Prospective Cohort Study

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Influence of surgical start time on the quality of surgery for middle and low rectal cancer: a post hoc analysis of the real trial

Guodong He, PhD[a,b], Zhuojian Zhang, MM[a], Weitang Yuan, MD[c], Taiyuan Li, PhD[d], Bo Tang, PhD[e], Baoqing Jia, PhD[f], Yanbing Zhou, PhD[g], Wei Zhang, PhD[h], Ren Zhao, PhD[i], Cheng Zhang, PhD[j], Longwei Cheng, MD[k], Xiaoqiao Zhang, PhD[l], Fei Liang, PhD[m], Ye Wei, PhD[n], Qingyang Feng, MD[a,b,*], Jianmin Xu, PhD[a,b,*]

Background: Surgical start time is considered to influence the quality of surgery due to surgeon fatigue. High-quality studies on middle and low rectal cancer are lacking. The analysis aims to find out the influence of surgical start time on the quality of surgery for middle and low rectal cancer, and whether robotic surgery could avoid the influence.

Materials and methods: This study was a post hoc analysis of the REAL (robotic vs. laparoscopic surgery for middle and low rectal cancer) study, a multicenter, randomized, controlled, unblinded, parallel group, superiority trial. This analysis included the modified intention-to-treat population of the REAL study, who were divided into Group I (the surgeon's first surgery of the day), Group II (the surgeon's second surgery of the day), and Group III (the surgeon's third and subsequent surgeries of the day) based on surgical information registered in the REAL study. The primary outcome was the percentage of patients with a positive circumferential resection margin. The second outcomes were the macroscopic completeness of resection the incidence of intraoperative complications and 30-day postoperative complications.

Results: A total of 1171 patients from the REAL study were included and divided into three groups: 547 (46.7%) in Group I (the surgeon's first surgery), 420 (35.9%) in Group II (the surgeon's second surgery), and 204 (17.4%) in Group III (the surgeon's third and subsequent surgeries). There was a lower percentage of circumferential resection margin (CRM)-positive patients in Group I (3.9%) than in Group II (6.6%, unadjusted $P = 0.069$) and Group III (8.1%, unadjusted $P = 0.027$, adjusted $P = 0.081$). Group I also had fewer intraoperative complications (5.3%) than Group II (8.3%, unadjusted $P = 0.060$) and Group III (9.3%, unadjusted $P = 0.046$, adjusted $P = 0.138$). Macroscopic completeness of resection was not significantly different among the three groups (complete rate: Group I vs. Group II, 94.9% vs. 92.4%, unadjusted $P = 0.254$; Group I vs. Group III, 94.9% vs. 92.6%, unadjusted $P = 0.334$; Group II vs. Group III, 92.4% vs. 92.6%, unadjusted $P = 0.488$). The incidence of 30-day postoperative complications showed no significant difference among the three groups (Group I vs. Group II, 18.5% vs. 20.0%, unadjusted $P = 0.547$; Group I vs. Group III, 18.5% vs. 22.1%, unadjusted $P = 0.268$; Group II vs. Group III, 20.0% vs. 22.1%, unadjusted $P = 0.551$). The quality of robotic surgery was not significantly influenced by surgical start time. For laparoscopic surgery, Group I had a lower CRM positivity rate (4.3%) than Group II (9.4%, unadjusted $P = 0.029$, adjusted $P = 0.087$) and Group III (10.4%, unadjusted $P = 0.031$, adjusted $P = 0.047$).

Conclusion: According to this post hoc analysis of the REAL study, for middle and low rectal cancer surgery, surgical start time could influence surgical quality by affecting surgeon fatigue. Surgeries start later in a day bring worse quality compared to those early in a day. Robotic surgery could reduce this influence to some extent, while laparoscopic surgery is more susceptible.

