerly the Intergroup Rhabdomyosarcoma Study Group) staging system [9]. Forty-seven patients came to our hospital because of recurrence or disease persistence after multimodal treatments. General information is shown in Table 1. This study was approved by the Medicine Institutional Review Board of Zhujiang Hospital of Southern Medical University, and informed consent was obtained from a parent or guardian on behalf of the child.

Table 1 – Preoperative characteristics

Variable	Results
Patients (*n*)	62
Median age at surgery (mo)	46.9 ± 32.7
Gender (male/female)	53/9
Preoperative therapy, *n* (%)	
Chemotherapy	61 (98.4)
Radiotherapy	18 (29.0)
Partial cystectomy	14 (22.6)
Cystectomy and ureterocutaneostomy	2 (3.2)
Tumour size (cm), *n* (%)	
≤5	41 (66.1)
>5	21 (33.9)
COG staging, *n* (%)	
Stage 2	40 (64.5)
Stage 3	22 (35.5)

COG = Children's Oncology Group.

2.1. Surgical procedure

The surgical procedure is similar to that of adults, as we reported previously [7,10]. A five-port transperitoneal approach in dorsal lithotomy with a steep Trendelenburg of 15–25° was used. Trocars were placed in a bow shape. Radical cystectomy started by performing a pelvic lymph node dissection. The peritoneum was incised laterally to the iliac artery. Organs in children are immature, but the corresponding anatomical landmarks are the same as those in adults. The field of dissection was the same as that used in standard lymph node dissection for bladder cancer [11]. The umbilical arteries on both sides were sealed and divided during dissection. The ureter was then identified and isolated to the ureterovesical junction. After clipping with Hem-o-lok, the ureter margin was sent for frozen inspection. The Douglas pouch was then incised to expose the vas deferens and seminal vesicles that were used as the landmark for dissection. Separate bluntly along the Denonvillier's fascia to the posterior plane of underdeveloped prostate. The fat tissue on the anterior rectal surface is usually inconspicuous in children. For girls, the vaginal-wall integrity is important for preventing postoperative vaginal fistula. Thermal energy was used sparingly for treating lateral ligaments to prevent nerve damage, and nerve sparing was attempted in all patients. Absorbable clips and scissors were used to treat the lateral ligaments down to the endopelvic fascia. The next step was exposure of the anterior layer, which can be achieved easily by incision of the umbilical ligaments. The Retzius space was expanded forward to the puboprostatic/pubovesical ligament and the endopelvic fascia, which was then incised to expose the urethra. A ligation-free technique was used to control the dorsal vascular complex in boys [12,13], and the periurethral tissue was dissociated until complete isolation of the membranous urethra. After removal of the catheter, a Hem-o-lok clip was used routinely to close the stump before separating the urethra. Frozen sections of the urethral stump were also taken to confirm that these had not been invaded. The specimen was placed in an Endo Catch bag (Metronics, Minneapolis, MN, USA) and brought out through a lower-abdomen

midline incision. Considering the child's pelvic structure, six intermittent stitches prethreaded at the lithotomy 10, 8, 12, 2, 4, and 6 o'clock positions under laparoscopic monitoring were prepared for enterourethral anastomosis. Typically, 2-0 Monocryl with a UR-6 needle was used.

For neobladder reconstruction, an estimated 15–20 cm segment of the sigmoid colon was isolated initially. A circular stapler was then used in an end-to-end manner to restore intestinal continuity. The isolated segment was irrigated repeatedly using a dilute iodine solution to eliminate impurities and arranged in a U-shape configuration without detubularisation. We used a semicircular blade to delineate the detaenial field by drawing an outline along the edge of the isolated sigmoid mesentery. The serosal layer was incised as deeply as the plane between the smooth muscle and the submucosal layer. A circular area with a 1.5-cm diameter at the centre and areas of 2 cm × 1 cm at both ends of the free intestinal canal were preserved for enterourethral and ureteroenteric anastomoses. The two colonic bands and the serosal muscle tissue between them were then detached from the submucosal layer and removed continuously using the semicircular blade. The instant capacity and leak tightness were assessed by filling with 200 ml iodine solution. Neither of the ureters needs to be transposed below the sigmoid mesocolon to the other side. After proper spatulation, two F6 single J stents were inserted upwards into the renal pelvis, and then each stent was passed through the neobladder and exteriorised. We used a modification of the Leadbetter and Clarke [14] method for complete ureteroenteric anastomosis with a 4-0 polyglactin suture. The ends of the intestinal canals on both sides were closed subsequently. Enterourethral anastomosis was carried out at the corresponding position of the previous prethreading. Last but not least, side peritoneum petals were reperitonealised, which might be conductive to restore normal physiological structure and reduce postoperative complications. The surgical process was detailed in Figures 1 and 2. A drainage tube was placed in the pelvis.

2.2. Follow-up

In the early stage, patients were hospitalised until the catheter and stents were all removed. In the past 5 yr, with the promotion of the concept of enhanced recovery after surgery, children normally resumed bowel function and started oral feeding 5 d after surgery. After the removal of the drainage tube, the patient can be discharged with the catheter and stents. Cystography was performed to determine whether the catheter and stents could be removed 1 mo after surgery.

