Randomised Controlled Trial

INTERNATIONAL JOURNAL OF SURGERY

OPEN

Robotic versus open surgery for simultaneous resection of rectal cancer and liver metastases: a randomized controlled trial

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Objective: This study aimed to compare the short-term and long-term outcomes between robotic-assisted simultaneous resection and open surgery in patients with rectal cancer and liver metastases.

Background: Open simultaneous resection of colorectal cancer and synchronous liver metastases is widely performed and the potential cure for eligible patients. However, the feasibility of robotic simultaneous resection of primary and secondary liver lesions has not been established as a treatment option for metastatic rectal cancer.

Patients and methods: A single-center randomized controlled trial was conducted at a hospital in China. Enrolling patients were aged from 18 to 75 years and diagnosed with surgically resectable metastatic rectal cancer (distal extension to $\leq$15 cm from the anal margin). Patients selected for simultaneous resection were randomly assigned to have robotic or open surgery at a 1:1 ratio. The primary endpoint was the incidence rate of complications within 30 days after surgery. Secondary endpoints were bladder, sexual function, 3-year disease-free survival, and overall survival.

Results: A total of 171 patients were enrolled in this trial with 86 in the robotic group and 85 in the open group. As a result, patients in the robotic group demonstrated fewer complications within 30 days after surgery than those in the open group (31.4 vs. 57.6%, $P=0.014$) and no mortality seen in either group. Patients in the robotic group had less blood loss [mean (SD), 125.5 (38.3) vs. 211.6 (68.7) ml; $P<0.001$], faster bowel function recovery [mean (SD), 63.7 (27.4) vs. 93.8 (33.5) h $P<0.001$] and shorter hospital stay [mean (SD), 8.0 (2.2) vs. 10.7 (5.4) days; $P<0.001$] compared with those in the open group. The robotic group had a faster recovery of bladder and sexual function at 3 months after surgery than that of the open group. The 3-year disease-free survival rate (39.5 vs. 35.3%, $P=0.739$) and the 3-year overall survival rate (76.7 vs. 72.9%, $P=0.712$) were not statistically significant between the two groups.

Conclusions: In our randomized clinical trial, robotic simultaneous resection treatment of patients with rectal cancer and liver metastases resulted in fewer surgical complications, and a faster recovery to those of open surgery. Oncological outcomes showed no significant difference between the two groups.

Keywords: clinical trial, disease-free survival, liver metastases, overall survival, rectal cancer, robotic surgery, simultaneous resection, surgical complication

Introduction

Colorectal cancer (CRC) remains one of the leading causes of cancer-related deaths worldwide. The liver is the most common organ of metastasis from CRC. Approximately, 15–20% of CRC patients have synchronous colorectal liver metastases (SCRLM) at the time of initial diagnosis[1]. Complete radical resection of primary and metastatic lesions is currently the only potential cure for SCRLM patients[2].

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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International Journal of Surgery (2023) 109:3346–3353

Received 16 December 2022; Accepted 25 June 2023

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, www.lww.com/international-journal-of-surgery.

Published online 5 October 2023

http://dx.doi.org/10.1097/JS9.0000000000000581

Robotic surgery is increasingly used for treating rectal cancer and may offer short-term benefits, such as less blood loss, reduced surgical complications, and a shortened recovery time to open surgery[3]. When compared with open surgery, robotic surgery also enables better preservation of bladder and sexual function, with comparable long-term oncologic outcomes[4,5].

Since the first robotic liver resection was reported in 2011, a growing number of studies showed that robotic surgery is also a safe and feasible approach for radical resection of liver cancer and metastases[6,7]. Moreover, two retrospective studies reported that robotic simultaneous resection of the primary and metastatic lesions may be a feasible operation strategy for SCRLM patients[8,9]. However, evidence from a randomized clinical trial is needed to confirm the safety and efficacy of robotic simultaneous resection.

Open simultaneous resection for SCRLM requires two incisions mostly whereas robotic surgery requires a small incision about 5 cm, or even no incision when combined with the Natural Orifice Specimen Extraction Surgery (NOSES) technology, resulting in reduced trauma symptoms. Our group has more than 10 years of surgical experience in robotic CRC and liver cancer surgery[6,7]. Here, by conducting a randomized controlled study, we compare the postoperative complications of robotic simultaneous resection with that of open surgery for SCRLM patients, and the secondary endpoint includes disease-free survival (DFS), overall survival (OS), urinary, and sexual function.

