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Research Article

Prophylactic Urethrectomy Could Further Shorten the Female Bladder Cancer Recurrence and Metastasis

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ABSTRACT

Objective: To compare the clinical effects and safety of two methods of laparoscopic total cystectomy for female bladder cancer patients with retention and resection of the urethra.**Methods:** Female bladder cancer patients with bladder invasive urothelial carcinoma were selected in grade II~III from January 2008 to March 2018. Patients were divided into two groups based on the surgical method: group A laparoscopic radical cystectomy, and group B laparoscopic radical cystectomy + urethrectomy, to observe the clinical efficacy, operation duration, blood loss during surgery, hospitalization time, and complications.**Results:** The operation times in groups A and B were 262.54 ± 27.95 min and 310.28 ± 32.99 min, respectively. The volumes of intraoperative blood loss in groups A and B were 439.46 ± 44.52 mL and 456.74 ± 47.18 mL, respectively. There were no discernable differences in the probability of postoperative complications in the two groups. In group A, four patients experienced bladder cancer recurrence and metastasis, and 50% of these cases had a urethral recurrence. In group B, one patient experienced bladder cancer recurrence and metastasis; however, there was no urethral recurrence.**Conclusion:** Although laparoscopic radical cystectomy + urethrectomy extended the operation times; prophylactic urethrectomy can further shorten the bladder cancer recurrence and metastasis and improve patient prognosis without an increase in complications. However, its long-term clinical efficacy needs further study and supplement.

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Introduction

Bladder cancer is one of the most common malignant tumors in the urinary system, ranking ninth among the international malignant tumors. The incidence of bladder cancer in China is relatively low compared with that in western countries, but recently its incidence has been increasing annually. The incidence of bladder cancer in women is lower than that in men by 1/3, but the malignant degree of bladder cancer in women is higher with a worse prognosis [1-3]. In recent years, with the development of endoscopic technology, laparoscopic radical cystectomy

with urinary diversion is the standard procedure for treating superficial bladder tumors, which are not sensitive to bladder infusion chemotherapy and muscle-invasive bladder cancer [4]. The standard procedures for female radical cystectomy include bladder, uterus, double attachment, and anterior vaginal wall resection, and pelvic lymph node dissection. With the increase of in-depth studies about bladder cancer in women, the discussion about whether to preventively resect urethra during surgery is increasing. Herein, we aimed to examine the operation time, intraoperative blood loss, postoperative complications, the complete healing time of the incision, and surgical satisfaction in order to evaluate the surgical outcomes between only laparoscopic radical

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cystectomy and laparoscopic radical cystectomy + urethrectomy in female bladder cancer patients.

Materials and Methods

I Study Population

A total of 42 females with bladder invasive urothelial carcinoma II~III grade undergoing laparoscopic radical cystectomy at the Second People's Hospital of Changzhou between January 2008 and March 2018 were recruited for the current study. In accordance with the different surgical methods, the patients were divided into two groups: group A

and group B. The patient characteristics of the two groups are illustrated in (Table 1). The study was approved by the ethics committee of our hospital, and all participants provided written informed consent. In both groups, distant metastasis before the operation was excluded, and patients with stage $\geq T2$ required a cystoscopy to exclude posterior urethral metastasis. In addition, both groups of patients did not have severe cardiopulmonary or cerebrovascular disease. There was no significant statistical difference in the patients age and the number of $\geq T2$ cases. Three days before the operation began, a low-residue diet and oral metronidazole 0.2 g t.i.d. + levofloxacin 0.5 g q.d., and a cleansing enema were prescribed the night before the operation and on the morning of the operation. The postoperative follow-up lasted 24 months.

Table 1: General information about the two groups of female bladder cancer patients.

Group	n	Age (yr)	Pathological stage		primary	palindromia
			<T2	$\geq T2$		
A	22	57.22 $\pm$ 11.36	12	10	13	9
B	20	58.54 $\pm$ 9.45	11	9	12	8
Statistical quantity	0.318	0.496	1.867		0.781	
P value	0.573	0.311	0.325		0.431	

Group A: laparoscopic radical cystectomy; Group B: laparoscopic radical cystectomy+urethrectomy.

II Surgical Methods

Two groups of patients underwent the same preoperative preparation: routine preparation of the skin, routine field disinfection with povidone-iodine, spreading of a towel, general anaesthesia with tracheal intubation, put in the Trendelenburg position and the body shaped like an X. Group A used the supine position, and group B used the lithotomy position.

