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Original Article

Clinical effect of robot-assisted radical cystectomy in bladder cancer

Yuzhu Lin[1], Ying Zhang[2], Liumei Luo[1], Xin Zhang[3]

[1]Department of Urology, Hainan Provincial People's Hospital, Haikou 570311, Hainan Province, China; [2]Nursing Department of Hainan Provincial People's Hospital, Haikou 570311, Hainan Province, China; [3]Department of Urology, The Second Affiliated Hospital of Shandong University of Traditional Chinese Medicine, Jinan 250000, Shandong Province, China

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Abstract: Objective: This study aimed to determine whether robot-assisted radical cystectomy (RARC) can accelerate recovery, improve pelvic lymph node dissection effects, and reduce serum tumor marker tumor specific growth factor (TSGF) levels in patients with bladder cancer. Methods: A total of 96 patients with bladder cancer admitted to our hospital were recruited as the research participants. Among them, 43 patients who adopted radical cystectomy were enrolled in the control group (CG), and 53 patients treated with RARC were included in the research group (RG). The operation time, intraoperative blood loss, postoperative bowel recovery time, gastrointestinal function recovery, complication rate, clinical efficacy, changes of TSGF levels before and after operation, postoperative satisfaction and quality of life were observed. Results: Compared with the CG, patients in the RG experienced longer operation times ($P<0.05$), less intraoperative blood loss ($P<0.05$), and faster time to bowel recovery, anal exhaust, and anal defecation ($P<0.05$); moreover, the RG had a lower incidence rate of complications ($P=0.025$) and TSGF levels ($P<0.05$), higher effective cure rate ($P=0.023$) and satisfaction degree ($P=0.048$), as well as superior quality of life scores in six dimensions ($P<0.05$). Conclusion: The application of RARC can accelerate the recovery of patients with bladder cancer, improve the pelvic lymph node dissection effects, and reduce the serum levels of tumor marker TSGF.

Keywords: Robot-assisted radical cystectomy, bladder cancer, effect of pelvic lymph node dissection

Introduction

Bladder cancer is a malignancy originating from the bladder, which is associated with substantial morbidity, mortality and cost, and is one of the most prevalent cancers worldwide [1]. According to statistics from the World Health Organization, in 2016, there were 770,000 new cases of bladder cancer, and its high prevalence and tendency to recur and relapse has brought a massive burden on health services, as well as a serious threat to patients' lives [2, 3]. Previous data show that carcinogens such as tobacco and environmental or occupational exposure are major risk factors for bladder cancer [4]. The disease can occur at any age, mostly above 50 years of age, and the incidence tends to increase with age [5]. Asymptomatic hematuria is its most common clinical manifestation, and there may also be symptoms such as urinary frequency, urinary urgency, urinary pain and difficulty in urination [6]. Most patients are diagnosed with non-muscle invasive bladder cancer (NMIBC), and transurethral resection of the bladder tumor is the first stage of treatment after diagnosis [7], while radical cystectomy is indicated when NMIBC progresses to high risk or locally advanced stages [8]. Recently, increasing studies have pointed out that although radical cystectomy is effective in treating early-stage patients, it is a complex and invasive procedure that increases the risk of postoperative complications, which seriously affects the prognosis of patient survival [9]. In the meanwhile, clinical research and improvement of surgical skills for bladder cancer have kept pace with the continuous advances in medicine.

Although open surgery remains the most frequently used surgical method, the application of robot-assisted radical cystectomy (RARC) has gained acceptance in patients with bladder cancer in recent years [10]. With the development of Da Vinci robot-assisted Surgical System and surgical techniques, a growing number of urologists are embarking on an in-depth study of RARC [11]. For example, the team of Bochner BH revealed that RARC can effectively improve the perioperative curative effect [12]. Also that RARC has more obvious advantages in treating patients with complicated conditions [13]. However, a large number of studies focus on the success rate of surgery and the long-term survival of patients, while ignoring the recovery of patients' physical function and the changes of tumor markers. Tumor specific growth factor (TSGF), a peptide produced by tumor cells that is closely related to cell growth, infiltration and metastasis, is also a product of the massive expansion of malignant tumors and surrounding blood vessels [14]. It can be released into the blood at the early stage of malignant transformation, and can be detected at the early stage of malignant tumor formation. Hence, TSGF is not only a specific marker for malignant tumors, but also of great clinical value in the early diagnosis of tumors [15]. Therefore, this time, the effects of RARC on recovery, pelvic lymph node dissection, and serum tumor marker TSGF levels were explored, so as to provide a reliable theoretical basis to optimize surgery and increase patient acceptance.

Methods

Patient data

A total of 96 patients with bladder cancer admitted to the Hainan Provincial people's Hospital from May 2016 to June 2019 were recruited as research participants for prospective analysis. Among them, 43 patients who adopted radical cystectomy were enrolled in the control group (CG), and 53 patients treated with RARC were included in the research group (RG). This study was approved by the Ethics Committee of the Hainan Provincial people's Hospital, and all patients and their family members were informed and signed the inform consent.