The children received hospital follow-up every 3–6 mo in the first 2 yr. As these children received different degrees of chemoradiotherapy at a very young age, we paid more attention to bone development and corresponding growth problems. During the follow-up period, the children received enhanced computed tomography and cystoscopy to determine whether there was a tumour recurrence or urinary tract disorder. Day- and night-time urinary control was evaluated at each visit. Continence was defined as the use of zero or one safety pad, whereas incontinence was defined as the use of more than one wet pad. Complications, defined according to the standardised criteria recommended by the European Association of Urology guidelines, were reported and grouped in postoperative day periods of 0–30 and >30 d [15].

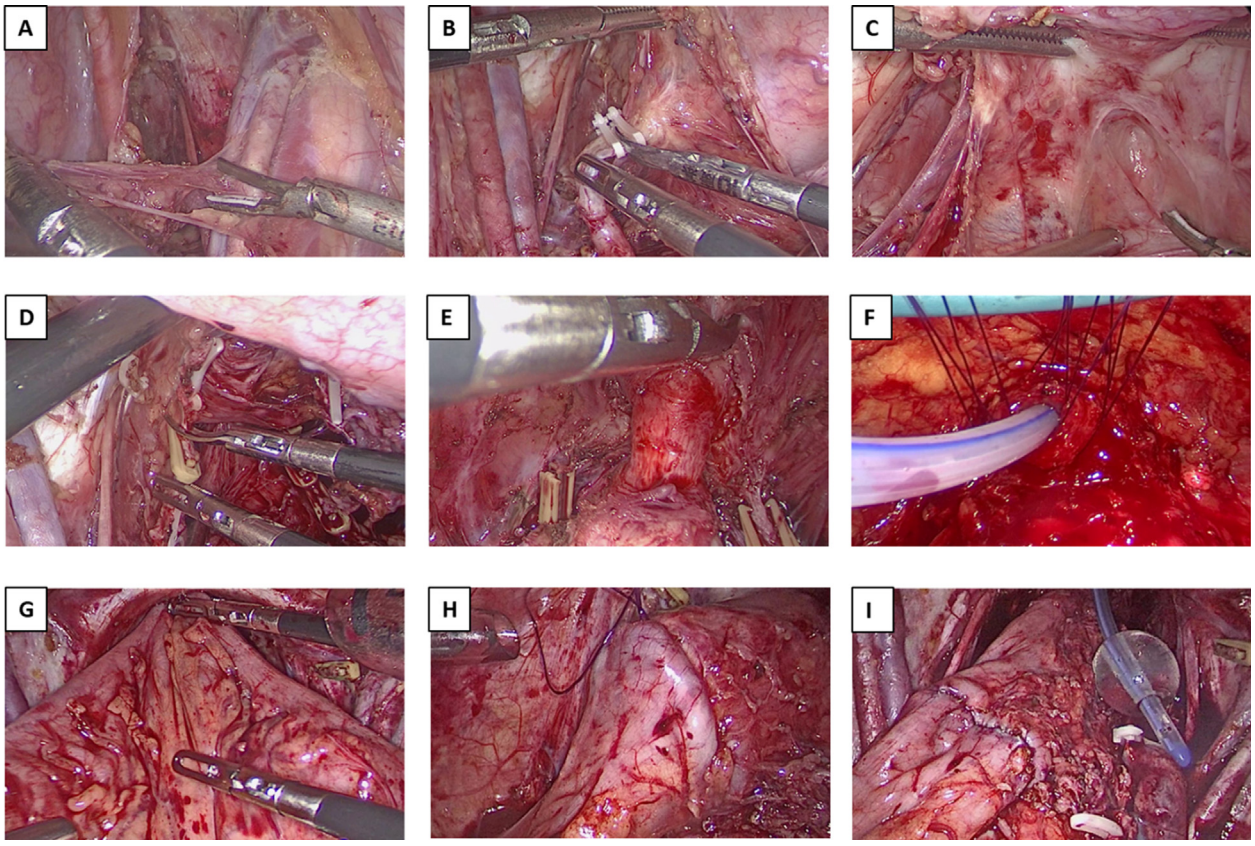

Fig. 1 – Step-by-step of radical cystoprostatectomy for B/P RMS. (A) Pelvic lymph node dissection; the field of dissection is the same as that of standard dissection for bladder cancer. (B) Ureteral disconnection; the margin is sent for frozen inspection. (C) Separation of the Denonvillier's fascia and establishment of the posterior plane. (D) Treatment of the lateral ligaments and establishment of the lateral plane. (E) Dissection of the apex of the prostate and urethra, and establishment of the anterior plane. (F) Prethreading under laparoscopic monitoring; six intermittent stitches are evenly distributed around the urethra. (G) Interception of a sigmoid colon and placement of a U-shaped neobladder. (H and I) Intestinal continuity was restored by a circular stapler. B/P RMS = bladder and prostate rhabdomyosarcoma.