HIGHLIGHTS

- The first randomized controlled trial comparing robotic versus open simultaneous resection.
- Robotic surgery had better short-term outcomes in reducing complications.
- Oncological outcomes were similar between robotic and open surgery.

Patients and methods

Trial design

This is a single-center, randomized, unblinded, parallel-group trial comparing robotic versus open surgery for simultaneous resection of both rectal cancer and liver metastases. This trial was registered with ClinicalTrials.gov. This report is compliant with the CONSORT guideline[10] (Supplemental Digital Content 1, http://links.lww.com/JS9/B135) (Supplemental Digital Content 2, http://links.lww.com/JS9/B136).

This study was approved by the Institutional Review Board of our center. All patients signed the informed consent prior to the selection. Patients were randomly assigned to either robot-assisted or open surgery in a one-to-one ratio.

The detailed study protocol is available in supplementary contents (*Supplementary Trial protocol*, Supplemental Digital Content 3, http://links.lww.com/JS9/B137).

Participants

As we previously reported[11], patients being considered for liver resection were discussed at a multidisciplinary meeting, and those patients with metastatic rectal cancer (distal extent ≤ 15 cm of the anal margin) deemed surgically resectable were considered for simultaneous resection. All patients had liver metastases already present when first diagnosed. The diagnosis of the tumor stage was based on clinical presentation and radiologic imaging. Primary tumor and liver lesions were evaluated using MRI and positron emission computed tomography (PET-CT). Liver biopsies and assessments were not routine. This study is expected to be completed within 3 years of enrollment (actual patient enrollment time: January 2016–May 2019).

The inclusion criteria were patients aged from 18 to 75 years, with histologically proven adenocarcinoma of the rectum, no severe major organ dysfunction, Child-Pugh A, and an Eastern Cooperative Oncology Group performance status of 0 or 1. The resectability of liver lesions was evaluated by liver surgeons of the MDT team, with indications of tumor numbers less than or equal to 5 and the maximum diameter of one tumor less than or equal to 10 cm. Eligible patients were randomly assigned into one of the treatment groups described in the following text (Fig. 1). Exclusion criteria were extrahepatic metastases; multiple liver metastases (number > 5); unable to tolerate simultaneous resection (ASA score > 3, chronic liver disease, physical or mental disability, etc.); tumors assessed as clinical complete response after preoperative radiotherapy or chemoradiotherapy; tumor assessed as cT1N0 and suitable for local excision; patients requiring emergency surgery; multiple colorectal tumors or other schedules requiring synchronous colon surgery; hereditary CRC; coexisting inflammatory bowel disease; pregnancy or lactation; or receiving treatment other than preoperative radiotherapy or chemoradiotherapy.

Preoperative radiotherapy or chemoradiotherapy was included in the protocol. However, if preoperative treatment had been received, only patients who had received long-course radiotherapy were enrolled. Patients' treatment followed the principles of long-course preoperative radiotherapy in the Chinese Standards of Diagnosis and Treatment for Colorectal Cancer (by the Chinese National Health Commission): a recommended dose of 45–50.4 Gy in 25–28 fractions; after 45 Gy a tumor bed boost with a 2 cm margin of 5.4 Gy in three fractions could be considered. During the radiotherapy, capecitabine was given orally. Surgery was done 8 weeks after the finish of radiotherapy. During the waiting period, fluorouracil or capecitabine-based chemotherapy was permitted.

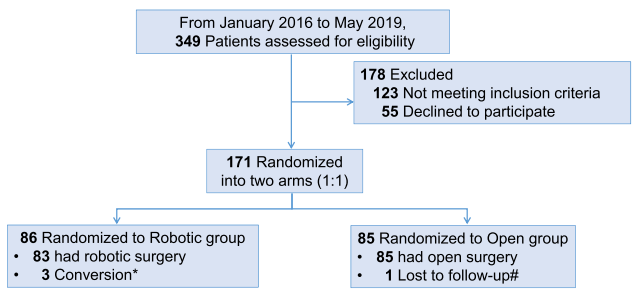

Figure 1. Consolidated Standards of Reporting Trials (CONSORT) Flow Diagram. (*All 86 patients in the robotic group were included in the ITT analysis; #All 85 patients in the open group were included in the ITT analysis).