Keywords: quality of surgery, rectal cancer, robotic surgery

[a]Department of Colorectal Surgery, Zhongshan Hospital Fudan University, Shanghai, China, [b]Shanghai Engineering Research Center of Colorectal Cancer Minimally Invasive, Shanghai, China, [c]Department of Colorectal Surgery, The First Affiliated Hospital of Zhengzhou University, Zhengzho, Henan Province, China, [d]Department of General Surgery, The First Affiliated Hospital of Nanchang University, Nanchang, Jiangxi Province, China, [e]Department of General Surgery, Southwest Hospital, Army Medical University, Chongqing, China, [f]Department of General Surgery, The First Medical Center, PLA General Hospital, Beijing, China, [g]Department of Gastrointestinal Surgery, The Affiliated Hospital of Qingdao University, Qingdao, Shandong Province, China, [h]Department of Colorectal Surgery, Changhai Hospital, Navy Medical University, Shanghai, China, [i]Department of General Surgery, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, [j]Department of General Surgery, Northern Theater Command General Hospital, Shenyang, Liaoning Province, China, [k]Second Department of Gastrointestinal Surgery, Jilin Cancer Hospital, Changchun, Jilin Province, China, [l]Department of General Surgery, Shandong Provincial Hospital affiliated to the Shandong First Medical University, Jinan, Shandong Province, China, [m]Department of Biostatistics, Zhongshan Hospital Fudan University, Shanghai, China and [n]Department of General Surgery, Huadong Hospital Fudan University, Shanghai, China

G.H. and Z.Z. contributed equally to this article.

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**Corresponding author. Address: Department of Colorectal Surgery, Zhongshan Hospital Fudan University, and Shanghai Engineering Research Center of Colorectal Cancer Minimally Invasive, No. 180 Fenglin Road, Shanghai 200032, China. E-mail: xujmin@aliyun.com (J. Xu); fqy198921@163.com (Q. Feng).*

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Introduction

Colorectal cancer is one of the most common malignancies worldwide. Laparoscopic surgery is widely recognized for the treatment of colon cancer. However, its efficacy for treating rectal cancer is still the subject of debate, mainly because of the potential for incomplete mesorectal excision and circumferential resection margin (CRM) positivity[1–3]. These findings are closely related to the quality of the total mesorectal excision (TME) procedure. Robotic surgery may be the solution to these problems[4,5]. We conducted a multicenter randomized controlled trial, the REAL study. The reported short-term outcomes revealed the significant advantages of robotic surgery over laparoscopy, such as a lower CRM positivity rate, lower postoperative complication rate, faster postoperative recovery, and shorter postoperative hospital stay[6].

Surgeons' fatigue is considered to affect the quality of surgery and has been reported previously for various types of surgery[7–9]. There are also a few reports on colorectal cancer, but all the previous studies were retrospective with a low level of evidence[10,11]. Additionally, previous studies have not analyzed colon and rectal cancer surgeries separately. Previous studies have shown that robotic surgery may reduce surgeon fatigue and thus improve surgical quality, but high-quality studies supporting such a notion are lacking[12–14].

When the protocols of the REAL study were designed initially, data of surgical start time was recorded, but the REAL study did not consider it as an outcome. When we were collecting and analyzing data of the REAL study, we found that quality of surgery might be influenced by the surgical start time. Therefore, we conducted this post hoc analysis using data from the REAL study to find out whether surgical start time could influence the quality of surgery, and compared with laparoscopic surgery, whether robotic surgery could reduce surgeon fatigue and improve surgical quality of middle and low rectal cancer.

HIGHLIGHTS

- The quality of surgery for rectal cancer is affected by surgical start time.
- Circumferential resection margin positivity, intraoperative and postoperative complications are influenced.
- Robotic surgery could avoid the influence of surgical start time to some extent.

Methods

Study design and participants

This study was a post hoc analysis of the REAL study. The REAL study is a multicenter, randomized, controlled, unblinded, parallel group, superiority trial comparing robotic surgery with conventional laparoscopic surgery for radical resection of middle and low rectal cancer. The REAL study was registered with ClinicalTrials.gov and was approved by the institutional review board and ethics committee of each participating center. All patients participated provided written informed consent. Surgical start time was not designed as an endpoint of the REAL study.

A total of 11 centers in eight provinces in China participated in the REAL study. Of the 11 centers in the study, only 2 centers had two chief surgeons participating. In the other nine centers, each center had only one chief surgeon participating. All chief surgeons participated in the REAL study work in the Department of General Surgery/Gastrointestinal Surgery/Colorectal Surgery in their hospital, and all of their operations were gastric or colorectal cancer surgeries.

The major inclusion criteria were as follows: middle (>5–10 cm from the anal verge) or low (≤5 cm from the anal verge) rectal cancer; aged 18–80 years; American Society of Anesthesiologists Classes I to III; histologically proven rectal adenocarcinoma; tumors assessed as cT1-T3 (the mesorectal fascia was not involved) N0-N1 or ycT1-T3 Nx after preoperative radiotherapy or chemotherapy (measured by enhanced pelvic MRI); no evidence of distant metastasis; no other malignancies in the medical history; and suitable for both robotic and laparoscopic surgery. Eligible patients were randomly assigned (1:1) to robotic and laparoscopic groups. All robotic surgeries used the da Vinci Si Surgery System.