Inclusion and exclusion criteria

The patients included were diagnosed with bladder cancer by cystoscopy, urine and imaging, and received treatment in our hospital, and all of them showed clinical symptoms for the first time, with complete data and high compliance. If patients had serious disorders of heart, lung, liver or kidney function, extreme physical weakness, surgical intolerance, mental disorders, communication disorders or immunodeficiency they were excluded.

Methods

CG: preoperative anesthesia was performed after determining the patient's posture, and a catheter was indwelled. Then, puncture was performed at 2 cm above the umbilicus of the patient, and the intraperitoneal pressure was maintained at 10-15 mmHg. A laparoscope was placed, and dissection and cystectomy were performed. The ileum was taken as the efferent loops, and the ureteral-ileum anastomosis was performed to form a catheter, which was then fixed. Patients were given routine medication guidance after the operation.

RG: The patient was placed in a satisfactory position for general anesthesia, and a four-arm Da Vinci robot-assisted Surgical System was applied. (1) Establishment of channels: the patient was placed in a Trendelenburg position at 20-30°. After the robot was locked, monopolar electrocoagulation curved scissors and bipolar electrocoagulation forceps were connected to arms 1 and 2, respectively. The first incision was made at the superior margin of the umbilicus, and a 12 mm trocar was placed as the camera lens hole. The pneumoperitoneum pressure was maintained at 12-15 mmHg (1 mmHg =0.133 kPa). The other five operating channels were established under direct vision: the second and third holes were made 2 cm below the umbilicus and the lateral margins of the right and left rectus abdominis muscles, respectively, for the 8 mm channels of the robotic arms 1 and 2; the 12 mm trocar was placed 4 cm below the left costal margin as the first auxiliary hole, and the 5 mm trocar was placed above the left anterior superior iliac spine as the second auxiliary hole; the 12 mm trocar was placed above the right anterior superior iliac spine as the alternate auxiliary hole. (2) Ligation of bilateral ureters: the posterior peritoneum was opened above the iliac vessels, and the bilaterally ureters were first freed to the inner segment of the bladder wall, and then cut off with Hem-o-lok clamping. (3)

Dissection of the lateral bladder ligaments: the ligaments were separated downward along the internal iliac vessels to the pelvic floor, and laterally along the medial umbilical ligaments to the pelvic floor, and then the lateral umbilical ligaments and the superior arterial vein of the bladder were ligated in turn with Hem-o-lock. (4) Separation and opening of Denonvillier's fascia: the peritoneum of the posterior wall of urinary bladder was opened to separate the vas deferens and seminal vesicles. The Denonvillier's fascia was opened along the seminal vesicles and vas deferens downward, and separated downward to the tip of the prostate. (5) Free of anterior wall of urinary bladder and dissection of prostate ligament: the anterior wall of urinary bladder was lifted to separate the loose tissue of prevesical space. The pelvic fascia was opened to expose the pubic prostatic ligament and severed. The lateral ligaments of the prostate were freed by lifting the seminal vesicles and then dissected by LigaSure electrocoagulation in turn. (6) Dissection of the urethra and resection of the specimen: the penile deep dorsal vein complex was dissected after LigaSure electrocoagulation, the urethra was dissected after Hem-o-lok clamping of the urethra, and the specimen was completely resected. (7) Pelvic lymph node dissection: the external iliac artery, vein, obturator nerve and lymph nodes of internal iliac artery were successively dissected at the iliac vessel bifurcation, and the obturator nerve was carefully protected. (8) Urinary diversion: ureterocutaneous anastomosis was performed [16].

Outcome measures

The operation time, intraoperative blood loss, postoperative bowel recovery time, gastrointestinal function recovery and complication rate of two groups of patients were observed, as well as the clinical efficacy. The clinical efficacy was assessed as follows: complete response: patients with clear urine color, no visible hematuria, and urine routine showing red blood cells (-) or (+), and their clinical symptoms and lesions completely disappeared and maintained for more than 4 weeks. Partial response: patients with significantly reduced hematuria, no visible hematuria, routine urine tests showing red blood cells (++) or (++++), and their tumor lesion reduced (the sum of the longest diameter reduced ≥30%) and maintained for more than 4 weeks. Stable disease: patients with no significant change in hematuria, and the sum of the longest diameter was reduced less than 30%. Progressive disease: the increase of the sum of the longest diameters of tumors ≥10%. The effective cure rate = (complete response + partial response) cases/total number of cases ×100%. The levels of tumor marker TSGF before and after operation, postoperative satisfaction were recorded, and the quality of life scores were calculated (the higher the score, the higher the quality of life).

Statistical analysis

All results were recorded as (mean ± standard deviation) and were statistically analyzed by SPSS 22.0 software. Comparison between groups was performed with t test. Comparison among multiple groups was done by one-way analysis of variance and LSD post-hoc test. $P<0.05$ was considered as statistically significant.

Results

Clinical data

The two groups of patients were compared in terms of general information of age, body mass index (BMI), gender, course of disease, smoking history, hypertension history, obesity, living environment, and ethnicity, and the results showed no statistical difference ($P>0.05$) (**Table 1**).