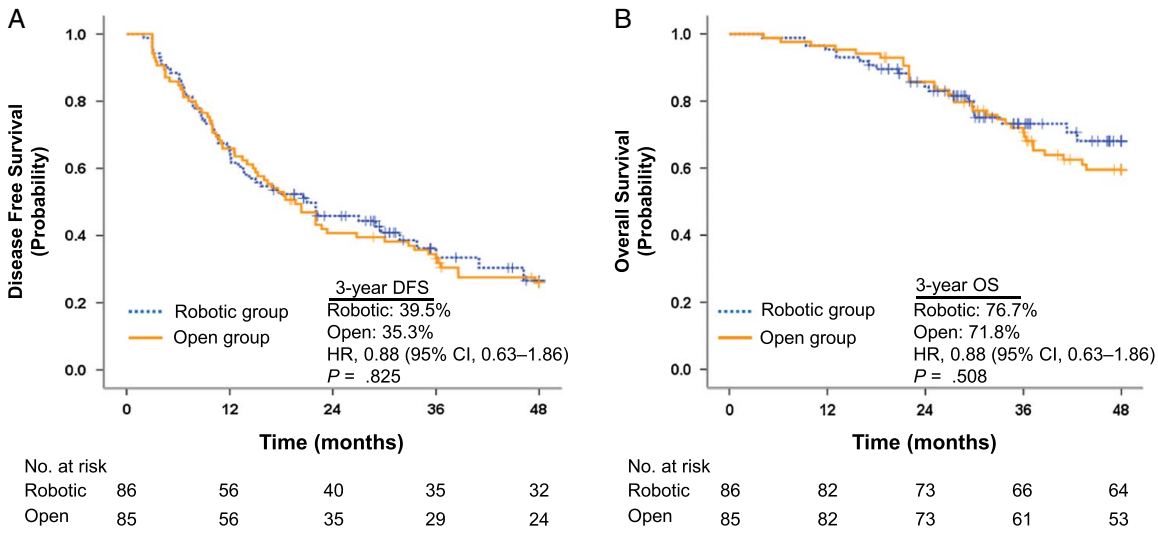

Figure 2. Kaplan–Meier survival curves. Kaplan–Meier survival curves of both groups on DFS (A); Kaplan–Meier survival curves of both groups on OS (B). DFS, disease-free survival; HR, hazard ratio; OS, overall survival.

Operative techniques

Photos of the dissection of the No.253 lymph nodes during the surgery, the complete surgical specimen (liver and rectum), the flattening of the resected mesorectum, and the inside and outside of the dissected specimen were taken and uploaded to review surgical quality. All photos of the specimen were taken with a ruler. Unedited video recordings were required for all operations and were uploaded to review the surgical process and quality. All photos and videos were uploaded within 6 months after surgery.

Rectum resection

The single-docking technique with four or five ports was used as described in our previous studies[3,12]. A detailed description of the robotic surgical procedures was shown in Figure S1 (Supplemental Digital Content 4, http://links.lww.com/JS9/B138). We performed high dissection and low ligation for treatment of No.253 lymph node and preserved the left colic artery during both robotic and open surgery. Once the sigmoid colon, mesocolon, entire rectum, and mesorectum were completely mobilized, anterior resection with the double-staple technique or abdominoperineal resection was performed subsequently. We used the 'PST' technique (Preservation of the left colic artery, Stitching reinforcement of anastomosis, and Transanal drainage tube) routinely, which significantly reduce the incidence rate of anastomotic leak[12].

Liver resection

The detailed surgery step was shown in Figure S2 (Supplemental Digital Content 5, http://links.lww.com/JS9/B139). Lesions located in the peripheral segments of the liver were considered for segmental or nonanatomic resection. Patients requiring a hemihepatectomy are considered suitable for the robotic approach when the lesions are not involved in the transaction plane and major structures (vena cava).