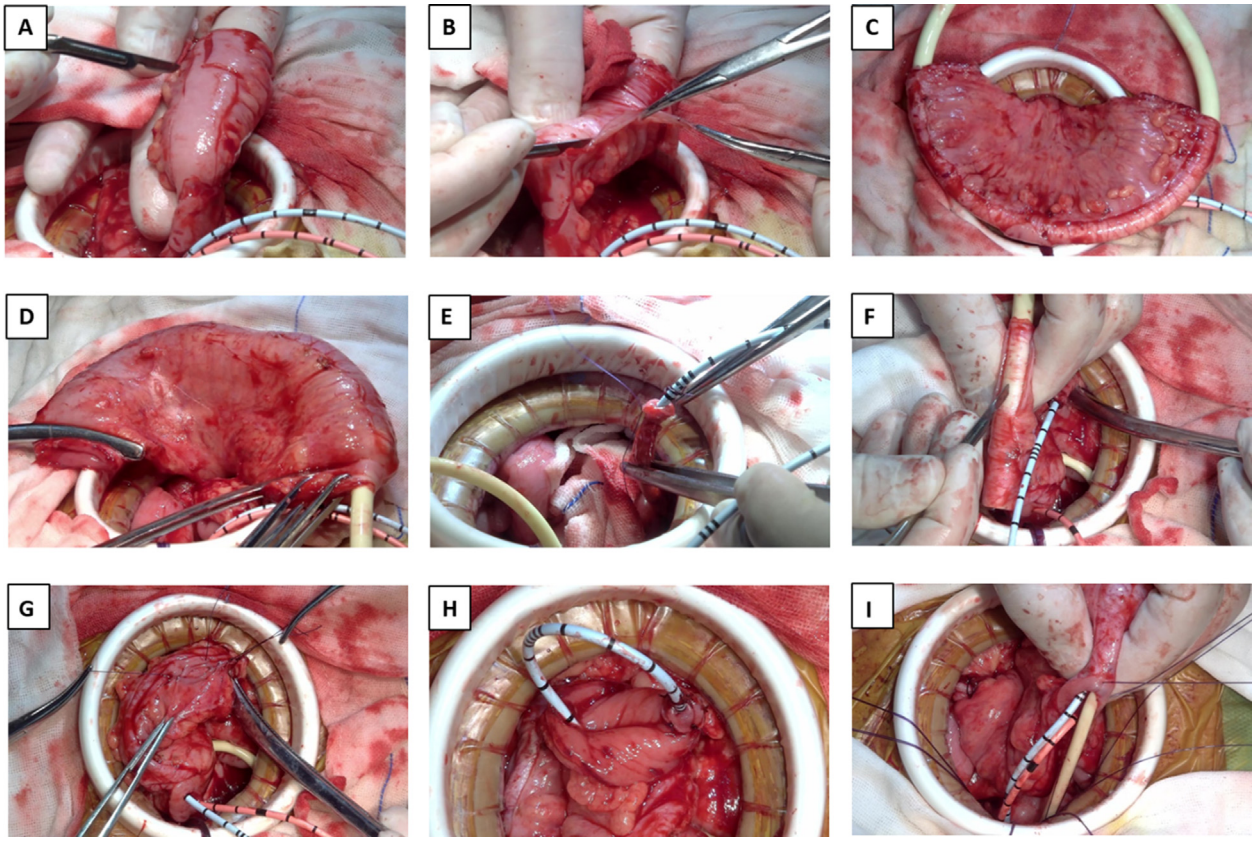

Fig. 2 – Step-by-step configuration of a detaenial sigmoid neobladder for children. (A) Delineate the detaenial field by using a semicircular blade to draw an outline along the edge of the isolated sigmoid mesentery. Areas at the centre and both ends of the free intestinal canal are preserved for enterourethral and ureteroenteric anastomoses. (B and C) Two colonic bands and serosal muscle tissue between them are detached from the submucosal layer and removed continuously. (D) After the stripping procedure, instant capacity and leak tightness are assessed. (E) After proper spatulation, a single J stent was inserted upwards into the renal pelvis and fixed to the ureter. (F and G) Antireflux treatment (Leadbetter-Clarke method) is performed on the previously reserved colon bands at both ends. (H) Mucosal-to-mucosal suture to avoid postoperative anastomotic stenosis and necrosis. (I) Enterourethral anastomosis is carried out at the corresponding position of the previous prethreading.

2.3. Statistical analysis

IBM SPSS Statistics 22.0 (IBM Corp., Armonk, NY, USA) was used for the statistical analysis. Descriptive statistics were mainly used. Continuous variables were presented as mean ± standard deviation, and categorical variables were presented as ratios. The Kaplan-Meier method was used for the analysis of overall survival (OS), recurrence-free survival (RFS), and continence rate. Univariate logistic regressions were performed to test the effect of baseline and perioperative characteristics on oncological outcomes.