Operation time and intraoperative blood loss in the two groups

The statistical comparison of the operation time and intraoperative blood loss between the two groups revealed that patients in the RG experienced longer operation times ($P<0.05$, **Figure 1A**) and had less intraoperative blood loss than those in the CG ($P<0.05$, **Figure 1B**).

Postoperative bowel recovery time and gastrointestinal function recovery

The comparison of postoperative bowel recovery time and gastrointestinal function recovery showed that patients in the RG experienced faster bowel recovery ($P<0.05$, **Figure 2A**), time of anal exhaust ($P<0.05$, **Figure 2B**), and anal

Table 1. Comparison of general data

	Research group (n=53)	Control group (n=43)	χ^2 or t/p
Age (years)	49.7±8.9	50.2±9.1	0.271/0.787
BMI (KG/cm^2)	23.2±2.4	23.5±2.1	0.644/0.521
Gender			0.038/0.845
Male	31 (58.49%)	26 (60.47%)	
Female	22 (41.51%)	17 (39.53%)	
Course of disease (year)	1.1±0.5	1.2±0.6	0.891/0.375
Smoking history			0.089/0.766
Present	38 (71.70%)	32 (74.42%)	
Absent	15 (28.30%)	11 (25.58%)	
Hypertension history			0.151/0.698
Present	35 (66.04%)	30 (69.77%)	
Absent	18 (33.96%)	13 (30.23%)	
Obesity			0.058/0.809
Present	32 (60.38%)	27 (62.79%)	
Absent	21 (39.62%)	16 (37.21%)	
Living environment			0.084/0.772
Town	36 (67.92%)	28 (65.12%)	
Countryside	17 (32.08%)	15 (34.88%)	
Ethnicity			0.211/0.646
Han	45 (84.91%)	35 (81.40%)	
Minority	8 (15.09%)	8 (18.60%)	

defecation (P<0.05, **Figure 2C**) than those in the CG.

Postoperative complications in the two groups

Postoperative complications such as incision infection, intestinal obstruction, thrombosis, ileostomy ischemia, and catheter blockage were counted in both groups. The total incidence of postoperative complication was 5.66% in the RG, which was notably lower than that in the CG (20.93%), with a statistically significant difference (P=0.025) (**Table 2**).

Comparison of clinical efficacy

The effective cure rate of patients in the RG was 86.79%, which was higher than that in the CG (67.44%) (P=0.023), as shown in **Table 3**.

Changes of tumor marker TSGF levels before and after operation in the two groups

We detected the levels of tumor marker TSGF in the two groups, and found no marked difference in TSGF level between the two groups before operation (P>0.05). After operation, TSGF level decreased significantly in both groups, and was lower in the RG than in the CG (P<0.05) (**Figure 3**).

Comparison of postoperative satisfaction

The postoperative satisfaction of the two groups was counted. The total satisfaction was 94.34% in the RG, which was notably higher than that in the CG (81.40%) (P=0.048), as shown in **Table 4**.

Quality of life of the two groups

Postoperative quality of life of patients was assessed from the six dimensions of physiology, psychology, interpersonal relationship, social function, independence, and environmental impact. The RG exhibited higher scores in all aspects than the CG, with statistical differences (P<0.05), as shown in **Figure 4**.

Discussion

Bladder cancer is the first and second most common urological malignancy in China and the United States, respectively [17]. It is characterized by painless hematuria, and its diagnosis is determined by urine cytology and transurethral resection of the bladder tumor [18]. Intravesical treatment was applied for carcinoma in situ and other non-muscular invasive tumors [19]. The standard treatment for muscle-invasive disease is radical cystectomy and several urinary diversion services [20]. With the popularization of minimally invasive techniques and the continuous advancement of medicine, robot-assisted laparoscopic techniques have gradually become increasingly popular in clinical practice [21]. This study, compared the value of RARC in patients with bladder cancer, and is of great significance for clinical practice.

The results of this experiment showed that patients in the RG who had RARC experienced longer operation time and less intraoperative blood loss than patients in the CG who received radical cystectomy, suggesting that RARC causes smaller incision and less bleeding,

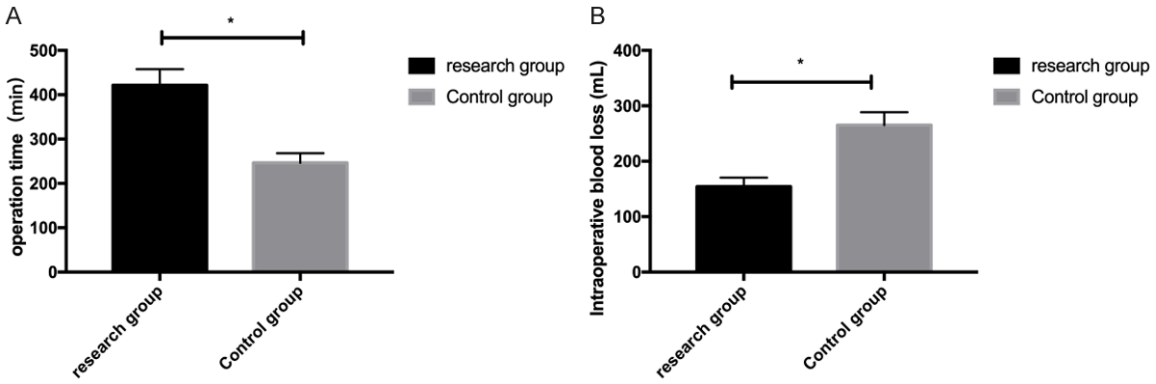

Figure 1. Operation time and intraoperative blood loss in the two groups. A. Operation time of the two groups of patients. B. Intraoperative blood loss of the two groups of patients. Note: *denotes P<0.05.