Outcomes

All case record forms were gathered and stored in the EasyClinical Information Management System (Hangzhou, Zhejiang Province, China). The primary endpoint of this study was surgical complication within 30 days after surgery, and the secondary endpoints included DFS, OS, urinary and sexual function by intent-to-treat analysis. DFS was calculated from the date of randomization to the date of tumor recurrence or death from any cause. OS was defined as the time from randomization to the date of death from any cause. Bladder function and sexual function were measured at baseline, 3 and 6 months following surgery according to the International Prostate Symptom Score (IPSS)[13], International Index of Erectile Function (IIEF)[14], and Female Sexual Function Index (FSFI)[15]. The first questionnaire was filled preoperatively in our wards as baseline data. Subsequently, the questionnaire was filled out again during outpatient follow-up at 3 and 6 months after surgery. Before filling out the questionnaire, doctors will provide guidance and explanations to patients and their families. Patients and their families must fully understand the questions in the questionnaire before filling it out. The completed questionnaire will be collected and registered by specialized personnel. Time of first flatus passage: time from the finish of surgery to the first flatus emission reported by the patient or the first time the stoma bag is obviously inflated (recorded in hour); Time of liquid diet: time from the finish of surgery to the first taking fluid diet (recorded in hour); Time of remove urinary catheter: time from the finish of surgery (we put the urinary catheter after anesthesia) to the first time patient can control the urination by himself and remove the urinary catheter (recorded in hour); Postoperative hospital staystime from the finish of surgery to the discharge (recorded in day), including the time readmission within 30 days after the surgery; Total hospital cost: all costs related to the treatment will be classified and counted, including examination, surgery, medication, nursing, etc. once admitted; Postoperative hospital cost: all costs related to the treatment will be classified and counted, including examination, medication, nursing, etc. from the finish of surgery.

Surgical complications

The surgical complications were recorded and classified according to the Clavien–Dindo system[16]. Only complications of Grade II or higher were registered and analyzed in this study. Major complications of grade III or IV include: (1) Major gastrointestinal complications: bowel obstruction requiring reoperation, anastomotic leakage requiring percutaneous drainage or reoperation, intestinal necrosis, peritonitis, and intra-abdominal abscess; (2) Major hepatic complications: bile leakage requiring percutaneous drainage or reoperation, subphrenic effusion requiring percutaneous drainage or reoperation, and severe liver failure defined by Factor V less than 30% on postoperative day-3; (3) Major respiratory complications: pleural effusion requiring percutaneous drainage or reoperation, respiratory distress requiring intubation; (4) Major cardiac complications: congestive heart failure, or myocardial infarction; (5) Major urinary complications: ureterostenosis requiring stent or operation, renal insufficiency requiring dialysis; 6) Major general complications: intraoperative or postoperative hemorrhage requiring transfusion at least 1 blood unit transfusion or reoperation, surgical site infection requiring debridement and suturing, or reoperation.

Randomization and blinding

This study used a randomized, parallel design. A sample size of 176 patients (assume 10% lost) was calculated on the basis of the assumptions of a surgical complication rate of 55% in the open group, and 35% in the robotic group, with a value of 0.05, and statistical power of 80% and one-sided P values on the basis of the Z test.

Patients were randomly assigned into the robotic group and the open group at a ratio of 1:1. The block randomization method is used in this trial with a block size of six. No stratified method is used. Random sequences for each block were generated by the computer (using the RAND function, Microsoft Excel software).

This study was not blinded and all the patient were informed about the surgical approach before surgery.

Statistical analysis

Patient baseline characteristics and outcome factors were summarized and calculated using descriptive statistics. A Student t-test was used for the continuous variable data analysis. The Pearson x^2 test or Fisher exact test was used to analyze the categorical parameters, as appropriate. According to the Kaplan–Meier method and the log-rank test, survival statistics on time-to-event variables were calculated and compared. SPSS software (version 19.0; SPSS) was used for statistical analyses. The tests were considered significant when a P-value of less than 0.05 was obtained. We used a COX regression model to assess risk factors for surgical complications, a multivariate model including factors that were statistically significant ($P < 0.05$) in a univariate analysis.

Results

Patient baseline characteristics

A total of 171 patients were enrolled in this trial between January 2016 and May 2019. Of all the patients, 86 patients were randomly assigned to the robotic group and 85 patients to the open group, and all were then assembled in the intent-to-treat (ITT) population accordingly. Among the ITT population, three patients in the robotic group were transferred to open surgery and one patient in the open group was lost during the follow-up period (Fig. 1). Patient clinical characteristics at baseline were similar between the two groups (Table 1). 44 (51.2%) of 86 patients in the robotic group and 45 (52.9%) of 85 patients in the open group had tumors located in the middle-low rectum. 20 patients (23.2%) in the robotic group and 18 patients (21.1%) in the open group received preoperative radiotherapy or chemoradiotherapy. The median follow-up time of the entire trial was 36 months, ranging from 8 to 52 months.