The study population of this analysis was the entire modified intention-to-treat (mITT) population of the REAL study, defined according to the original assigned groups and excluding patients who did not undergo surgery or no longer met the inclusion criteria after randomization. Patients in this study were categorized into Group I (the surgeon's first surgery of the day), Group II (the surgeon's second surgery of the day), and Group III (the surgeon's third and subsequent surgeries of the day) based on surgical information registered in the REAL study.

For the same center, surgeries in 1 day were performed by the same surgeon consistently, and were divided into three groups according to the registered start time and order. For the convenience of operating room management, robotic surgery was scheduled to be performed on the same day, also was the laparoscopic surgery. This meant that in 1 day, all surgeries were robotic surgeries, or laparoscopic surgeries. There was no situation that robotic and laparoscopic surgeries performed in the same day. The volume of surgeries by each surgeon was balanced between the three groups (Supplemental Digital Content Table S1, available at: http://links.lww.com/JS9/E41).

This study was reported in line with the Strengthening the Reporting of Cohort Studies in Surgery criteria[15].

Outcomes

The primary outcome of this study was CRM positivity, which was defined as a CRM 1 mm or less from the tumor[16]. When calculating the CRM positivity rate, the denominator was the number of patients without a complete response of the primary tumor. The secondary outcomes were macroscopic completeness of resection, intraoperative complications, and 30-day postoperative complications. The macroscopic completeness of resection was defined as: complete (intact mesorectum with only minor irregularities of a smooth mesorectal surface. No defect is deeper than 5 mm, and there is no coning toward the distal margin of the specimen), nearly complete (moderate bulk to the mesorectum, but irregularly of the mesorectal surface.

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Moderate coning of the specimen is allowed. At no site is the muscularis propria visible, except for the insertion of the levator muscles), or incomplete (little bulk to mesorectum with defects down onto muscularis propria or very irregular CRM).

Statistical analysis

Data from the whole mITT population of the REAL study was used in this study. For categorical variables, the two-sided Pearson's χ^2 test or Fisher's exact test (expected frequency <5) was used, as appropriate. The difference in rate and the corresponding 95% CI were calculated using the Miettinen–Nurminen method. For continuous variables, Student's *t* test (normal distribution, reported as the mean and SD) or the Mann–Whitney *U* test (nonnormal distribution, reported as the median and interquartile range) was used, as appropriate. The difference in the median and the corresponding 95% CI were calculated using the Hodges–Lehmann method. SPSS version 26.0 was used for the statistical analyses. All *P* values were two-sided and were considered significant when they were less than 0.05. For multiple testing with *P* value <0.05, the Benjamini–Hochberg False Discovery Rate method was performed for adjustment.

Role of the funding source

This study was a post hoc analysis of the REAL study. The funders of the REAL study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. We declare no potential conflicts of interest.

Results

In this post hoc analysis, the study population included 1171 patients from the total mITT population of the REAL study. Patients were divided into three groups according to the surgical start time: 547 (46.7%) from the surgeon's first surgery (Group I), 420 (35.9%) from the surgeon's second surgery (Group II), and 204 (17.4%) from the surgeon's third and subsequent surgeries (Group III) (Fig. 1). The patients' clinical characteristics at baseline were similar among the three groups (Table 1). A total of 258 (47.2%) of 545 patients in Group I, 212 (50.5%) of 418 patients in Group II, and 95 (46.6%) of 208 patients in Group III had tumors located in the lower rectum. A total of 229 (41.9%) of 545 patients in Group I, 196 (46.7%) of 418 patients in Group II, and 86 (42.2%) of 208 patients in Group III received preoperative radiotherapy or chemoradiotherapy.

The outcomes are shown in Table 2. The CRM-positivity rate in Group I was 3.9%, lower than in Group II (6.6%, unadjusted $P = 0.069$) and in Group III (8.1%, unadjusted $P = 0.027$, adjusted $P = 0.081$). Group I also had lower intraoperative complication rate (5.3%) than Group II (8.3%, unadjusted $P = 0.060$) and Group III (9.3%, unadjusted $P = 0.046$, adjusted $P = 0.138$). The macroscopic completeness of resection was not significantly different among the three groups (complete rate: Group I vs. Group II, 94.9% vs. 92.4%, unadjusted $P = 0.254$; Group I vs. Group III, 94.9% vs. 92.6%, unadjusted $P = 0.334$; Group II vs. Group III, 92.4% vs. 92.6%, unadjusted $P = 0.488$). The incidence of postoperative complications showed no significant difference among the three groups (Group I vs. Group II, 18.5% vs. 20.0%, unadjusted $P = 0.547$; Group I vs. Group III, 18.5% vs. 22.1%, unadjusted $P = 0.268$; Group II vs. Group III, 20.0% vs. 22.1%, unadjusted $P = 0.551$). The other pathological outcomes are shown in Supplemental Digital Content Table S2, available at: http://links.lww.com/JS9/E41.