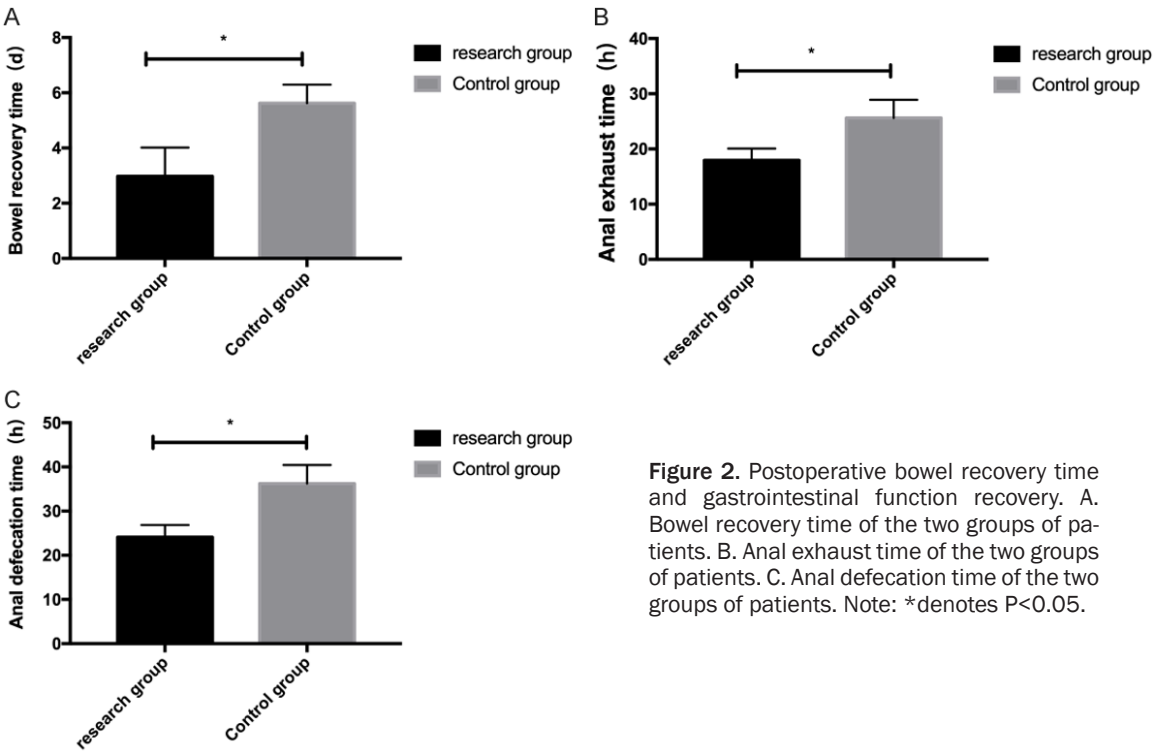

Figure 2. Postoperative bowel recovery time and gastrointestinal function recovery. A. Bowel recovery time of the two groups of patients. B. Anal exhaust time of the two groups of patients. C. Anal defecation time of the two groups of patients. Note: *denotes P<0.05.

which can effectively reduce postoperative pain and accelerate wound healing. Operation time has always been an important indicator for surgeons [22]. However, it is worth noting that RARC requires a lot of instrument docking and position adjustment [23], which we speculate may also be an important factor affecting the duration. Previous studies have shown that the average operation time for radical cystectomy has been continuously shortened with the development of minimally invasive surgical techniques and the increase in the volume of robotic bladder cancer procedures [24]. The team of Tang JQ [25] showed that the operation time of RARC was within the acceptable range and did not cause poor prognosis of patients, which can prove our results. Then, the postoperative bowel recovery time and gastrointestinal function recovery of the two groups were statistically compared. Patients in the RG experienced faster recovery time of bowel, and shorter time of anal exhaust and defecation than those in the CG, indicating that RARC is effective in treating patients with bladder can-

Table 2. Postoperative complications in the two groups

	Research group (n=53)	Control group (n=43)	χ^2	p
Incision infection	0 (0.00%)	1 (2.33%)		
Intestinal obstruction	0 (0.00%)	2 (4.65%)		
Thrombosis	1 (1.89%)	2 (4.65%)		
Ileostomy ischemia	1 (1.89%)	2 (4.65%)		
Catheter blockage	1 (1.89%)	2 (4.65%)		
Total incidence	3 (5.66%)	9 (20.93%)	5.061	0.025*

Note: *denotes P<0.05.

