Is Robot-assisted Radical Cystectomy the Preferred Minimal Invasive Procedure for Non-advanced Bladder Urothelial Carcinoma(T1-T2N0M0)? A Single Center Retrospective Study.

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Research

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Abstract

Background: To investigate the perioperative efficacy and cost of robot-assisted radical cystectomy(RARC) and laparoscopic RC(LRC) in patients with non-advanced bladder urothelial carcinoma

Methods: 156 patients with non-advanced bladder urothelial carcinoma undergoing minimally invasive radical cystectomy in our center between January 2015 and April 2020 were included. Perioperative data and hospitalization expenses were extracted from our database. All analyses were performed using SPSS 23.0 software, and $p < 0.05$ was considered statistically significant.

Results: The proportion of male patients was 86.5%(135/156) and the median age was 65(IQR 59-71) years old. RARC had a lower PSM rate (0 vs 5.3%,P=0.051), longer median operation time(370 vs 305 min,P<0.001) and higher median hospitalization cost(20565.2 vs 15532.4$,P<0.001). There were no significant differences in intraoperative transfusion rate, anesthesia resuscitation in ICU, postoperative hospital stay, 30-d complications and postoperative treatment expenses between the two groups(P=0.815,0.715, 0.817,0.92 and 0.543,respectively.)

Conclusion: Short operation time and low hospitalization costs are favorable factors for LRC, but RARC may be the preferred surgical procedure for non-advanced bladder urothelial carcinoma considering the potentially low PSM rate.

Trial registration: A complete informed consent was obtained from the patient and their families before the surgery.Informed consent was signed for all patients.This study was approved by the Ethics Review Committee of the Second Xiangya Hospital of Central South University

Background

Bladder cancer(BC), a common and intractable malignancy, is a challenge facing urologists around the world, with an predicted 81400 additional BC patients in the USA within 2020[1]. Radical cystectomy(RC) is the paramount treatment for muscle-invasive BC(MIBC) and highest risk non-muscle invasive BC(NMIBC) is one of its indications[2]. The application of laparoscope in bladder resection can be tracked to 1992[3], which has a huge advance in improving postoperative analgesia and rehabilitation but needs highly adept anatomical structure and intraperitoneal skills[4]. In 1994, the robot was approved into clinical surgery[5]. In the past, robotic surgeries were inclined to the early patients without coexisting illness and achieved encouraging results[5–8]. The current views on the perioperative effects and oncologic outcomes between robot-assisted RC(RARC) and laparoscopic RC(LRC) are sharply divided[9, 10]. Patients with stage T1-T4 were included indiscriminately in previous analysis, ignoring the subtle differences between different surgical tools in the bladder resection of advanced tumors[11–13]. Here, we stratified patients according to the 8th AJCC Cancer Manual[14] followed by comparing the merits of RARC and LRC, to provide a new view and clinical evidence for the formulation of surgical strategy in patients with non-advanced urothelium carcinoma.

Methods

341 patients without metastatic lesion underwent RC in our center between January 2016 and April 2020. All patients agreed to RC, as the results of the transurethralresection of bladder tumor suggested MIBC or NMIBC with highest progression risk. Tumor stage depended on the pathologic results after RC. The exclusion criteria were as follows: 1.Open surgery, conversion to open surgery or palliative surgery. 2.Combined with other malignant tumors. 3.Non urothelial carcinoma. 4.High stage of tumor(T3/T4) or positive lymph nodes. Tumor stage, comorbidities and economic condition determined the choice of surgical tools and urinary diversion.

All data were obtained from our electronic medical record systems. The histologic type, tumor stage, number of lymph node, positive surgical margin(PSM) and presence of lymphovascular invasion were derived from postoperative pathological reports. Physical condition and anesthesia risk were analyzed using age, American Society of Anesthesiologists(ASA) score and underling diseases. Baseline hemoglobin and albumin level were used to assess anemia and nutritional status followed by transfusion volume and perioperative changes in hemoglobin for estimating intraoperative blood loss. The maximum value of hemoglobin in patients before operation and the value on the day of discharge were obtained, and calculated the decreased value. The postoperative 30-day complications were collected and evaluated by comprehensive complication index(CCI) and Clavien-Dindo classification(CDC) system[15]. The expenses of diagnosis, anesthesia, surgery, blood transfusion, postoperative treatment and consumables were calculated respectively. Other perioperative indicators include gender, operation time, incidence of anesthesia resuscitation in ICU, restart autonomous deambulation and postoperative hospital stay.