Table 1

Patient baseline characteristics.[a]

Variable baseline	Robotic surgery ($n = 86$)	Open surgery ($n = 85$)
Age, mean (SD), year	65.5 (11.93)	64.4 (10.98)
ASA classification, No. (%)		
I	51 (59.3)	55 (64.7)
II	33 (38.4)	28 (32.9)
III	2 (2.3)	2 (2.4)
Sex, No. (%)		
Male	56 (65.1)	59 (69.4)
Female	30 (34.9)	26 (30.6)
BMI, mean (SD), kg/m^2	23.7 (2.7)	23.9 (2.1)
Preoperative adjuvant therapy, No. (%)[b]	20 (23.2)	18 (21.1)
CRS scores, No. (%)[c]		
< 3	60 (69.8)	62 (73.0)
≥ 3	26 (30.2)	23 (27.0)
CEA at diagnosis, ng/ml,		
< 5	24 (27.9)	22(25.8)
≥ 5	62 (72.1)	63(74.2)
Height of tumor from anal verge, No. (%)		
High rectum, > 10–15 cm	42 (48.8)	40 (47.1)
Middle rectum, > 5–10	20 (23.3)	19 (22.4)
Low rectum, ≤ 5 cm	24 (27.9)	26 (30.5)
Liver metastases location		
1 segment	52 (60.5)	50 (58.8)
2 segments	24 (27.9)	23 (27.1)
3 segments	10 (11.6)	12 (14.1)

[a]There were no significant differences between the groups.
[b]Patients accepted chemoradiotherapy or chemotherapy before operations.
[c]CRS (clinical risk score) included five clinical criteria—nodal status of primary, disease-free interval from the primary to discovery of the liver metastases of <12 months, number of tumors >1, preoperative CEA level >200 ng/ml, and size of the largest tumor >5 cm as reported in Fong's work. (Fong *et al.* 1999[17]).
ASA, American Society of Anesthesiologists; CEA, carcino-embryonic antigen; CRS, clinical risk score.

Surgical complications

Table 2 shows the complication rates monitored up to 30 days postoperatively. Of 171 patients, 76 patients (44.4%) had surgical complications: 27 (31.4%) in the robotic group and 49 (57.6%) in the open group ($P = 0.014$). The most common surgical complications were pleural effusion (12.2%) and surgical site infection (10.5%). Overall, 24 patients (14.0%) reported a major complication (grade III/IV): 7 (8.1%) in the robotic group and 17 (20%) in the open group ($P = 0.029$). No mortality was seen in either group within 30 days after surgery. Rehospitalization was a rare event, among of them, three patients (3.5%) in the robotic group were hospitalized due to have

Table 2
Surgical complications.

Variable	Robotic surgery ($n=86$)	Open surgery ($n=85$)	P
Overall, *n* (%)	27 (31.4)	49 (57.6)	0.014*
Gastrointestinal complications			
Bowel obstruction	2	4	
Anastomotic leakage	3	3	
Intestinal necrosis	0	0	
Peritonitis	0	0	
Intra-abdominal abscess	0	0	
Hepatic complications			
Bile leakage	0	1	
Subphrenic effusion	6	8	
Severe liver failure	0	0	
General complications			
Hemorrhage	2	3	
Surgical site infection	5	13	
Respiratory complications			
Pleural effusion	7	14	
Respiratory distress	0	0	
Cardiac complications	1	1	
Urinary complications	1	2	
Major complications, n (%)[a]	7 (8.1)	17 (20)	0.029*
Mortality, *n* (%)	0 (0)	0 (0)	1.000
Reoperation, *n* (%)[b]	1 (1.2)	3 (3.5)	0.305
Rehospitalization, *n* (%)[c]	3 (3.5)	5 (5.9)	0.874

We collected the complications, mortality, rehospitalization events in 30 days after surgery.
*Statistically significant ($P<0.05$).
[a]The surgical complications were recorded and classified according to the Clavien–Dindo system. Major complications includes grade III or IV complications.
[b]One patient had transverse colostomy within 30 days because of anastomotic leak in the robotic group; and Two patients had transverse colostomy because of anastomotic leak and one patient had exploratory laparotomy due to bleeding in the open group.
[c]Three patients re-admitted within 30 days because of anastomotic leak in the robotic group, and five patients suffered gastrointestinal bleeding and small bowel obstruction in the open group.

Table 3
Pathological outcomes.