Table 3. Comparison of clinical efficacy between the two groups

	Research group (n=53)	Control group (n=43)	χ^2	p
Complete response	27 (50.94%)	15 (34.88%)		
Partial response	19 (35.85%)	14 (32.56%)		
Stable disease	3 (5.66%)	6 (13.95%)		
Progressive disease	4 (7.55%)	8 (18.60%)		
Effective cure rate (%)	86.79%	67.44%	5.201	0.023*

Note: *denotes P<0.05.

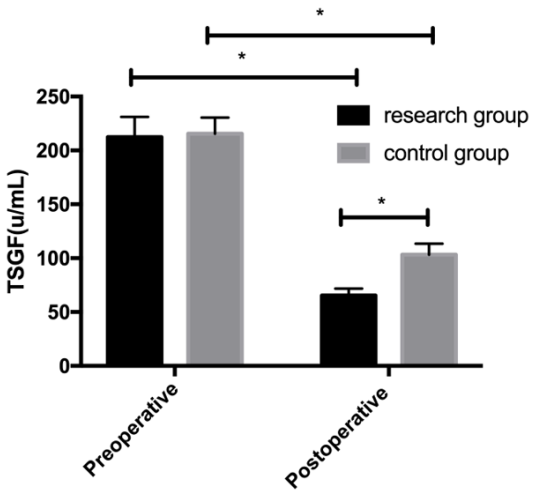

Figure 3. Changes of tumor marker TSGF levels before and after operation in the two groups. Note: *denotes P<0.05.

cer, which reduces the amount of intraoperative blood loss, causes less damage to the patient's body, and promotes the recovery of the patient's bowel and other functions. It is also suggested that the gastrointestinal function of patients undergoing RARC recovers quickly after operation [26], which is similar to the results of this experiment. Furthermore, postoperative complications such as incision infection, intestinal obstruction, thrombosis, ileostomy ischemia and catheter blockage were statistically analyzed. The total incidence of complications in the RG was 5.66%, which was notably lower than that in the CG (20.93%), indicating that RARC can effectively reduce the incidence of adverse reactions and is of great significance to improve the clinical efficacy. We speculate that its value lies in the fact that the procedure takes advantage of the robotic system, its anatomical precision, its ability to maintain a sufficient length of urethral stump intraoperatively, and its reduced use of opioid analgesics during surgery [27], which reduces complications and accelerates patient recovery. Further, we found an effective cure rate of 86.79% in the RG, which was higher than that of CG (67.44%), suggesting that RARC has an extremely high application value for bladder cancer. Such results are also in line with the team of Hussein AA [28] on RARC in bladder cancer, which can support the results of this experiment. TSGF, a tumor-specific growth factor, is the result of the expansion of malignant tumor and its peripheral capillaries [29]. According to previous studies, TSGF, secreted by tumor tissues during vascular proliferation, will be released into the peripheral blood along with the formation and growth of tumors, resulting in increased serum levels, which has been therefore used as a tumor marker in clinical screening of tumor diseases [30]. In this experiment, there was no significant difference in the TSGF levels between the two groups before operation. After operation, TSGF level decreased notably in both groups, especially in the RG. This suggests that RARC can clean the tumor tissue thoroughly, which is beneficial to reduce the level of tumor marker TSGF, and has a positive effect on promoting patients' self-confidence and increasing their satisfaction degree. We also counted the postoperative satisfaction of the two groups. The total satisfaction was 94.34% in the RG, which was notably higher than that in the CG (81.40%). Such results were consistent with the above, proving

Table 4. Comparison of postoperative satisfaction

	Research group (n=53)	Control group (n=43)	χ^2	p
Satisfied	38 (71.70)	19 (44.19)		
Basically satisfied	12 (22.64)	16 (37.21)		
Dissatisfied	3 (5.66)	8 (18.60)		
Total satisfaction (%)	50 (94.34)	35 (81.40)	3.921	0.048*

Note: *denotes P<0.05.