Data indicated that the quality of robotic surgery was not significantly influenced by the surgical start time (Table 3). The CRM percentage in Group I was 3.5%, while that in Group II was 3.9%

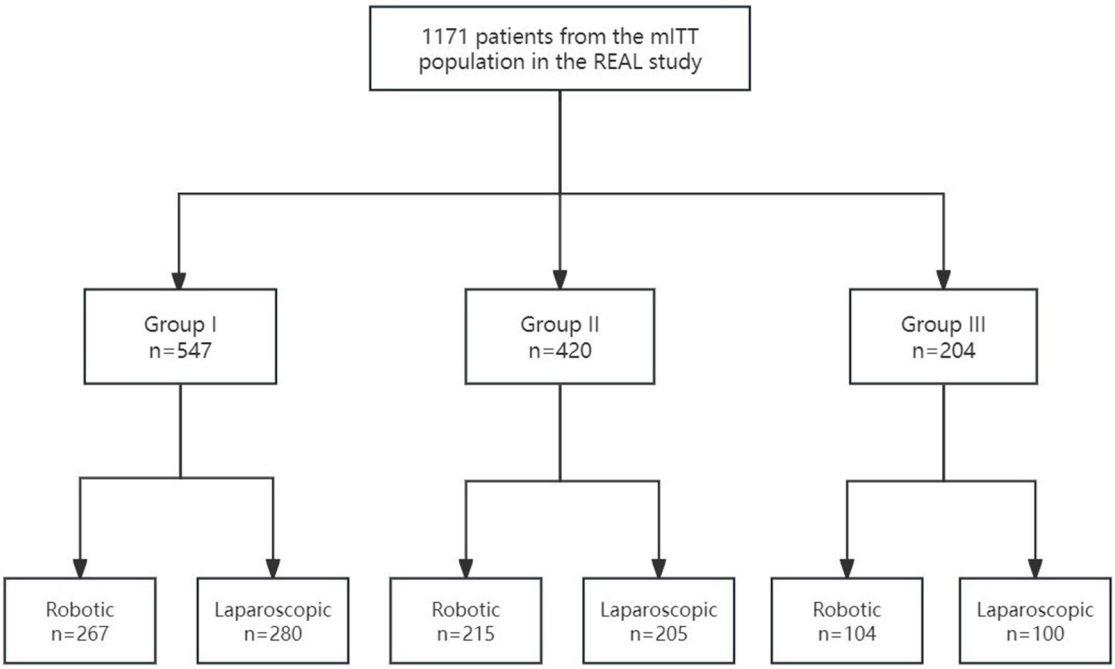

Figure 1. Trial profile. MITT, modified intent-to-treat, excluding patients who no longer met the inclusion criteria before or during the surgery or who did not undergo surgery.