3. Results

Approximately one-third of the patients were at stage 3 at the first visit to hospital. Nearly all patients had already received chemotherapy, and 17 patients had received both chemotherapy and radiotherapy (Table 1). All surgeries, including three intracorporeal laparoscopic surgeries, were completed successfully without severe intraoperative complications. Preservation of the reproductive system was performed in four girls. The mean operative time was 386.9 ± 95.4 min and the mean blood loss was 136.5 ± 77.4 ml. Lymph node metastases developed in three (4.8%) children. Of 53 male patients, 21 (39.6%) developed prostate infiltration. Unlike ileal neobladder, these children did not require routine pouch irrigation after surgery. The mean hospital stay was 21.5 d. Typically, single J stents and catheters were removed 5 wk following surgery after confirmation of watertight healing by cystography. Details are shown in Table 2.

3.1. Oncological outcomes

Of the 62 patients, 54 were alive without evidence of disease recurrence or metastasis at the last follow-up. For

Table 2 – Perioperative characteristics

Variable	Results
Total operative time (min)	386.9 ± 95.4
Estimated blood loss (ml)	136.5 ± 77.4
Number of retrieved lymph nodes	13.2 ± 7.2
Preservation of uterus and uterine appendages, *n* (%)	4 (44.4)
COG grouping, *n* (%)	
I	56 (90.3)
IIA	3 (4.8)
IIB	2 (3.2)
IIC	1 (1.6)
Tumour resection status, *n* (%)	
Microscopically complete	58 (93.5)
Microscopically incomplete	4 (6.5)
Macroscopically complete	62 (100)
Hospital stay (d)	21.5 ± 12.6
Catheter indwelling time (d)	37.8 ± 11.8

COG = Children's Oncology Group.

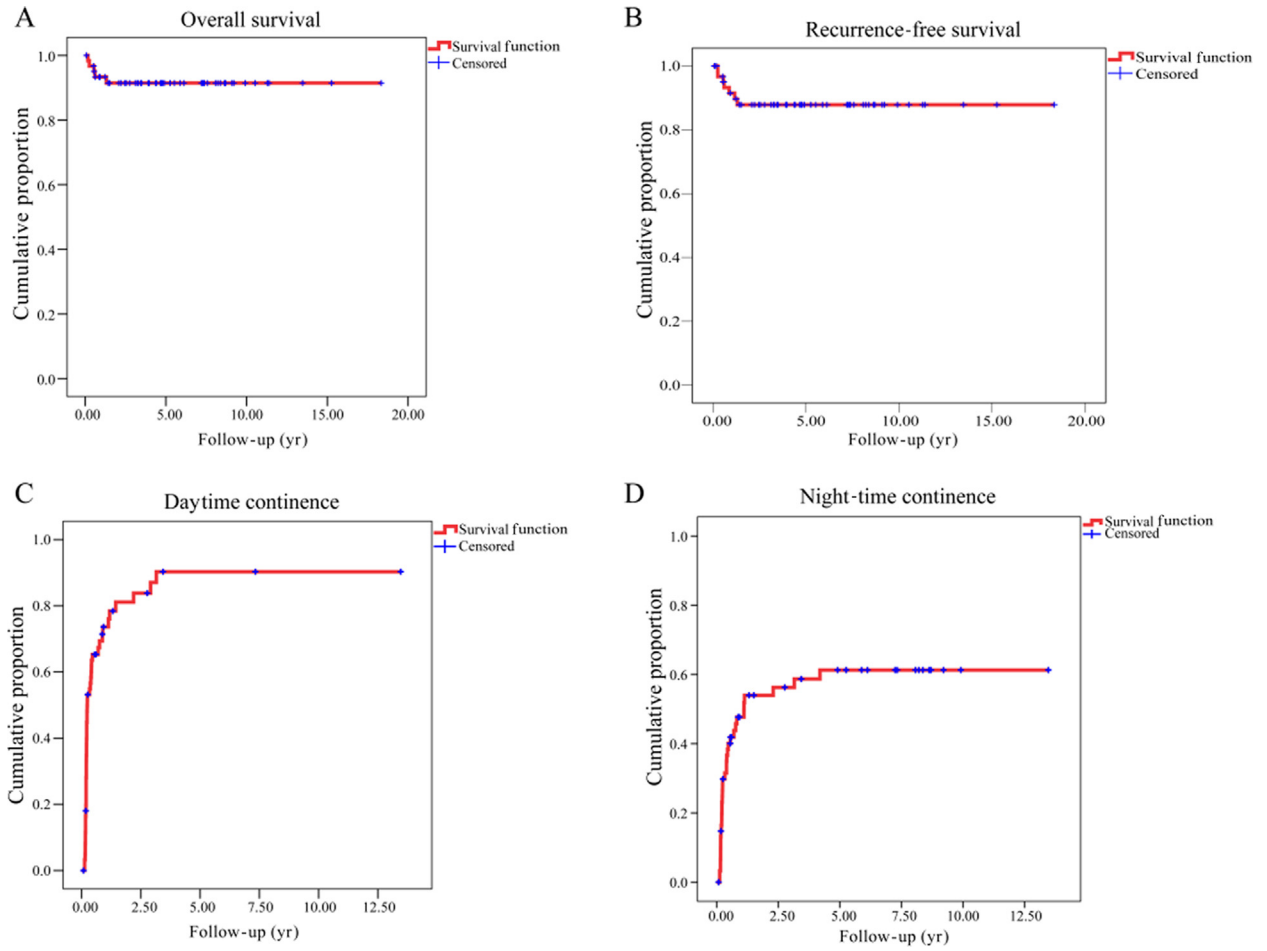

Fig. 3 – Kaplan-Meier estimates of (A) overall survival and (B) recurrence-free survival. Kaplan-Meier analyses depicting the (C) daytime and (D) night-time continence rates.