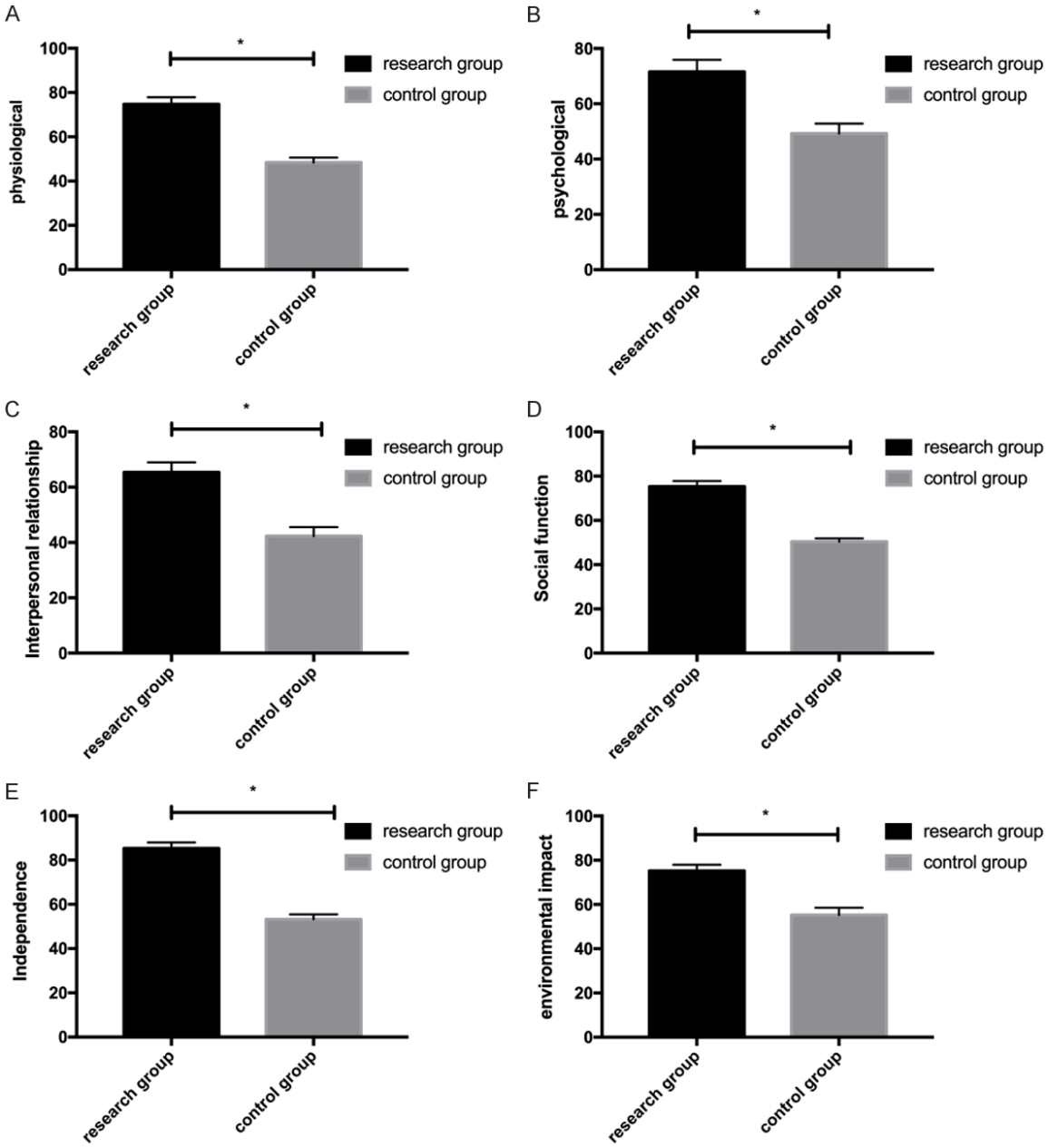

Figure 4. Quality of life of the two groups. A. Postoperative physiological scores of the two groups of patients. B. Postoperative psychological scores of the two groups of patients. C. Postoperative interpersonal relationship scores of the two groups of patients. D. Postoperative social function scores of the two groups of patients. E. Postoperative independence scores of the two groups of patients. F. Postoperative environmental impact scores of the two groups of patients. Note: *denotes P<0.05.

its application value. At the end of the study, the postoperative quality of life scores were compared from the six dimensions of physiology, psychology, interpersonal relationship, social function, independence, and environmental impact. The RG exhibited higher scores in all dimensions than the CG, indicating the obvious advantages of RARC in enhancing the surgical efficacy and prognosis.

There are many clinical treatments for bladder cancer, while in this study, only radical cystectomy was used as a control for comparison. Therefore, there is a possibility that RARC may not differ so significantly in all aspects compared with other treatment methods, which is a key direction of our future research. Besides, due to the short experimental period, we cannot determine the influence of RARC on the long-term prognosis of patients. Hence, we will follow up the participants in this study for a longer time to improve our results.

To sum up, the application of RARC can accelerate the recovery of patients with bladder cancer, improve pelvic lymph node dissection effect, and reduce the serum levels of tumor marker TSGF.

Disclosure of conflict of interest

None.

Address correspondence to: Ying Zhang, Nursing Department of Hainan Provincial People's Hospital, No. 19 Xiuhua Road, Xiuying District, Haikou 570311, Hainan Province, China. Tel: +86-138-76838020; E-mail: zhangying1262020@126.com; Xin Zhang, Department of Urology, The Second Affiliated Hospital of Shandong University of Traditional Chinese Medicine, No. 1, Jingba Road, Shizhong District, Jinan 250013, Shandong Province, China. Tel: +86-15098786067; E-mail: 15098786067@139.com

References

[1] Sanli O, Dobruch J, Knowles MA, Burger M, Alemozaffar M, Nielsen ME and Lotan Y. Bladder cancer. Nat Rev Dis Primers 2017; 3: 17022.

[2] Grayson M. Bladder cancer. Nature 2017; 551: S33.