Variable	Robotic surgery ($n=86$)	Open surgery ($n=85$)	P
pT stage, No. (%)			0.813
1	9 (10.5)	7 (8.2)	
2	40 (46.5)	38 (44.7)	
3	37 (43.0)	40 (47.1)	
pN stage, No. (%)			0.831
0	32 (37.2)	28 (32.9)	
1	40 (46.5)	43 (50.6)	
2	14 (16.3)	14 (16.5)	
Lymph node yield, Mean (SD), No.	24.1 (12.9)	23.2 (11.9)	0.936
R0 resection for rectum, No. (%)	86 (100)	85 (100)	1
Quality of mesorectum, No. (%)[a]			0.592
Complete	78 (90.7)	79 (92.9)	
Near complete	8 (9.3)	6 (7.1)	
Incomplete	0 (0)	0 (0)	
Maximal tumor size, Mean (SD), cm			
Rectum	4.1 (1.3)	4.3 (1.4)	0.924
Liver	3.4 (2.3)	3.4 (1.8)	1
R0 resection for Liver, No. (%)	86 (100)	85 (100)	1
Resection margin of liver, Mean (SD), cm	1.2 (0.7)	1.4 (0.7)	0.873

[a]According to Quirkes' criteria.

anastomotic leakage, and five patients (5.9%) suffering from anastomotic leakage, gastrointestinal bleeding or small bowel obstruction in the open surgery group.

Pathological outcomes, operative findings, and short-term outcomes

The pathological outcomes are shown in Table 3. There was no statistically significant difference between the two groups in lymph node yield, quality of mesorectum, and radical resection rate.

The detailed operative findings and short-term outcomes were shown in Table 4. In the ITT analysis, the mean operative time was 33.2 min longer in the robotic group than in the open group [mean (SD), 314.7 (82.6) vs. 281.5 (67.9) minutes; $P=0.007$]. After adjusting the extra time required for surgical instrument installation, the mean operative time between groups did not differ significantly [mean (SD), 288.3 (79.1) vs. 281.5 (67.9) minutes; $P=0.17$]. Mean blood loss was 125.5 (38.3) ml [mean (SD)] during robotic surgery and 211.6 (68.7) ml [mean (SD)] during open surgery ($P<0.001$). The first bowel movement occurred as early as the third day after robotic surgery, which is 30.1 h ahead of the open surgery group ($P<0.001$). Oral intake of more than 1 l of fluid was tolerated in the robotic surgery group at 17.6 h earlier ($P<0.001$). The median time of hospital stay after robotic surgery was 8 days, which is 2.7-day shorter than that after open surgery ($P<0.001$). The total hospital cost of the robotic group needed an additional 2472.9 US dollars when compared with open surgery ($P<0.001$), whereas the robotic group had fewer hospital costs after surgery (mean, 5261.6 vs. 5649.1 US dollars, $P<0.001$). In addition, robotic surgery had better recovery as evaluated by hematological biomarkers at days 1, 3, and 5 after surgery (Table S1, Supplemental Digital Content 8, http://links.lww.com/JS9/B142). In the robotic group, the serum levels of C-reactive protein (CRP), alanine aminotransferase (AST), and aspartate aminotransferase (ALT) were significantly lower than the open group at 1, 3, and 5 days after surgery ($P<0.01$), respectively. Furthermore, the robotic surgery resulted in an improved pre-albumin (PA) level at 5 days after surgery when compared with open surgery ($P<0.001$).

Postoperative bladder and sexual function

Patient self-reported assessment of bladder function at baseline, 3 months and 6 months postsurgery was complete in 155 out of 171 cases (90.6%). Patient self-reported assessment of sexual function was complete in 72.2% of the men (83 out of 115) and 76.8% of the women (43 out of 56). Data presented in Figure S3 (Supplemental Digital Content 6, http://links.lww.com/JS9/B140) include IPSS scores for bladder function (with higher scores indicating worse function on a scale of 0–35), the FSFI scores for female sexual function (with higher scores indicating better function on a scale of 2–36), and IIEF scores for male sexual function (with higher scores indicating better function on a scale of 5–75) for robotic and open surgery at baseline, 3 and 6 months. The 3-month scores of IPSS showed the robotic surgery offered better bladder function than the open group [mean (SD) IPSS score, 5.8 (1.4) vs. 7.9 (1.8); $P=0.02$]. In addition, the robotic group have better sexual function preservation for both male and female patients at 3 months after surgery when

Table 4

Operative findings and short-term outcomes.