Continuous variables conforming to the normal distribution and homoscedasticity were analyzed by T test and showed as mean ± standard deviation(SD), otherwise, Wilcoxon rank sum test and median(Interquartile range,IQR) were performed. Categorical variables were presented as the frequency(ratio) and compared by chi-squared or fisher exact method. SPSS 23.0 software was used for statistical analysis and $p < 0.05$ meant a statistical difference in the study.

Results

185 cases were exclude, including 67 open RC, 6 squamous cell carcinoma, 11 adenocarcinoma, 2 sarcoma, 5 prostate adenocarcinoma, 1 colon cancer, 5 palliative operation, 8 conversion to open operation, 3 radical ureterectomy and 77 locally advanced patients. In non-advanced group, 81 underwent RARC and 75 for LRC (Fig. 1).

Baseline data of 156 patients are shown in Table 1. The proportion of male patients was 86.5%(135/156) and the median age was 65(IQR 59–71) years old. Up to 50%(78/156) of patients were complicated with respiratory dysfunction. The hydronephrosis rate was higher in the LRC group (21.3 vs 8.6%,P = 0.025). While the RARC group had a higher median hemoglobin value (133 vs 130 g/L,P = 0.042), this mini

difference was not clinically significant. Gender, age, ASA score,albumin level and other comorbidities between the two groups were no significantly different(P all > 0.05).

Table 1
Baseline characteristics for RARC and LRC in non-advanced group

	Total	RARC	LRC	P
Number of patients	156	81	75	
Male gender,n(%)	135(86.5)	73(90.1)	62(82.7)	0.173
Age,median(IQR),years	65(59–71)	64(57.5–70)	66(60–71)	0.646
ASA scole ≥ 3,n(%)	81(51.9)	39(48.1)	42(56)	0.327
Hydronephrosis,n(%)	23(14.7)	7(8.6)	16(21.3)	0.025
Hypertention,n(%)	47(30.1)	21(25.9)	26(34.7)	0.235
Coronary heart disease,n(%)	12(7.7)	5(6.2)	7(9.3)	0.459
Diabetes,n(%)	15(9.6)	6(7.4)	9(12)	0.331
Respiratory dysfunction,n(%)	78(50)	42(51.9)	36(48)	0.631
Cerebrovascular disease,n(%)[1]	3(1.9)	0(0)	3(4)	0.109
Perior abdominal surgery,n(%)	24(15.4)	14(17.3)	10(13.3)	0.494
Albumin,median(IQR),g/L	38.2(36.1–40.1)	37.9(36.2–39.9)	38.6(36.1–40.5)	0.694
Hemoglobin,median(IQR),g/L	131(118.3-141.8)	133(121.5-144.5)	130(116–139)	0.042

1.Fisher exact method ASA = American Society of Anesthesiologists, LRC = laparoscopic radical cystectomy, RARC = robotic-assisted radical cystectomy, IQR = interquartile range.

Pathological outcomes are described in Table 2. The two groups achieved a good balance in histological subtype and tumor stage(P = 0.876,0.955). Patients receiving RARC seemed to have a lower PSM rate(0 vs 5.3%,P = 0.051) and higher median lymph node output (11 vs 10,P = 0.062).

Table 2
Pathological outcomes for RARC and LRC in non-advanced group

	Total n = 156	RARC n = 81	LRC n = 75	P
Histological subtype,n(%)[1]				0.876
UC without other differentiation	136(87.2)	69(85.2)	67(89.3)	
UC with squamous differentiation	8(5.1)	5(6.2)	3(4)	
UC with glandular differentiation	10(6.4)	6(7.4)	4(5.3)	
UC with other differentiation	2(1.3)	1(1.2)	1(1.3)	
Tumor stage,n(%)				0.955
T1	69(44.2)	36(44.4)	33(44)	
T2	87(55.8)	45(55.6)	42(56)	
Positive surgical margins, n(%)[1]	4(2.6)	0(0)	4(5.3)	0.051
Lymph node dissection,n(%)	128(82.1)	68(84)	60(80)	0.521
Lymph node yield,median(IQR)	10(7-13.8)	11(8–15)	10(6–12)	0.062
Lymphovascular Invasion[1],n(%)	9(5.8)	3(3.7)	6(8)	0.314

1.Fisher exact method.UC = urothelium carcinoma. LRC = laparoscopic radical cystectomy, RARC = robotic-assisted radical cystectomy, IQR = interquartile range.