To establish artificial pneumoperitoneum by incision in the lower edge of the umbilical cord (15 mmHg pressure), a 10 mm cannula was used and 30° lens from the incision, and 2-3 cm above the anterior superior iliac spine was penetrated into each of the 5 mm cannulas under-screen monitoring, 12 mm of cannula was placed on the McBurney point and the anti-McBurney point respectively. Ovarian suspension ligaments were isolated from the oviduct umbrella and lateral ovaries and ligated. The peritoneum was cut to free the ureter at the bifurcation of the iliac vessels and freed downward along the internal iliac artery and the umbilical artery dissociated, along the pelvic wall downstream of the broad ionic ligament and cut off from the main ligament of the uterus. The uterus was moved forward, and the sacral ligament was exposed and cut off, the rectum uterine depression was opened, the uterine artery next to the cervix was freed and tied, the uterus and double appendages were lifted with a gripper and the vaginal fornix cut horizontally. The posterior urethra was freed between the anterior wall of the vagina and the bladder as well as the lateral wall of the bladder to handle the lateral ligament of the bladder, and free up to the junction of the bladder urethra, exposing the pubic urethral ligament.

Group A used Hem-o-lok to close the bladder neck and cut off the distal urethra. Group B continued to free the distal urethra along the bladder neck, and the distal urethra was clamped with Hem-o-lok to remove all of the urethra. An incision was made on the anterior wall of the vagina at the anterior fornix. The specimen was placed in the specimen bag and

removed from the vagina. The vaginal incision was closed with an absorbable or barbed line.

The two groups both used extraperitoneal bilateral ureterocutaneostomy. After complete removal of the bladder, the left ureter was pulled to the right side along the lateral peritoneum path through the posterior peritoneum space of the presacral sigmoid colon and cropped with the right ureter. A single-J stent was used in the ureter, then extracted through the right rectus abdominal puncture point, and an interrupted suture for the ureter with the surrounding tissue. Both groups were immediately given "natriuretic heparin calcium" q.d., a subcutaneous injection, combined with lower extremity pneumatic therapy to prevent deep venous thrombosis.

III Evaluations

In order to evaluate the clinical outcomes, we measured and recorded various intraoperative and postoperative parameters, including the 1) operation duration, 2) blood loss during the operation, 3) length of hospitalization, 4) postoperative complications assessment.

IV Statistical Analysis

SPSS 22.0 statistical software was used to process the data. Measurement data are presented as means $\pm$ standard deviations. A q test was used for pairwise comparisons between groups, and the X2 test was used for the comparison of rates. P values <0.05 were accepted as statistically significant.

Results

I Operation Time, Volume of Intraoperative Blood Loss, and Length of Hospitalization

All operations were successfully completed and there was no transition to open surgery during the laparoscopic cystectomy. The total operative

time for group A was approximately 230-420 min, with an average of about 262 minutes. The volume of intraoperative bleeding was approximately 300-500 mL, with an average of 439 mL. The number of postoperative hospitalization days were approximately 10-22 days, with an average of 14 days. For group B, the total operative time was approximately 270-470 min, with an average of approximately 310

minutes. The volume of intraoperative bleeding was approximately 290-520 mL, with an average of 456 mL. The number of postoperative hospitalization days were about 8-19 days, with an average of 15 days (Table 2). The operation time for group A was shorter than that of the resection group B. The intraoperative bleeding and postoperative hospitalization days were similar between groups A and B.

Table 2: Comparison of operation time, intraoperative blood loss, and the length of hospitalization between the two groups of patients.

Group	Operation time (min)	Intraop blood loss (ml)	Length of hospitalization(d)
A	262.54±27.95	439.46±44.52	14.75±1.43
B	310.28±32.99	456.74±47.18	15.11±1.53
Statistical quantity	7.281	1.685	1.113
P value	0.000	0.095	0.269

Group A: laparoscopic radical cystectomy; Group B: laparoscopic radical cystectomy+urethrectomy.

II Postoperative Complications and Bladder Cancer Recurrence and Metastasis

The postoperative follow-up time for group A was 4-24 months, and 86.4% of the patients received follow-up. During follow-up, there were six patients with different degrees of hydronephrosis, two patients were bilateral, four were unilateral, two had severe hydronephrosis, two were relieved after percutaneous nephrostomy, and the rest of the patients were treated conservatively after regular review. Three patients had stoma stenosis after the operation and improved after ostomy; four patients had recurrence within 12 months after the operation, including patients with urethral metastasis, one with bone metastasis and one patient pelvic metastasis, who died with advanced tumors with multiple organ failure in 4, 6, 10 and 15 months after the operation.