Table 1

Clinical characteristics of the patients at baseline

	Group I (*n* = 547)	Group II (*n* = 420)	Group III (*n* = 204)	*P*
Sex				0.174
Male	327 (59.8%)	268 (63.8%)	115 (56.4%)	
Female	220 (40.2%)	152 (36.2%)	89 (43.6%)	
Age (SD), years	59.6 (10.6)	60.3 (10.1)	60 (10.8)	0.580
Body-mass index[a]				0.506
Mean (SD), kg/m^2	23.5 (3.3)	23.6 (3.2)	23.4 (3.2)	0.838
Underweight (<18.5 kg/m^2)	28 (5.1%)	20 (4.8%)	15 (7.4%)	
Normal (18.5–23.9 kg/m^2)	292 (53.4%)	207 (49.3%)	96 (47.1%)	
Overweight (24–27.9 kg/m^2)	184 (33.6%)	160 (38.1%)	79 (38.7%)	
Obese (≥28 kg/m^2)	43 (7.9%)	33 (7.9%)	14 (6.9%)	
American Society of Anesthesiology score				0.727
1	292 (53.4%)	236 (56.2%)	114 (55.9%)	
2	225 (41.1%)	167 (39.8%)	78 (38.2%)	
3	30 (5.5%)	17 (4.0%)	12 (5.9%)	
Comorbidity	200 (36.6%)	134 (31.9%)	67 (32.8%)	0.286
Hypertension	108 (19.7%)	75 (17.9%)	39 (19.1%)	0.758
Diabetes	46 (8.4%)	33 (7.9%)	16 (7.8%)	0.941
Cardiovascular diseases	35 (6.4%)	17 (4.0%)	11 (5.4%)	0.275
Cerebrovascular disease	19 (3.5%)	11 (2.6%)	5 (2.5%)	0.655
Pulmonary diseases	16 (2.9%)	5 (1.2%)	7 (3.4%)	0.122
Previous abdominal surgery	91 (16.6%)	83 (19.8%)	40 (19.6%)	0.397
Height of tumor from anal verge				0.516
Mean (SD), cm	5.9 (2.5)	5.7 (2.5)	5.9 (2.5)	0.329
Low rectum, ≤5 cm	258 (47.2%)	212 (50.5%)	95 (46.6%)	
Middle rectum, >5–10 cm	289 (52.8%)	208 (49.5%)	109 (53.4%)	
Preoperative radiotherapy or chemoradiotherapy	229 (41.9%)	196 (46.7%)	86 (42.2%)	0.294
Waiting period after radiotherapy				0.787
8–10 weeks	134 (24.5%)	117 (27.9%)	53 (26.0%)	
10–12 weeks	85 (15.5%)	70 (16.7%)	28 (13.7%)	
>12 weeks	10 (1.8%)	9 (2.1%)	5 (2.5%)	
Chemotherapy for waiting period after radiotherapy				0.572
Oral capecitabine	68 (12.4%)	51 (12.1%)	29 (14.2%)	
CAPEOX	95 (17.4%)	81 (19.3%)	31 (15.2%)	
FOLFOX	66 (12.1%)	64 (15.2%)	26 (12.7%)	
Clinical T stage				0.434
1–2	229 (41.9%)	174 (41.4%)	95 (46.6%)	
3	318 (58.1%)	246 (58.6%)	109 (53.4%)	
Clinical internal sphincter involvement	120 (21.9%)	98 (23.3%)	47 (23.0%)	0.866
Clinical N stage				0.277
0	387 (70.7%)	270 (64.3%)	143 (70.1%)	
1	125 (22.9%)	117 (27.9%)	49 (24.0%)	
2	35 (6.4%)	33 (7.9%)	12 (5.9%)	
Clinical TNM stage				0.196
I	190 (34.7%)	143 (34.0%)	75 (36.8%)	
II	197 (36.0%)	127 (30.2%)	68 (33.3%)	
III	160 (29.3%)	150 (35.7%)	61 (29.9%)	
Surgery method				0.732
Robotic	267 (48.8%)	215 (51.2%)	104 (51.0%)	
Laparoscopic	280 (51.2%)	205 (48.8%)	100 (49.0%)	

Data are *n* (%) unless otherwise specified.

[a]Classification according to the guidelines for the prevention and control of overweight and obesity in Chinese adults.

(Group I vs. Group II, unadjusted $P = 0.823$), and that in Group III was 5.6% (Group I vs. Group III, unadjusted $P = 0.406$). The incidence of intraoperative complications (Group I vs. Group II, 4.5% vs. 6.0%, unadjusted $P = 0.445$; Group I vs. Group III, 4.5% vs. 6.7%, unadjusted $P = 0.380$; Group II vs. Group III, 6.0% vs. 6.7%, unadjusted $P = 0.813$) and postoperative complications (Group I vs. Group II, 15.4% vs. 17.2%, unadjusted $P = 0.583$; Group I vs. Group III, 15.4% vs. 16.3%, unadjusted $P = 0.813$; Group II vs. Group III, 17.2% vs. 16.3%, unadjusted $P = 0.847$) did not significantly differ. Additionally, the difference in the completeness of resection was not related to the surgical start time (complete rate: Group I vs. Group II, 95.9% vs. 94.9%, unadjusted $P = 0.794$; Group I vs. Group III, 95.9% vs. 95.2%, unadjusted $P = 0.263$; Group II vs. Group III, 94.9% vs. 95.2%, unadjusted $P = 0.197$).