Perioperative data and cost are reported in Table 3. 12(14.8%) patients received ureterocutaneostomy in RARC group and 14(18.7%) in LRC group. Compared with the LRC group, the median operation time (370 vs 305 min,P < 0.001), median surgery cost (4661.9 vs 1160.6$,P < 0.001) and mean consumables fee(10271.7 vs 8505.5$,P < 0.001) in the RARC group were significantly higher. There were no significant differences in intraoperative transfusion rate, anesthesia resuscitation in ICU, postoperative hospital stay, 30-d complications and postoperative treatment expenses between the two groups(P = 0.815,0.715,0.817,0.92 and 0.543,respectively.)

Table 3
perioperative outcomes and cost for RARC and LRC in non-advanced group

	RARC n = 81	LRC n = 75	P
Diversion type,n(%)[1]			0.696
Ileal conduit	66(81.5)	57(76)	
Ureterocutaneostomy	12(14.8)	14(18.7)	
Orthotopic neobladder	3(3.7)	4(5.3)	
Operative time,median(IQR),min	370(302.5–455)	305(250–380)	< 0.001
Intraoperative transfusion,n(%)	15(18.5)	15(20)	0.815
Anesthesia resuscitation in ICU,n(%)	9(11.1)	7(9.3)	0.715
Restart deambulation,median(IQR),day	3(2–4)	3(2–5)	0.298
Postoperative hospital stay,median(IQR),day	11(9-13.5)	10(8–16)	0.817
Decrease of hemoglobin,median(IQR),g/L	27(17.5–43)	24(16–40)	0.489
30-d Complications,n(%)	61(75.3)	57(76)	0.92
Clavien 1–2	49(60.5)	46(61.3)	0.915
Clavien 3–5	12(14.8)	11(14.7)	0.979
CCI,median(IQR)	8.7(4.4–24.2)	12.2(8.7–24.2)	0.623
Cost,median(IQR),$	20565.2 (18837.4-22652.4)	15532.4 (14136.2-17313.6)	< 0.001
Diagnosis,median(IQR),$	1201.1(915.4-1658.4)	1345.6(940.7-1571.1)	0.557
Anesthesia,median(IQR),$	340.7(306.3-393.6)	335.2(298.1-391.8)	0.739
Surgery,median(IQR),$	4661.9(4336.1-4661.9)	1160.6(924.2-1560.6)	< 0.001

1.Fisher exact method 2.T test. LRC = laparoscopic radical cystectomy,RARC = robotic-assisted radical cystectomy,IQR = interquartile range.SD = Standard deviation ICU = Intensive care unit.CCI = Comprehensive compliance index

Fig 1 Patients selection process

1.RC = radical cystectomy 2 ORC = open radical cystectomy 3.MIRC = minimally invasive radical cystectomy

	RARC n = 81	LRC n = 75	P
Blood transfusion,median(IQR),$	36.7(33.8–39.5)	36.7(33.8-105.7)	0.898
Treatment,median(IQR),$	4305.7(3293.9-5198.2)	4221.9(3251.3-5880.7)	0.543
Consumables,mean(SD),$[2]	10271.7(1511.8)	8505.5(1504.1)	< 0.001
1.Fisher exact method 2.T test. LRC = laparoscopic radical cystectomy,RARC = robotic-assisted radical cystectomy,IQR = interquartile range.SD = Standard deviation ICU = Intensive care unit.CCI = Comprehensive compliance index			
Fig 1 Patients selection process			
1.RC = radical cystectomy 2 ORC = open radical cystectomy 3.MIRC = minimally invasive radical cystectomy			

Supplementary table 1 shows 247 complications in 156 patients. Intestinal obstruction (15.4%), lymphorrhagia(14.7%) and urinary tract infection (13.5%) were the most common postoperative complications.

Discussion

The perioperative values of RARC and LRC have been fully proved—less blood loss, rapid intestinal recovery, low analgesic needs and short hospital stay[16–19]. In theory, robotic devices could reduce muscle tremors caused by fatigue in the operators' arm, while weakening haptic feedback. However, two simultaneous mete-analysis comparing the perioperative and tumor outcomes of the two minimally invasive surgical approaches reached divergent conclusions[9, 10]. Feng et al[9] considered that RARC was superior to LRC in complications, length of stay, lymph node yield and mortality. Peng and colleagues found no significant difference on the efectiveness and safety between RARC and LRC. We hypothesized that heterogeneity of the included literature and neoplasm staging led to the above discrepancy. In our study, there was good comparability between the two groups in age, gender, ASA score, coexisting disease, tumor stage and histological type. Hydronephrosis is one of the secondary prognostic factors in BC patients and affects the choice of treatment options[20]. Only one of the 4 PSM patients had hydronephrosis before operation, so hydronephrosis was not a significant factor for PSM in this study(P = 0.475). Perioperative complications and postoperative survival outcomes were associated with tumor progress even with the use of minimally invasive surgical tools[11–13]. The PSM rate and 30-d mortality of pT4 patients increased to 31.5% and 4.2%[12]. Previous studies suggested that there was no significant difference in PSM between the RARC and LRC groups[16, 21, 22]. Here, RARC had a potentially lower PSM rate(0 vs 5.3%,P = 0.051) in patients with non-advanced diseases, which might owe to the flexible mechanical arms and stereoscopic vision. Although the median lymph node yield in the