[3] Antoni S, Ferlay J, Soerjomataram I, Znaor A, Jemal A and Bray F. Bladder cancer incidence and mortality: a global overview and recent trends. Eur Urol 2017; 71: 96-108.

[4] Cahn DB, Handorf EA, Ghiraldi EM, Ristau BT, Geynisman DM, Churilla TM, Horwitz EM, Sobczak ML, Chen DYT, Viterbo R, Greenberg RE, Kutikov A, Uzzo RG and Smaldone MC. Contemporary use trends and survival outcomes in patients undergoing radical cystectomy or bladder-preservation therapy for muscle-invasive bladder cancer. Cancer 2017; 123: 4337-4345.

[5] Cumberbatch MGK, Jubber I, Black PC, Esperto F, Figueroa JD, Kamat AM, Kiemeney L, Lotan Y, Pang K, Silverman DT, Znaor A and Catto JWF. Epidemiology of bladder cancer: a systematic review and contemporary update of risk factors in 2018. Eur Urol 2018; 74: 784-795.

[6] DeGeorge KC, Holt HR and Hodges SC. Bladder cancer: diagnosis and treatment. Am Fam Physician 2017; 96: 507-514.

[7] Kamoun A, de Reynies A, Allory Y, Sjodahl G, Robertson AG, Seiler R, Hoadley KA, Groeneveld CS, Al-Ahmadie H, Choi W, Castro MAA, Fontugne J, Eriksson P, Mo Q, Kardos J, Zlotta A, Hartmann A, Dinney CP, Bellmunt J, Powles T, Malats N, Chan KS, Kim WY, McConkey DJ, Black PC, Dyrskjot L, Hoglund M, Lerner SP, Real FX and Radvanyi F; Bladder Cancer Molecular Taxonomy Group. A consensus molecular classification of muscle-invasive bladder cancer. Eur Urol 2020; 77: 420-433.

[8] Mullenders J, de Jongh E, Brousali A, Roosen M, Blom JPA, Begthel H, Korving J, Jonges T, Kranenburg O, Meijer R and Clevers HC. Mouse and human urothelial cancer organoids: a tool for bladder cancer research. Proc Natl Acad Sci U S A 2019; 116: 4567-4574.

[9] Robertson AG, Kim J, Al-Ahmadie H, Bellmunt J, Guo G, Cherniack AD, Hinoue T, Laird PW, Hoadley KA, Akbani R, Castro MAA, Gibb EA, Kanchi RS, Gordenin DA, Shukla SA, Sanchez-Vega F, Hansel DE, Czerniak BA, Reuter VE, Su X, de Sa Carvalho B, Chagas VS, Mungall KL, Sadeghi S, Pedamallu CS, Lu Y, Klimczak LJ, Zhang J, Choo C, Ojesina AI, Bullman S, Leraas KM, Lichtenberg TM, Wu CJ, Schultz N, Getz G, Meyerson M, Mills GB, McConkey DJ; TCGA Research Network, Weinstein JN, Kwiatkowski DJ and Lerner SP. Comprehensive molecular characterization of muscle-invasive bladder cancer. Cell 2017; 171: 540-556, e525.

[10] Parekh DJ, Reis IM, Castle EP, Gonzalgo ML, Woods ME, Svatek RS, Weizer AZ, Konety BR, Tollefson M, Krupski TL, Smith ND, Shabsigh A, Barocas DA, Quek ML, Dash A, Kibel AS, Shemanski L, Pruthi RS, Montgomery JS, Weight CJ, Sharp DS, Chang SS, Cookson MS, Gupta GN, Gorbonos A, Uchio EM, Skinner E, Venkatramani V, Soodana-Prakash N, Kendrick K, Smith JA Jr and Thompson IM. Robot-assisted radical cystectomy versus open radical cystectomy in patients with bladder cancer (RAZOR): an open-label, randomised, phase 3, non-inferiority trial. Lancet 2018; 391: 2525-2536.

[11] Hussein AA, May PR, Jing Z, Ahmed YE, Wijburg CJ, Canda AE, Dasgupta P, Shamim Khan M, Menon M, Peabody JO, Hosseini A, Kelly J, Mottrie A, Kaouk J, Hemal A, Wiklund P and Guru KA; Collaborators. Outcomes of intracorporeal urinary diversion after robot-assisted radical cystectomy: results from the International Robotic Cystectomy Consortium. J Urol 2018; 199: 1302-1311.

[12] Bochner BH, Dalbagni G, Marzouk KH, Sjoberg DD, Lee J, Donat SM, Coleman JA, Vickers A, Herr HW and Laudone VP. Randomized trial comparing open radical cystectomy and robot-assisted laparoscopic radical cystectomy: oncologic outcomes. Eur Urol 2018; 74: 465-471.

[13] Catto JWF, Khetrapal P, Ambler G, Sarpong R, Khan MS, Tan M, Feber A, Dixon S, Goodwin L, Williams NR, McGrath J, Rowe E, Koupparis A, Brew-Graves C and Kelly JD. Robot-assisted radical cystectomy with intracorporeal urinary diversion versus open radical cystectomy (iROC): protocol for a randomised controlled trial with internal feasibility study. BMJ Open 2018; 8: e020500.