the five deaths, four patients died of tumour recurrence and one died of pneumonia 2 mo after surgery. Two children experienced recurrence and metastasis within 3 mo postoperatively, and one of the patients refused treatment. The other patient received further chemotherapy combined with targeted drug and had stable disease for 6 mo until progression was observed again. Salvage radiotherapy with bilateral nephrostomy was administered, but the patient ultimately died of malnutrition 1 yr after radical cystectomy. In addition, three relapsed patients are still on treatment. The 5-yr OS rate was 92%, with 88% RFS (Fig. 3A and B, Table 3, and Supplementary Tables 1 and 2). To date, the longest follow-up time was 18 yr. The median follow-up time was 53.4 mo (Table 3). Our univariate analysis showed that tumour invasiveness, COG grouping, and lymph node metastasis were potential predictors of a poor prognosis (Table 4).

3.2. *Functional outcomes*

Although three children developed varying degrees of postoperative hydronephrosis, all 57 survivors exhibited normal postoperative renal function (serum creatinine 44.3 ± 15.1

Table 3 – Oncological and functional outcomes

Variable	Results
Follow-up (mo), median (range)	53.4 (1–223)
Oncologic outcome[a] (%)	
1-yr OS	93
1-yr RFS	92
5-yr OS	92
5-yr RFS	88
10-yr OS	92
10-yr RFS	88
Sexual function (>12 yr old)	
Erectile function[b]	5/14
Regular menstruation[c]	2/2
Daytime continence[d]	
3 mo (%)	32/60 (53.3)
6 mo (%)	39/59 (66.1)
12 mo (%)	43/57 (75.4)
Night-time continence	
3 mo (%)	18/60 (30.0)
6 mo (%)	24/59 (40.7)
12 mo (%)	28/57 (49.1)

OS = overall survival; RFS = recurrence-free survival.
[a] Kaplan-Meier method was used.
[b] Only boys are assessed.
[c] Only girls with preserved the reproductive organs are assessed.
[d] Continence was defined as the use of zero or one safety pad.

Table 4 – Evaluation of prognostic factors in B/P RMS

Variables	OR	95% CI	*p* value
COG staging	5.6	1.0–31.7	0.052
Ki67/10	1.5	1.0–2.5	0.070
Lymph node metastasis	21.6	1.7–282.0	0.019
Adjuvant chemotherapy	0.5	0.1–2.7	0.462
Time to surgery (mo)	1.0	1.0–1.1	0.212
Tumour shrinks	0.3	0.1–3.9	0.389
Prostate invaded	2.3	0.5–11.4	0.318
Positive margin	2.9	0.3–32.4	0.389
Depth of tumour invasion	6.1	1.1–34.7	0.042
COG grouping above IIA	21.6	1.7–282.0	0.019
≥6 cycles' neoadjuvant chemotherapy	5.8	0.7–51.3	0.115

B/P RMS = bladder and prostate rhabdomyosarcoma. CI = confidence interval; COG = Children's Oncology Group; OR = odds ratio.
Tumour recurrence was the dependent variable.
Time to surgery: time from diagnosis to surgery.
Tumour shrinks: after neoadjuvant chemotherapy or/and radiotherapy.
Depth of tumour invasion: mucosa and submucosa versus muscle and deeper.

Table 5 – Early and late complications

Variable	Results
Early complications (38.7%), *n* (%)	
Urinary tract infection	10 (16.1)
Pneumonia	3 (4.8)
Surgical incision infection	5 (8.1)
Fistula	2 (3.2)
Urinary leak	2 (3.2)
Ileus	4 (6.5)
Late complications (37.1%)	
Urinary tract infection, *n* (%)	7 (11.3)
Enterourethral anastomotic stenosis, *n* (%)	9 (14.5)
Ureteroenteric anastomotic stenosis, *n* (%)	3 (4.8)
Neobladder stones, *n* (%)	2 (3.2)
Fistula, *n* (%)	4 (6.5)
Urethrovaginal fistula	3/9
Urethroscrotal fistula	1/53

μmol/l, estimated glomerular filtration rate 103.7 ± 26.6 ml/min/1.73 m^2). No severe metabolic disturbance was observed in the survivors. The continence rates were 75.4% (43/57) for the daytime and 49.1% (28/57) for the night-time 12 mo after surgery. Thereafter, the recovery of urinary control has been stabilised. Nevertheless, a small proportion of the children still experienced significant improvements (Fig. 3C and D). Five of the 14 >12-yr-old boys reported that they experienced erections. Two female patients >12 yr old reported that they menstruated.