RARC group was higher (11 vs 10,P = 0.062), but this failed to achieve statistical difference and significant clinical significance. And the lymph node yield depended on the extent of pelvic lymph node dissection.

The surgery time of RARC and LRC fluctuated in 328–511 and 301–533 minutes respectively[10]. There are many factors affecting intraoperative time[23]. Although the time-consuming of RARC tends to be shortened[23], it doesn't omit the necessary surgical steps but requires more time in assembling, debugging and disassembling instruments compared with LRC. RARC required obviously longer median operative time than LRC in non-advanced group (370 vs 305 min,P < 0.001), while it did not significantly increase the risk of anaesthetic resuscitation(11.1 vs 9.3%,P = 0.715). Some scholars pointed out that intraoperative blood transfusion was associated with survival parameters and robots were expected to reduce the demand for blood products[24]. In non-advanced patients, the intraoperative blood transfusion rate was similar in the RARC and LRC groups(20 vs 18.5%,P = 0.815), which is line with Su's retrospective study of 315 patients[21]. And there was no statistically significant difference in hemoglobin decline and transfusion cost (P = 0.489,0.898), suggesting similar intraoperative blood loss.

Khan et al[22] showed no significant difference in 30-d major complication(Clavien 3–5) among open surgery and minimally invasive surgical approaches(P = 0.20). Peng and colleagues[10] further demonstrated that the postoperative complication rates were similar between RARC and LRC(P = 0.61). However, other voices insisted that LRC was associated with a higher complication rates(p = 0.02)[9]. There existed a higher morbidity in LRC group(50% vs 36.5%,P = 0.017)[21]. Vetterlein and colleagues[15] reported that 99% of patients with RC would experience some complications, with a fatality rate of 2.4% within 30 days after surgery. However, the concept of postoperative meaningful complications has not been clearly defined, resulting in a wide variation in the reported rate of complications in different institutions. We found no statistically significant difference in the rate and severity of 30-d complications between RARC and LRC in patients stratified for tumor stage. Likewise, postoperative hospital stay was similar. Inconsistent with the above studies, lymphorrhagia was a common issue in minimal Invasive RC in our retrospective study(supplement Table 1). Compared with open surgery, RARC has advantages in the less blood loss, mild complication and short hospital stay, which cannot completely counteract the high cost of equipment[25]. Patients with RARC spend much more than those with LRC[21]. There is no study about cost analysis between RARC and LRC. The costs of surgery and consumables were the reason for the expensive hospitalization fees of RARC.

Therefore, we has compared the effectiveness and cost of RARC and LRC. Compared with previous studies, LRC and RARC had better comparability in terms of intraoperative transfusion rates, complications, postoperative hospital stay and treatment costs. Meantime, RARC showed better pathological outcomes, which need to be further validated with long-term survival data.

Inevitably, there were several limitations in this study. First, Our study was a single-center retrospective study with its inherent drawbacks, but we provided much detailed perioperative data. Second, different surgical habits and treatment ideas among the five surgeons may lead to some bias. Third, instead of

collecting estimated blood lose, we assessed the intraoperative blood transfusion, perioperative hemoglobin level and blood fees, which we believe can reflect intraoperative condition objectively. Nevertheless, this study enriches the perioperative data of LRC and RARC and opens a new perspective for patients to choose surgical tools.

Conclusion

- Short operation time and low hospitalization costs are favorable factors for LRC, but RARC may be the preferred surgical procedure for non-advanced bladder urothelial carcinoma considering the potentially low PSM rate.

Abbreviations

BC = Bladder cancer

RC = Radical cystectomy

RARC = Robot assisted radical cystectomy

LRC = Laparoscopic radical cystectomy

PSM = Positive surgical margin

ASA = American Society of Anesthesiologists

CCI = Comprehensive complication index

CDC = Clavien-Dindo classification

SD = Standard deviation

IQR = Interquartile range

ICU = Intensive care unit

AJCC = American Joint Committee on Cancer

Declarations

Ethical approval and consent to participate

This study was approved by the Ethics Review Committee of the Second Xiangya Hospital of Central South University.