Variable	Robotic surgery ($n=86$)	Open surgery ($n=85$)	P
Type of rectum surgery, No. (%)			0.704
High anterior resection	42 (48.8)	40 (47.1)	
Low anterior resection	30 (34.9)	27 (31.8)	
Abdominoperineal resection	14 (16.3)	18 (21.1)	
Type of liver surgery, No. (%)			0.738
Wedge resection	50 (58.1)	45 (52.9)	
Segmentectomy	30 (34.9)	32 (37.6)	
Hemihepatectomy	6 (7.0)	8 (9.5)	
Protective Stoma, No. (%)	1 (1.2)	1 (1.2)	0.993
Conversion to open	3 (3.5%)	/	0.082
Operative time, Mean (SD), min	314.7 (82.6)	281.5 (67.9)	0.007
Estimated blood loss, Mean (SD), ml	125.5 (38.3)	211.6 (68.7)	< 0.001
Blood transfusion, *n* (%)	2 (2.3)	1 (1.8)	0.874
Time of first flatus passage, Mean (SD), hour	63.7 (27.4)	93.8 (33.5)	< 0.001
Time of liquid diet, Mean (SD), hour	14.2 (10.7)	31.8 (20.4)	< 0.001
Time of remove urinary catheter, Mean (SD), hour	77.8 (36.2)	84.5 (50.3)	0.384
Postoperative hospital stays, Mean (SD), day	8.0 (2.2)	10.7 (5.4)	< 0.001
Total hospital cost, Mean (SD), US dollar	13,272.5 (2393.2)	10,799.6 (3204.1)	< 0.001
Postoperative hospital cost, Mean (SD), US dollar	5,261.6 (1,0234)	5,649.1 (1,273.8)	< 0.001
Time to start adjuvant chemotherapy			0.026
< 4 weeks	76	64	
≥ 4 weeks	10	21	
Cycles of adjuvant chemotherapy			0.131
None	1	1	
< 6	4	9	
6–12	81	73	

compared with the open group [mean (SD) IIEF scores, 22.6 (2.5) vs. 12.5 (2.8), $P=0.001$; mean (SD) FSFI score, 7.7 (2.2) vs. 13.5 (2.9), $P=0.008$]. The IPSS, IIEF, and FSFI scores had no significant difference between both groups at 6 months after surgery. These data demonstrated that compared with open surgery, robotic surgery enabled patients to have faster recovery of bladder and sexual function from operation injury.

Disease-free survival and overall survival

Of the ITT population, 115 of 171 (67.3%) suffered from treatment failures, defined as distant metastasis, local recurrence, or death. All other patients were censored at the time of the last follow-up. All the first relapse events are listed in Table S2 (Supplemental Digital Content 8, http://links.lww.com/JS9/B142), and no significant difference was found between the two groups (robotic surgery vs. open surgery: 61.6 vs. 67.1%). The Kaplan–Meier survival curves of all 171 patients are presented in Figure 2. Both the 3-year DFS and OS rate of the robotic group did not reach statistically significance to that of the open group [DFS: 39.5 vs. 35.3%, HR = 0.94 (95% CI: 0.64–1.36), $P=0.739$]; [OS: 76.7 vs. 72.9%, HR = 0.88 (95% CI: 0.63–1.86), $P=0.712$].

Discussion

Our study is the first randomized controlled trial that reports robotic simultaneous resection of rectal cancer and liver metastases had better short-term outcomes than traditional open surgery in reducing postoperative complications and accelerating postoperative recovery. Besides, long-term oncological outcomes did not reach statistically significance.

Traditionally, simultaneous resection of primary rectal cancer with liver metastases is performed by open surgery. It requires two incisions (shown in Figure S4A, Supplemental Digital Content 7, http://links.lww.com/JS9/B141) for adequate exposure to the operative field, which often leads to severe pain, more physical and psychological trauma for patients. Robotic surgery only requires an incision of 5–10 cm (Figure S4B, Supplemental Digital Content 7, http://links.lww.com/JS9/B141), or even no incision is needed when combined with the NOSES technology (Figure S4C, Supplemental Digital Content 7, http://links.lww.com/JS9/B141), which can be more esthetically pleasing with minimal trauma.