3.3. *Complications*

The major early complications included urinary tract infection (16.1%), pneumonia (4.8%), and incisional infection (8.1%). Especially, the first child who underwent the surgery in 2003 suffered severe early complications; an additional surgery was performed to treat intestinal obstruction. Fortunately, she recovered uneventfully and was discharged home on day 34, without recurrences observed during the 18-yr follow-up. Benign anastomotic stenosis was the most common late complication, which occurred in 12 children (including nine enterourethral anastomotic stenoses and three ureteroenteric anastomotic stenoses). For the patients with enterourethral anastomotic stenosis, continued antagonistic urethral dilation was necessary. Usually after three times of dilation, the patients can achieve a satisfactory urination. For ureteroenteric anastomotic stenosis, we adopted dynamic monitoring of renal resistive index to evaluate obstruction [16,17]; the results did not show a significant increase. During the follow-up process, the hydrops gradually decreased without surgical intervention. Vaginal fistula was another common complication that occurred in three out of nine girls. Overall, 24 (38.7%) and 23 (37.1%) children developed early (<30 d) and late (>30 d) complications, respectively (Table 5).

4. Discussion

For B/P RMS, the COG reported that the 5-yr OS was 86% and the 5-yr event-free survival (EFS) was 79% [18]. Chemotherapy and radiotherapy are the preferred treatment strategies that are thought to preserve normal bladder function while curing the patient. With the advent of new radiotherapeutic modalities, brachytherapy combined with partial cystectomy has gradually been recommended by researchers [19–21]. However, the bladder preservation reported in the literature has mainly been performed for tumours that were not above the level of the bladder trigone and had not infiltrated bladder vessels. Moreover, the recovery of bladder function has been uneven after comprehensive therapy, which reached only 40–60% [22]. Meanwhile, the application of radiotherapy in China has lagged far behind the use of surgery. Doctors and patients both regard radiotherapy as an auxiliary treatment that does not have a dominant role, and its adverse side effects are very obvious. Two of the patients in this group had received excessively heavy dosages of radiation, which resulted in freezing of the pelvis during the operation. Furthermore, among our follow-up patients, some had abnormal skeletal development caused by previous radiotherapy, which resulted in a serious delay in the growth stage. Lautz et al. [23] declared that surgical complications are immediately measurable but that the full impact of radiation therapy is often delayed by years.

Children comprise a special group that will benefit greatly from longer-term survival expectations. Complete resection of the primary tumour is an important factor for prognosis [6]. Radical cystectomy is undoubtedly more reliable than partial resection in terms of oncological control. Hays et al [24] reported that 40% of patients without visible tumour cells at second surgeries experienced tumour relapse, which indicated the malignancy and concealment of RMS. In the present group, six boys with negative frozen section results developed recurrence with or without metastasis during the follow-up. We thought that due to the previous treatment, the activity of tumour cells and tissues may be hidden, but its invasive properties are maintained. Nevertheless, given that no invasion of the uterus and appendages was found in the preoperative examination, also considering future endocrine function and reproductive function [3], we preserved the reproductive organs in four girls, and none experienced a recurrence.

Orthotopic neobladder is undoubtedly the preferred method of urinary diversion in children. Detubularised ileal spherical neobladders often require repeated folding and suturing, which is complicated and time consuming. However, detaenial sigmoid neobladder only requires a 15–20 cm length of colon without potential adverse effects

on gastrointestinal absorption. By stripping the seromuscular tissue of the isolated colon, a large-capacity and low-pressure reservoir can be created. More importantly, routine neobladder irrigation is not required after surgery. Long-term follow-up results showed no overdistension of the neobladder and deteriorating renal function. Postoperative recovery is faster and better in children than in adults, which may depend on the high histocompatibility and tissue adaptability of children.

Whether or not the neobladder should be reconstructed primarily remains controversial [4]. Some authors have suggested that neobladder reconstruction should be delayed until the patient has achieved a durable disease-free status after radical cystectomy in case of tumour relapse [25]. However, Castagnetti et al. [5] reported that none of the patients undergoing delayed Padua ileal neobladder reconstruction after attaining disease-free status achieved autonomous urination. Fibrostenosis might develop in the urethral stump and external sphincter after radical cystectomy. Consequently, the difficulty of second-stage surgery is greatly increased, and physiological activities of the tissues around the urethra and ureter are weakened, which are not conducive to postoperative functional recovery. In the present study, detaenial sigmoid neobladder was constructed immediately after radical cystectomy. Our results showed that single-stage neobladder reconstruction can provide patients with good quality of life without significantly increasing recurrence and complications.

Functional recovery of the upper urinary tract is also associated with postoperative quality of life, which mainly depends on the ureteroenteric anastomosis. We used a modified Leadbetter and Clarke [14] method to accomplish ureteroenteric anastomosis, which achieved extremely good results in the children. Only three children developed varying degrees of postoperative hydronephrosis with normal renal function, which may be related to the high histocompatibility and tissue adaptability of children in general. Moreover, the design of the U-shaped neobladder can also enable a low-tension anastomosis and effectively protect the blood supply of the bowel and ureters.