Consent fore publication

A complete informed consent was obtained from the patient and their families before the surgery.Informed consent was signed for all patients.

Availability of date and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request

Competing interests

Xiao Ming, Zhong Zhaohui, Ren Jiannan, Xiong Wei have no conflict of interest to declare.

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Authors' contribution

Xiao Ming was responsible for study concepts,study design and the writing of the manuscript. Zhong Z was responsible for reviewing the article and proposing changes. Ren J collected and analyzed data. Xiong W was responsible for the starring revision of the article and study design. All authors read and approved the final manuscript.

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Figures

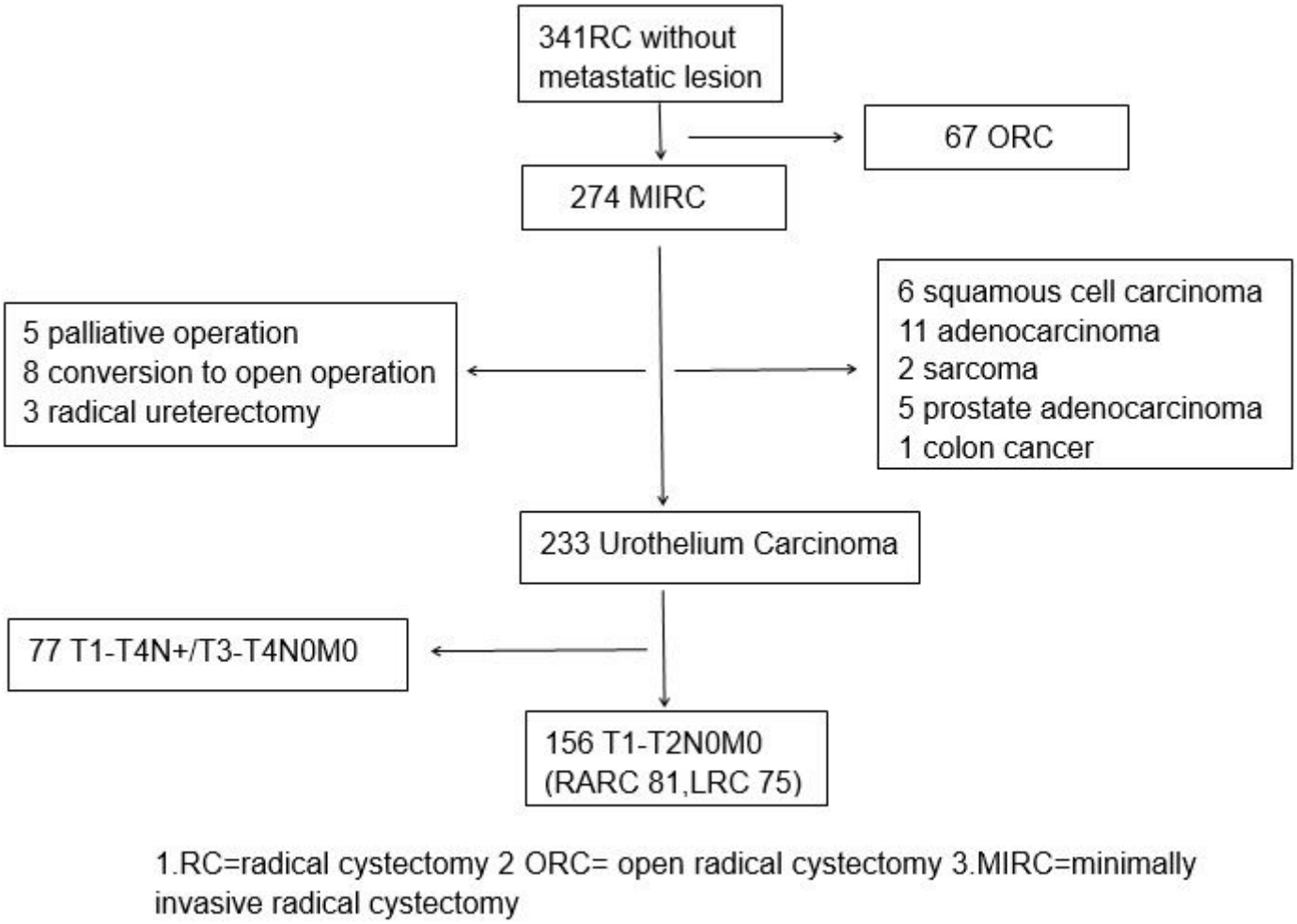

Figure 1

Patients selection process

Supplementary Files

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