Group B was followed up for 6-24 years after surgery, and 85% of the patients were followed up. During follow-up, there were six patients with different degrees of hydronephrosis, three were bilateral, three were unilateral, and the degree of the majority of hydronephrosis was mild and given conservative treatment. Two patients had stoma stenosis after the operation and improved after stoma dilatation; one patient had bone metastasis within 12 months after the operation and died of an advanced tumor with multiple organ failure 15 months after the operation, and no urethral metastasis occurred (Table 3). The recurrence of urethral tumor in the resection group was significantly less than that in the retention group; there was no significant difference in the incidence of other complications in the two groups.

Table 3: Comparison of postoperative complications and bladder cancer recurrence and metastasis between the two groups of patients.

Group	Infection (n)	stoma stenosis (n)	Hydronephrosis (n)	recurrence and metastasis (n)
A	2	3	6	4
B	3	3	5	2
Statistical quantity	0.249	0.007	0.046	4.220
P value	0.588	0.934	0.830	0.040

Group A: laparoscopic radical cystectomy; Group B: laparoscopic radical cystectomy+urethrectomy.

Discussion

With the development of endoscopic technology in urology, laparoscopic radical cystectomy with urinary diversion has become important treatments for muscle-invasive bladder cancer or high-grade bladder cancer. Due to the unique anatomical structure of women, the scope of standard total cystectomy also includes anterior pelvic organs, but patients undergoing radical cystectomy still have a lifetime risk of recurrence of urothelial cancer [5, 6].

Among them, urethral tumor recurrence is a rare complication after radical bladder cancer resection. The average incidence is between 1-8%, and the incidence for female patients is 2-4%. Most urethral recurrences occur before surgery within 2 years [7, 8]. Although the recurrence rate of urethral tumors is low, the prognosis is extremely poor. Studies have shown that the median overall survival of patients after urethral recurrence is 6-54 months, and the 5-year disease-specific survival rate is 0-83% [9]. In female patients, the involvement of the bladder neck and anterior vaginal wall is associated with an increased

risk of recurrence of urethral tumors. As early as 1995, Stein *et al.* examined the medical records of 67 female bladder cancer patients who underwent total cystectomy and found that the involvement of the anterior vaginal wall and bladder neck was highly correlated with urethral recurrence. Chen *et al.* then further demonstrated the association between bladder neck involvement and urethral recurrence. They retrospectively studied 115 female patients who underwent radical surgery for bladder cancer, of which nine patients had a recurrence of urethral tumors and involvement of the bladder neck was the only risk factor for urethral involvement. It is worth mentioning that there were two patients with recurrent urethra without bladder neck involvement [10, 11].

When radical cystectomy was first performed in the 1950s to treat bladder tumors, prophylactic urethral resection was a common practice for men with risk factors for urethral recurrence, including prostate involvement, multifocal tumors, and bladder neck involvement. Until the 1990s, due to concerns about the recurrence of urethral tumors, considering the short length of the female urethra and close to the bladder

neck, urethral resection and anterior pelvic resection was performed on women routinely [12, 13]. In recent years, with the recent increase in the use of orthotopic bladder replacement and the suspicious benefits of prophylactic urethral resection, the identification of patients with high-risk urethral recurrence, the management of residual urethra, and the treatment of urethral recurrence have become key issues again. This article compares the intraoperative preventive urethral resection with the traditional surgical scope to evaluate the efficacy, advantages and disadvantages of these two surgical scopes in the treatment of female invasive bladder cancer.

In this study, two groups of patients chose laparoscopic radical cystectomy, which was less invasive and better than traditional open surgery; the urinary diversion method was selected for the extraperitoneal bilateral ureterocutaneostomy with better tolerance from patients [14]. In the resection group, the distal urethra was freed and removed on the basis of the original operation of female bladder cancer radical resection, which extended the operation time on the original basis, but there was no significant increase in intraoperative bleeding. In terms of postoperative complications, ostomy stenosis and hydronephrosis occurred to different degrees in both groups, but the difference was not statistically significant and improved after treatment. In terms of postoperative tumor recurrence, the resection group performed significantly better, with only one case of tumor recurrence and metastasis, while four patients in the retention group developed tumor recurrence and metastasis, which included two cases of urethral metastasis. It is suggested that preventive resection of the female urethra during operation can significantly reduce the probability of postoperative tumor recurrence and metastasis, which is beneficial for patient prognosis.

Conclusion

In conclusion, female bladder cancer patients undergoing prophylactic urethrectomy compared with preserving the urethra during laparoscopic radical cystectomy, except for the slightly longer operation time, there is no significant difference in the remaining perioperative aspects. In terms of short-term oncology prognosis, prophylactic urethrectomy is obviously the better choice. However, due to the lack of long-term follow-up results, its long-term clinical efficacy requires further research and increased sample size.

Conflicts of Interest

None.

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