Children are too young to complete effective pelvic floor muscle exercises, so urinary function recovery mostly depends on precise intraoperative manipulation. Active stimulation of the perianal muscles by a parent was also performed in some children. Our follow-up results showed that the 3-mo daytime urinary continence rate was 53.3% and reached as high as 75.4% at the 1-yr follow-up. On the one hand, these results were influenced by the powerful regenerative ability of children. On the other hand, our results also depended on the effective protection of the support structure during the operation, especially in the urethral stump and area around the neurovascular bundle. Moreover, we are currently conducting a study on the neural remodelling mechanism of neobladder urination behaviour, and the initial results revealed that urinary control innervation of the sigmoid neobladder may resemble normal physiology more closely [10].

Children were more prone to postoperative complications due to hypoimmunity caused by the history of chemoradiotherapy and surgical stress after urinary diversion. Overall, about 35% children developed early and late complications. Formation of neobladder stones occurred in two patients in the early stage. During the process of endoscopic lithotripsy, we found that both cases of neobladder stones were caused by the Hem-o-lok clips in the neobladder. Clips' erosion from the lateral ligament was highly suspected [26]. After the use of absorbable clips, neobladder stones were not observed subsequently.

Previous studies from the COG found that the primary site, tumour size, tumour invasiveness, and positive lymph nodes were important prognostic parameters for EFS and OS of patients with RMS (all sites) [27], and we obtained similar results in the present study. Our previous immunohistochemistry results had shown that PD-L1–positive staining was observed in 47.1% of the patients; metastatic tumour cells in the lymph nodes were positive for PD-L1 expression [28]. Thus, we speculated that PD-1/PD-L1 inhibitors may be potential therapeutic agents for patients with B/P RMS. We expect and are committed to develop very specific treatments through technologies, such as genetic testing in the future.

4.1. Limitations

Although the surgical cohort in this study comprised one of the largest reported series of neobladder reconstructions for B/P RMS, the sample size was still small. The study spanned a long time and the preoperative characteristics of the children varied greatly, which could have introduced a bias in the analysis. Studies in larger samples would provide results with a greater degree of reproducibility. Moreover, this was a single-centre retrospective study with limited surgeon experience.

5. Conclusions

Our results confirmed the safety and feasibility of primary orthotopic sigmoid neobladder reconstruction after radical cystectomy for paediatric patients with B/P RMS. Good outcomes in terms of oncological control and functional recovery were achieved. The high histocompatibility and tissue adaptability of children are inspiring. Individualised treatment for B/P RMS may become possible after exploration of genetic testing in the future.

***Author contributions*:** Abai Xu had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: A. Xu, Ch Liu, P. Xu.
Acquisition of data: C. Chen, Du, Z. Liu, Lan, Cao, Y. Liu, Huang, Shen, Cu Liu.
Analysis and interpretation of data: P. Xu, Ch Liu, A. Xu, C. Chen, B. Chen, Bi, Jiang, Du, Huang.
Drafting of the manuscript: P. Xu, C. Chen.
Critical revision of the manuscript for important intellectual content: P. Xu, Ch Liu, A. Xu, C. Chen, B. Chen.
Statistical analysis: C. Chen, Bi, Jiang, Z. Liu, Cu Liu.
Obtaining funding: P. Xu, Ch Liu, A. Xu.

Administrative, technical, or material support: A. Xu, Ch Liu, P. Xu, B. Chen, Lan, Cao, Y. Liu, Shen.
Supervision: A. Xu, Ch Liu, B. Chen.
Other: None.

Financial disclosures: Abai Xu certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

***Funding/Support and role of the sponsor*:** This work was supported by the Sino-German Mobility Programme (grant no. M-0299) and the Medical Science and Technique Foundation of Guangdong province of China (grant no. A2020241).

Peer Review Summary

Peer Review Summary and Supplementary data to this article can be found online at https://doi.org/10.1016/j.eururo.2022.08.015.