However, the statistical data from laparoscopic surgery showed different tendencies (Table 4). Group I had a lower percentage of CRM-positivity (4.3%) than Group II (9.4%, unadjusted

Table 2

Quality of surgeries at different surgical starting time

	Group I (*n* = 547)	Group II (*n* = 420)	Group III (*n* = 204)	Unadjusted *P* value (Group I vs. Group II)	Adjusted *P* value (Group I vs. Group II)	Unadjusted *P* value (Group I vs. Group III)	Adjusted *P* value (Group I vs. Group III)	Unadjusted *P* value (Group II vs. Group III)	Adjusted *P* value (Group II vs. Group III)
Circumferential resection margin ≤1 mm[a]	20/510 (3.9%)	26/394 (6.6%)	15/186 (8.1%)	0.069	··	0.027	0.081	0.520	··
Intraoperative complication[b]	29 (5.3%)	35 (8.3%)	19 (9.3%)	0.060	··	0.046	0.138	0.683	··
Macroscopic completeness of resection	··	··	··	0.254	··	0.334	··	0.488	··
Complete	519 (94.9%)	388 (92.4%)	189 (92.6%)	··	··	··	··	··	··
Nearly complete	19 (3.5%)	20 (4.8%)	12 (5.9%)	··	··	··	··	··	··
Incomplete	9 (1.6%)	12 (2.9%)	3 (1.5%)	··	··	··	··	··	··
Complications within 30 days after operation[c]	101 (18.5%)	84 (20.0%)	45 (22.1%)	0.547	··	0.268	··	0.551	··

Data are *n* (%) unless otherwise specified. Unadjusted *P* value: the original *P* value. Adjusted *P* value: Benjamini–Hochberg corrected *P* value.

[a]The denominator is patients without complete response of the primary tumor.

[b]Patients could have more than one intraoperative complication.

[c]Complications of Clavien–Dindo Grade II or higher grade. Patients could have more than one complication after operation.

P = 0.029, adjusted *P* = 0.087) and Group III (10.4%, unadjusted *P* = 0.031, adjusted *P* = 0.047). Intraoperative complications (Group I vs. Group II, 6.1% vs. 10.7%, unadjusted *P* = 0.062; Group I vs. Group III, 6.1% vs. 12.0%, unadjusted *P* = 0.055; Group II vs. Group III, 10.7% vs. 12.0%, unadjusted *P* = 0.741) and postoperative complications (Group I vs. Group II, 21.4% vs. 22.9%, unadjusted *P* = 0.694; Group I vs. Group III, 21.4% vs. 28.0%, unadjusted *P* = 0.181; Group II vs. Group III, 22.9% vs. 28.0%, unadjusted *P* = 0.334) increased with surgical duration, but not significantly. There was also no significant difference in the completeness of resection among the groups (complete rate: Group I vs. Group II, 93.9% vs. 89.8%, unadjusted *P* = 0.232; Group I vs. Group III, 93.9% vs. 90.0%, unadjusted *P* = 0.422; Group II vs. Group III, 89.8% vs. 90.0%, unadjusted *P* = 0.981).

Statistical data for robotic surgery and laparoscopic surgery from the same group were subsequently analyzed. The comparisons showed that, in Group I (Supplemental Digital Content Table S3, available at: http://links.lww.com/JS9/E41), the quality of surgeries was almost the same. However, in Group II (Supplemental Digital Content Table S4, available at: http://links.lww.com/JS9/E41), the percentages of CRM-positive patients were different between the robotic and laparoscopic

Table 3

Quality of robotic surgery in different surgical starting time

	Group I (*n* = 267)	Group II (*n* = 215)	Group III (*n* = 104)	Unadjusted *P* value (Group I vs. Group II)	Adjusted *P* value (Group I vs. Group II)	Unadjusted *P* value (Group I vs. Group III)	Adjusted *P* value (Group I vs. Group III)	Unadjusted *P* value (Group II vs. Group III)	Adjusted *P* value (Group II vs. Group III)
Circumferential resection margin ≤1 mm[a]	9/254 (3.5%)	8/203 (3.9%)	5/90 (5.6%)	0.823	··	0.406	··	0.547	··
Intraoperative complication[b]	12 (4.5%)	13 (6.0%)	7 (6.7%)	0.445	··	0.380	··	0.813	··
Macroscopic completeness of resection	··	··	··	0.794	··	0.263	··	0.197	··
Complete	256 (95.9%)	204 (94.9%)	99 (95.2%)	··	··	··	··	··	··
Nearly complete	7 (2.6%)	6 (2.8%)	5 (4.8%)	··	··	··	··	··	··
Incomplete	4 (1.5%)	5 (2.3%)	0	··	··	··	··	··	··
Complications within 30 days after operation[c]	41 (15.4%)	37 (17.2%)	17 (16.3%)	0.583	··	0.813	··	0.847	··

Data are *n* (%) unless otherwise specified. Unadjusted *P* value: the original *P* value. Adjusted *P* value: Benjamini–Hochberg corrected *P* value.

