Ann Surg Oncol (2019) 26:4390–4396
https://doi.org/10.1245/s10434-019-07794-x

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – COLORECTAL CANCER

Safety of Single-Site Laparoscopic Surgery Requiring Perioperative Heparinization in Colorectal Cancer: Propensity Score-Matched Analysis

Kazuya Iwamoto, MD[1], Hidekazu Takahashi, MD[1], Makoto Fujii, MD[2], Naotsugu Haraguchi, MD[1], Taishi Hata, MD[1], Chu Matsuda, MD[1], Hirofumi Yamamoto, MD[1], Tsunekazu Mizushima, MD[1], Masaki Mori, MD[1,3], and Doki Yuichiro, MD[1]

[1]Department of Gastroenterological Surgery, Osaka University Graduate School of Medicine, Osaka, Japan; [2]Department of Mathematical Health Science, Osaka University Graduate School of Medicine Division of Health Sciences, Osaka, Japan; [3]Department of Surgery and Science, Kyushu University Graduate School of Medical Sciences, Osaka, Japan

ABSTRACT

Background. We assessed the feasibility and safety of single-site laparoscopic surgery for patients with colorectal cancer who required perioperative heparinization.

Methods. This retrospective study reviewed the medical records of 390 patients who underwent single-site laparoscopic surgery for colorectal cancer from January 2010 to December 2016. Antithrombotic drugs were stopped preoperatively and heparin was administered according to the operative risk of each patient, based on consultation with the cardiologist physician or neurosurgeon. Propensity score modeling was utilized to adjust for baseline characteristics.

Results. Of 390 patients, 29 were treated with standard bridging intravenous heparin therapy. Propensity matching identified 119 patients: 22 patients in the heparinization group and 97 in the control group. The matched groups were not significantly different in operation times, bleeding volumes, or conversion rate. The mean postoperative hospital stay was 17.9 days in the heparinization group and 9.5 days in the control group ($p = 0.034$). Postoperative bleeding was observed in 4 patients (18.2%) in the heparinization group and 11 patients (11.4%) in the control group ($p = 0.646$), while other complications were similar in the two study groups ($p = 0.502$). Of these other complications, thromboembolic events were observed in two patients in the heparinization group and one patient in the control group.

Conclusions. We found that single-site laparoscopic surgery for colorectal cancer with heparinization was feasible and safe. Heparinization did not increase the risk of postoperative bleeding complications, but postoperative hospital stay was prolonged.

The colectomy procedure for colorectal cancer has undergone advances over the years, particularly in minimally invasive surgery techniques.[1] The rising use of minimally invasive surgical approaches, including single-site laparoscopic colectomy, signals the start of a new age in the field of colorectal cancer surgery. Single-site laparoscopic colectomy was designed to minimize invasiveness, and is reportedly at least equivalent to conventional multiport laparoscopic colectomy with regard to safety, feasibility, postoperative pain, cosmetic outcome, postoperative delirium, length of hospital stay, and long-term outcomes.[2–5]

Recent reports have shown that complete mesocolic excision (CME) with central vascular ligation (CVL) was feasible and safe under laparoscopic settings.[6–8] In a previous study, we applied the principles of CME to single-site laparoscopic colectomy for colon cancer and confirmed the safety, feasibility, and oncological clearance efficacy of

Electronic supplementary material The online version of this article (https://doi.org/10.1245/s10434-019-07794-x) contains supplementary material, which is available to authorized users.

First Received: 1 May 2019;
Published Online: 6 September 2019

H. Takahashi, MD
e-mail: htakahashi@gesurg.med.osaka-u.ac.jp

this procedure.[2] Moreover, these procedures have been standardized.[9] Those findings suggested that to achieve better oncological outcomes, the principles of CME + CVL should be observed, regardless of the patient's condition.