[14] Shao T, Huang J, Zheng Z, Wu Q, Liu T and Lv X. SCCA, TSGF, and the long non-coding RNA AC007271.3 are effective biomarkers for diagnosing oral squamous cell carcinoma. Cell Physiol Biochem 2018; 47: 26-38.

[15] Song X, Liang B, Wang C and Shi S. Clinical value of color Doppler ultrasound combined with serum CA153, CEA and TSGF detection in the diagnosis of breast cancer. Exp Ther Med 2020; 20: 1822-1828.

[16] Perera M, McGrath S, Sengupta S, Crozier J, Bolton D and Lawrentschuk N. Pelvic lymph node dissection during radical cystectomy for muscle-invasive bladder cancer. Nat Rev Urol 2018; 15: 686-692.

[17] Woldu SL, Bagrodia A and Lotan Y. Guideline of guidelines: non-muscle-invasive bladder cancer. BJU Int 2017; 119: 371-380.

[18] Abufaraj M, Foerster B, Schernhammer E, Moschini M, Kimura S, Hassler MR, Preston MA, Karakiewicz PI, Remzi M and Shariat SF. Micropapillary urothelial carcinoma of the bladder: a systematic review and meta-analysis of disease characteristics and treatment outcomes. Eur Urol 2019; 75: 649-658.

[19] Warrick JI, Sjodahl G, Kaag M, Raman JD, Merrill S, Shuman L, Chen G, Walter V and DeGraff DJ. Intratumoral heterogeneity of bladder cancer by molecular subtypes and histologic variants. Eur Urol 2019; 75: 18-22.

[20] Seiler R, Ashab HAD, Erho N, van Rhijn BWG, Winters B, Douglas J, Van Kessel KE, Fransen van de Putte EE, Sommerlad M, Wang NQ, Choeurng V, Gibb EA, Palmer-Aronsten B, Lam LL, Buerki C, Davicioni E, Sjodahl G, Kardos J, Hoadley KA, Lerner SP, McConkey DJ, Choi W, Kim WY, Kiss B, Thalmann GN, Todenhofer T, Crabb SJ, North S, Zwarthoff EC, Boormans JL, Wright J, Dall'Era M, van der Heijden MS and Black PC. Impact of molecular subtypes in muscle-invasive bladder cancer on predicting response and survival after neoadjuvant chemotherapy. Eur Urol 2017; 72: 544-554.

[21] Juo YY, Mantha A, Abiri A, Lin A and Dutson E. Diffusion of robotic-assisted laparoscopic technology across specialties: a national study from 2008 to 2013. Surg Endosc 2018; 32: 1405-1413.

[22] Matsumoto K, Tabata KI, Hirayama T, Shimura S, Nishi M, Ishii D, Fujita T and Iwamura M. Robot-assisted laparoscopic radical cystectomy is a safe and effective procedure for patients with bladder cancer compared to laparoscopic and open surgery: perioperative outcomes of a single-center experience. Asian J Surg 2019; 42: 189-196.

[23] Pak JS, Lee JJ, Bilal K, Finkelstein M and Palese MA. Utilization trends and short-term outcomes of robotic versus open radical cystectomy for bladder cancer. Urology 2017; 103: 117-123.

[24] Wijburg CJ, Michels CTJ, Oddens JR, Grutters JPC, Witjes JA and Rovers MM. Robot assisted radical cystectomy versus open radical cystectomy in bladder cancer (RACE): study protocol of a non-randomized comparative effectiveness study. BMC Cancer 2018; 18: 861.

[25] Tang JQ, Zhao Z, Liang Y and Liao G. Robotic-assisted versus open radical cystectomy in bladder cancer: a meta-analysis of four randomized controlled trails. Int J Med Robot 2018; 14: 1.

[26] Satkunasivam R, Tallman CT, Taylor JM, Miles BJ, Klaassen Z and Wallis CJD. Robot-assisted radical cystectomy versus open radical cystectomy: a meta-analysis of oncologic, perioperative, and complication-related outcomes. Eur Urol Oncol 2019; 2: 443-447.

[27] Attalla K, Kent M, Waingankar N and Mehrazin R. Robotic-assisted radical cystectomy versus open radical cystectomy for management of bladder cancer: review of literature and randomized trials. Future Oncol 2017; 13: 1195-1204.

[28] Baghdadi A, Hussein AA, Ahmed Y, Cavuoto LA and Guru KA. A computer vision technique for automated assessment of surgical performance using surgeons' console-feed videos. Int J Comput Assist Radiol Surg 2019; 14: 697-707.

[29] Cao R, Wu Q, Li Q, Yao M and Zhou H. A 3-mRNA-based prognostic signature of survival in oral squamous cell carcinoma. PeerJ 2019; 7: e7360.

[30] Nakamichi E, Sakakura H, Mii S, Yamamoto N, Hibi H, Asai M and Takahashi M. Detection of serum/salivary exosomal Alix in patients with oral squamous cell carcinoma. Oral Dis 2020; 27: 439-447.