[a]The denominator is patients without complete response of the primary tumor.

[b]Patients could have more than one intraoperative complication.

[c]Complications of Clavien–Dindo Grade II or higher grade. Patients could have more than one complication after operation.

Table 4

Quality of laparoscopic surgery at different operative starting time

	Group I (*n* = 280)	Group II (*n* = 205)	Group III (*n* = 100)	Unadjusted *P* value (Group I vs. Group II)	Adjusted *P* value (Group I vs. Group II)	Unadjusted *P* value (Group I vs. Group III)	Adjusted *P* value (Group I vs. Group III)	Unadjusted *P* value (Group II vs. Group III)	Adjusted *P* value (Group II vs. Group III)
Circumferential resection margin ≤1 mm[a]	11/256 (4.3%)	18/191 (9.4%)	10/96 (10.4%)	0.029	0.087	0.031	0.047	0.789	··
Intraoperative complications[b]	17 (6.1%)	22 (10.7%)	12 (12.0%)	0.062	··	0.055	··	0.741	··
Macroscopic completeness of resection	··	··	··	0.232	··	0.422	··	0.981	··
Complete	263 (93.9%)	184 (89.8%)	90 (90.0%)	··	··	··	··	··	··
Nearly complete	12 (4.3%)	14 (6.8%)	7 (7.0%)	··	··	··	··	··	··
Incomplete	5 (1.8%)	7 (3.4%)	3 (3.0%)	··	··	··	··	··	··
Complications within 30 days after operation[c]	60 (21.4%)	47 (22.9%)	28 (28.0%)	0.694	··	0.181	··	0.334	··

Data are *n* (%) unless otherwise specified. Unadjusted *P* value: the original *P* value. Adjusted *P* value: Benjamini–Hochberg corrected *P* value.

[a]The denominator is patients without complete response of the primary tumor.

[b]Patients could have more than one intraoperative complication.

[c]Complications of Clavien–Dindo Grade II or higher grade. Patients could have more than one complication after operation.

surgery groups (3.9% vs. 9.4%, P = 0.028). In Group III (Supplemental Digital Content Table S5, available at: http://links.lww.com/JS9/E41), the rate of complications within 30 days after the operation was different (16.3% vs. 28.0%, P = 0.045).

Discussion

This post hoc analysis of the REAL study is the first to show the influence of surgical start time on the quality of surgery for middle and low rectal cancer.

The continuous development of minimally invasive surgery has led to laparoscopic and robotic surgery becoming the mainstays of surgery for colorectal cancer resection. However, utility of laparoscopic surgery for rectal cancer, especially for middle and low rectal cancer, remains a subject of debate. The REAL study showed that for middle and low rectal cancer patients, robotic surgery could lead to better macroscopic completeness of resection, a lower CRM positivity rate, and fewer intraoperative and postoperative complications than laparoscopic surgery. Therefore, robotic surgery could improve the quality of surgery[6]. In addition to three-dimensional visibility, a stable camera platform, and flexible robotic arms, robotic surgery is advantageous in reducing the likelihood of surgeon fatigue[17,18]. In robotic surgery, surgeons are seated for most of the major steps, which is more comfortable than standing as in laparoscopic surgery. Moreover, the robotic surgical system allows surgeons to operate comfortably, without having to prioritize sterility. In addition, the flexibility and feasibility of robotic surgery can reduce its difficulty and the surgeons' mental stress. Previous studies have also shown that robotic surgery can reduce surgeon fatigue in a variety of surgeries, including surgeries for colorectal cancer[19,20]. However, there is a lack of high-quality studies on surgical quality and surgeon fatigue.

In this study, the authors analyzed the data from 1171 surgeries for middle and low rectal cancer and revealed that the surgical start time can affect the quality of surgery, as evidenced by CRM positivity and the incidences of intraoperative and postoperative complications. The data suggest that patients who underwent surgeries scheduled at later times in the day are more likely to have CRM positivity as well as intraoperative and postoperative complications. CRM positivity and intraoperative and postoperative complications more frequently occurred in patients who underwent laparoscopic surgery and did not occur in those who underwent robotic surgery, suggesting that the quality of robotic surgery is less influenced by surgical start time compared to those of laparoscopic surgery.