The primary endpoint was met as shown by a statistically significant decrease of surgical complications within 30 days after surgery. We showed that robotic surgery offers significantly decreased overall complication rates by 45.5% and major complication rates by 59.5% when compared with open surgery. The complication rates in our study were slightly higher than the previous retrospective studies due to the nature and type of clinical trials[8,9]. Compared with open surgery, robotic surgery has some advantages, like enlarged 3D vision and a flexible mechanical arm, which makes it more conducive to operate and to protect the vascular and neural[18,19]. This may be the technical reason why robotic surgery reduces postoperative complications. Besides, it has been reported that robotic surgery had the advantages of a quick recovery of bowel functions and an earlier postoperative discharge,[20] consistent with the current study.

The previous reports that robotic surgery offered short-term benefits over open surgery in rectal or liver surgery[3,7,21]. Our recent study showed robotic surgery for rectal cancer had lower postoperative complication, a higher rate of sphincter preservation, and a shorter duration of hospitalization, than that of the laparoscopic group[14]. Here, in this study, we demonstrated that robotic simultaneous resection of SCRLM arrived at a faster recovery of bowel movement with less blood loss. As for function preservation, our results showed the robotic surgery preserved better bladder and sexual function than open surgery at 3 months after surgery, suggesting that the surgeons using the robotic system could offer a high-quality autonomic nerve preservation operation, which is also supported by some previous studies[22–24].

Previous results suggest that robotic surgery is unlikely to be cost-saving[3,11]. In the current study, the total hospital costs of robotic surgery needed an additional 2472.9 US dollars, but it led to a faster recovery and a shorter hospital stay. As many large health economics analyses have shown[25,26], like any other new technology, the use of robotic surgery resulted in added costs but also brought actual benefits to patients. Therefore, making the absolute result might depends on the specific setting and long-term follow-up.

In terms of oncologic outcomes, which was one of the secondary endpoints of our study. The DFS rates at 3 years in our study were 39.5% after robotic surgery and 35.3% after open

surgery ($P = 0.825$), and OS rates of both groups were 76.7 and 71.8%, respectively ($P = 0.508$), which did not reach the significant statistical test between the two group. The result need to be interpreted carefully due to our study design and limited sample size. Whether robotic surgery can be superior to open surgery in oncologic outcome of SCRLM remains to be proved in further study.

The limitations of this study may include that it is a single-center study with a limited sample size, patients enrolled had limited liver metastases.

In conclusion, for patients with SCRLM, robotic surgery reduced surgical complications and had a faster recovery than open surgery. And oncological outcomes showed no significant difference between the two groups. When performed by experienced surgeons in selected patients, the robotic surgery is a feasible approach in simultaneous resection of rectal cancer and liver metastases.

Ethical approval

Ethical approval for this study was provided by the Ethical Committee of Zhongshan Hospital Fudan University, Shanghai, China on 20 December 2015 (B2015-124R2).

Consent

The study was approved by the Ethics Committee of Zhongshan hospital (B2015-124R2) and complied with the standards of the Declaration of Helsinki. All patients provided informed consent. Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Sources of funding

This trial was funded by the National Natural Science Foundation of China (82072653, 81602035); Clinical Research Plan of SHDC (No. SHDC2020CR5006); Shanghai Science and Technology Committee Project (19511121300); Clinical Research Plan of SHDC (No. SHDC2020CR3037B); Fujian Provincial Health Commission Project (2021GGB032); Xiamen Science and technology Agency program (3502Z20224ZD1067).

Author contributions

W.J.C., Q.H.Y., X.Y.W., and J.M.X.: concept and design; Y.L., S.Z.Z., L.R., G.D.H., G.F.Z., F.L., Y.W., X.Y.W., and J.M.X.: acquisition, analysis, or interpretation of data; W.J.C., Q.H.Y., Y.L., S.Z.Z., D.H.X., and F.L.: drafting of the manuscript; W.J.C., X.Y.W., and J.M.X.: critical revision of the manuscript for important intellectual content; F.L. and W.J.C.: statistical analysis; L.R., G.D.H., G.F.Z., F.L., and Y.W.: administrative, technical, or material support; J.M.X.: supervision.

Conflicts of interest disclosures

None.

Research registration unique identifying number (UIN)

1. Name of the registry: ClinicalTrials.gov.
2. Unique identifying number or registration ID: NCT02642978.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://clinicaltrials.gov/ct2/show/NCT02642978?term=NCT02642978&draw=2&rank=1.

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Data availability statement

Dr Jianmin Xu had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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