References

[1] Leaphart C, Rodeberg D. Pediatric surgical oncology: management of rhabdomyosarcoma. Surg Oncol 2007;16:173–85.
[2] Schmidt A, Warmann SW, Eckert F, et al. The role of reconstructive surgery and brachytherapy in pediatric bladder/prostate rhabdomyosarcoma. J Urol 2020;204:825–34.
[3] Lautz TB, Martelli H, Fuchs J, et al. Local treatment of rhabdomyosarcoma of the female genital tract: Expert consensus from the Children's Oncology Group, the European Soft-Tissue Sarcoma Group, and the Cooperative Weichteilsarkom Studiengruppe. Pediatr Blood Cancer 2020:e28601.
[4] Castagnetti M, Herbst KW, Esposito C. Current treatment of pediatric bladder and prostate rhabdomyosarcoma (bladder preserving vs. radical cystectomy). Curr Opin Urol 2019;29:487–92.
[5] Castagnetti M, Angelini L, Alaggio R, Scarzello G, Bisogno G, Rigamonti W. Oncologic outcome and urinary function after radical cystectomy for rhabdomyosarcoma in children: role of the orthotopic ileal neobladder based on 15-year experience at a single center. J Urol 2014;191:1850–5.
[6] Seitz G, Dantonello TM, Int-Veen C, et al. Treatment efficiency, outcome and surgical treatment problems in patients suffering from localized embryonal bladder/prostate rhabdomyosarcoma: a report from the Cooperative Soft Tissue Sarcoma trial CWS-96. Pediatr Blood Cancer 2011;56:718–24.
[7] Xu K, Liu CX, Zheng SB, et al. Orthotopic detaenial sigmoid neobladder after radical cystectomy: technical considerations, complications and functional outcomes. J Urol 2013;190:928–34.
[8] Xu A, Li B, Li H, et al. Comparison of seromuscular tunnel and split-cuff nipple antireflux ureteroenteral anastomosis techniques in orthotopic taenia myectomy sigmoid neobladder: a prospective, randomized study. Urology 2013;81:669–74.
[9] Lopes RI, Mello MF, Lorenzo AJJF. Recent advances in pediatric bladder malignancies. F1000Res 2020;9, F1000 Faculty Rev-147.
[10] Xu P, Chen B, Xu A, Yuan D, Zhang Y, Liu C. Initial experience with intracorporeal laparoscopic radical cystectomy and detaenial sigmoid neobladder reconstruction. Eur Urol 2021;79:545–51.
[11] Perera M, McGrath S, Sengupta S, et al. Pelvic lymph node dissection during radical cystectomy for muscle-invasive bladder cancer. Nat Rev Urol 2018;15:686–92.
[12] Xu P, Xu A, Chen B, et al. Ligation-free technique for dorsal vascular complex control during laparoscopic radical prostatectomy: a single-center experience from China. World J Urol 2017;35:395–402.
[13] Xu P, Chen B, Xu A, et al. Short-term outcomes and clinical efficacy of ligation-free technique used in laparoscopic radical cystectomy. World J Urol 2019;37(Suppl 1):81.
[14] Leadbetter WF, Clarke BG. Five years' experience with uretero-enterostomy by the combined technique. J Urol 1955;73:67–82.
[15] Mitropoulos D, Artibani W, Biyani CS, Bjerggaard Jensen J, Rouprêt M, Truss M. Validation of the Clavien-Dindo grading system in urology by the European Association of Urology Guidelines Ad Hoc Panel. Eur Urol Focus 2018;4:608–13.
[16] Patti G, Menghini ML, Todini AR, Marrocco G, Calisti A. The role of the renal resistive index ratio in diagnosing obstruction and in the follow-up of children with unilateral hydronephrosis. BJU Int 2000;85:308–12.
[17] Brkljacić B, Kuzmić AC, Dmitrović R, Rados M, Vidjak V. Doppler sonographic renal resistance index and resistance index ratio in children and adolescents with unilateral hydronephrosis. Eur Radiol 2002;12:2747–51.
[18] Saltzman AF, Cost NG. Current treatment of pediatric bladder and prostate rhabdomyosarcoma. Curr Urol Rep 2018;19:11.
[19] Michel J, Sauter L, Neunhoeffer F, et al. Sedation practices during high dose rate brachytherapy for children with urogenital and perianal rhabdomyosarcoma. J Pediatr Surg 2022;57:1432–8.
[20] Ozden E, Mercimek MN, Sarikaya S. Laparoscopic bladder-sparing approach in patients with prostatic rhabdomyosarcoma: a case series of two pediatric patients. Urol J 2019;17:525–7.
[21] Lobo S, Gaze MN, Slater O, et al. Bladder function after conservative surgery and high-dose rate brachytherapy for bladder-prostate rhabdomyosarcoma. Pediatr Blood Cancer 2022;69:e29574.
[22] Seitz G, Fuchs J, Sparber-Sauer M, et al. Improvements in the treatment of patients suffering from bladder-prostate rhabdomyosarcoma: a report from the CWS-2002P trial. Ann Surg Oncol 2016;23:4067–72.
[23] Lautz TB, Chi YY, Li M, et al. Benefit of delayed primary excision in rhabdomyosarcoma: a report from the Children's Oncology Group. Cancer 2021;127:275–83.
[24] Hays DM, Raney RB, Crist WM, et al. Secondary surgical procedures to evaluate primary tumor status in patients with chemotherapy-responsive stage III and IV sarcomas: a report from the Intergroup Rhabdomyosarcoma Study. J Pediatr Surg 1990;25:1100–5.
[25] Stein R, Frees S, Schröder A, et al. Radical surgery and different types of urinary diversion in patients with rhabdomyosarcoma of bladder or prostate—a single institution experience. J Pediatr Urol 2013;9(6 Pt A):932–9.
[26] Xu P, Binshen C, Abai X, Chunxiao Liu. Postoperative complications and treatment of detaenial sigmoid neobladder (20 years experience from a single center). Eur Urol Open Sci 2020;19(Suppl 2):e2352.
[27] Rodeberg DA, Garcia-Henriquez N, Lyden ER, et al. Prognostic significance and tumor biology of regional lymph node disease in patients with rhabdomyosarcoma: a report from the Children's Oncology Group. J Clin Oncol 2011;29:1304–11.
[28] Zhou P, Wang Q, Wang C, et al. Programmed death ligand 1 expression in bladder rhabdomyosarcoma and its association with clinicopathological features. Int J Clin Exp Pathol 2017;10:10565–70.