We consider that compared to laparoscopic surgery, robotic surgery has some advantages in technology and surgical procedures. When using robotic system, the surgical fields are controlled by the chief surgeon him/herself, which could suit the demands with less delay and avoid the probable poor coordination between the chief surgeon and the assistant. What's more, robotic arms have small mechanical "joints," so they can turn with flexibility after being put into trocars. For patients with narrow pelvic spaces due to factors such as obese and small pelvis, robotic tools could give more space for surgeon to operate. Another possible reason is that robotic surgery allows surgeon to deal with part of the surgery without directly in touch with patients, which could improve efficiency by taking less time on asepsis. When tired, robotic system allows surgeon work while sitting on a chair, which laparoscopic surgery could not and surgeon always have to stand until all procedures are over. There are also studies reporting that learning robotic surgery could take less time compared with laparoscopics[21,22], which showed that robotic surgery could offer better opportunities for young surgeons to become professional.

This study is a post hoc analysis of REAL study. Considering that REAL study did not select and include patients according to

surgical start time, we cannot confirm that the conclusion applicable to all patients undergoing rectal cancer surgery. However, as the enrollment criteria of REAL study were relatively broad, we have included most of the patients with rectal cancer, which was also consistent with recommendations of guidelines. So we believe this conclusion could be applicable to most of middle and low rectal cancer surgeries. Also, compared to rectal cancer with high position and colon cancer, surgeries for middle and low rectal cancer are more difficult and lead to more fatigue. Thus application of robotic surgery in middle and low rectal cancer would show more advantages, which was agreed by previous studies.

This study has several limitations. First, this is a post hoc analysis of a previously designed clinical trial. When the clinical trial was designed, surgical start time was not taken into consideration as an outcome. Thus, the statistical efficacy of this post hoc analysis is limited. Also, in the clinical trial, we did not design for long-term complications as outcomes, and there was a lack of corresponding data. So only the influence of surgical start time on short-term outcomes was reported. As for the statistical analysis, there were factors that we could not deal with perfectly. We tried to avoid the influence of different work arrangements by grouping patients to each group. However, there were still confounders such as work before surgery, surgeons' status, surgeries with different difficulties, and so on, that we could not avoid. These may influence the conclusion. Also, since different patients have different anatomical configurations and past histories, certain conditions such as pelvic stenosis, abdominal adhesions, edema of the rectum, and vascular variations can cause greater difficulty in surgery, which take more time and energy from surgeons and cause more fatigue.

In conclusion, according to this post hoc analysis of the REAL study, for middle and low rectal cancer surgery, surgical start time could influence surgical quality by affecting surgeon fatigue. Surgeries start later in a day bring worse quality compared to those early in a day. Robotic surgery could reduce this influence to some extent, while laparoscopic surgery is more susceptible. However, the data of this study shows low statistical power. High-quality subsequent researches focusing on the relationship between surgical start time and quality of surgery are required.

Ethical approval

This study analyzed data from the REAL trial, which was approved by the institutional review board and ethics committee of each participating center. This trial was done in accordance with the ethical principles of the Declaration of Helsinki and Good Clinical Practice guidelines.

Consent

All patients provided written informed consent.

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Author contributions

G.H. and Z.Z. contributed equally to this article as co-first authors. Q.F., W.Y., T.L., B.T., B.J., Y.Z., W.Z., R.Z., C.Z., L.C., X.Z., G.H., Y.W. and J.X. contributed to the conception and design of the REAL study and the collection of data. G. H. and Z.Z. contributed to the design of this post hoc analysis, the methodology and writing the manuscript. Z.Z. and F. L. contributed to the statistical analysis. Q.F. contributed to reviewing and approving the manuscript for submission. J. X. had full access to all underlying data and had final responsibility for the decision to submit the paper for publication.

Conflicts of interest disclosure

Not applicable.

Research registration unique identifying number (UIN)

This study is a post hoc analysis of the REAL trial. The REAL trial was registered with ClinicalTrials.gov, number NCT02817126.

Guarantor

Qingyang Feng and Jianmin Xu had full access to all underlying data and had final responsibility for the decision to submit the paper for publication.

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Data availability statement

All text, tables, and figures in this article are available to other researchers. For meta-analysis of individual participant data, individual-level deidentified patient data will be available after review and verification. Researchers should contact the corresponding author Prof. Jianmin Xu (xujmin@aliyun.com) to request data, providing the corresponding study protocol and the certificate of the institution. These will be verified and approved by the review committee of the trial collaboration group. All data will be available beginning with publication and ending 60 months after publication.

Assistance with the study

None.

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