Due to the aging of the population in recent years, the number of patients with cerebral infarction, atrial fibrillation, or ischemic heart disease has increased. Accordingly, the number of patients who receive antiplatelet and anticoagulation drugs has also increased, and these patients often require surgery. Because antithrombotic agents are associated with an increased risk of postoperative hemorrhage, the perioperative management of patients receiving antithrombotic therapy increases the difficulty of abdominal surgery. Studies have shown that heparinization for abdominal surgery could increase the risk of postoperative bleeding.[10-12] However, recent reports have shown that laparoscopic surgery was safe for patients who received antiplatelets or anticoagulants because it did not increase the risk of postoperative bleeding.[13,14]

Patients who undergo single-site laparoscopic surgery for colorectal cancer are often older and have comorbidities. It is not uncommon for these patients to be taking antiplatelet or anticoagulant therapy; however, even for these patients, surgery according to CME principles is necessary to improve oncological outcomes when performing single-site laparoscopic surgery with perioperative heparinization.

We evaluated the feasibility and safety of single-site laparoscopic surgery that conformed to a CME procedure for colorectal cancer in patients who required perioperative heparinization.

MATERIALS AND METHODS

Operative Procedures

Conventional multiport laparoscopic colectomy with CME was performed in a standard manner. Briefly, five ports, including the optical port, were placed. The first was the optical port, with a 12 mm trocar in the umbilicus, followed by one 12 mm trocar and three 5 mm trocars. For specimen extraction, the umbilical port was expanded to 2–5 cm, as previously described. According to a previous report, single-site laparoscopic colectomies were performed using standard laparoscopic instruments.[2] Briefly, a 2–3 cm extraction incision was performed in the umbilicus, and a multichannel access device, such as an EZ Access (Hakko, Nagano, Japan) or an SILS Port (Covidien, Mansfield, MA, USA), was fitted into the incision.

Patients and Data Collection

All experimental protocols described in this study were approved by the Institutional Ethical Review Committee (UMIN 15046-3: comprehensive agreement) and conform to the provisions of the Declaration of Helsinki. We retrospectively reviewed the medical records of 390 patients who underwent single-site laparoscopic surgery for colorectal cancer at our institution from January 2010 to December 2016. Of the 390 patients, 66 were taking anticoagulation and/or antiplatelet agents chronically for various comorbidities prior to surgery. A total of 29 patients received standard bridging intravenous heparin therapy (heparinization group) after consultation with the cardiologist physician or neurosurgeon who prescribed the antithrombotic drugs, and according to the operative risk of each patient. We compared the heparinization and untreated control groups with respect to patient background, perioperative characteristics, and postoperative outcomes. Postoperative complications were categorized using the Clavien–Dindo classification system, and we considered class III or higher as clinically significant.

Perioperative Management of Antithrombotic Drugs

When patients required perioperative heparinization, warfarin was stopped for 4 days, antiplatelet agents were stopped for 7 days, and direct oral anticoagulant drugs were stopped for 1 day before the planned surgery. Intravenous unfractionated heparin was started at 10,000–20,000 units per day. Intravenous unfractionated heparin was stopped 4 h before surgery and restarted 12–24 h after surgery, only after confirming the absence of any bleeding complications.

Definitions of Postoperative Bleeding

Bleeding was classified as major when at least one of the following occurred: fatal bleeding, retroperitoneal or intracranial bleeding, bleeding of critical organs (intraocular, adrenal, endocardial, or spinal bleeding), surgical-site bleeding that required surgical intervention, or clinically overt bleeding that caused at least a 20 g/L decline in hemoglobin or the need to transfuse $\geq$ 800 mL of red blood cells or whole blood. Minor bleeding was defined as bleeding that did not meet the major bleeding criteria.

Propensity Score Matching

Because the heparinization group was much smaller than the control group, an imbalance in crucial covariates related to outcomes could have biased the estimation of the heparinization effect. To adjust for these covariates, we

TABLE 1 Comparison of the characteristics of the two groups

	All patients (n =390)			Patient propensity matching (n =44)			Variable rate matching (n =119)		
	Control group (n =361)	Heparinization group (n =29)	p value	Control group (n =22)	Heparinization group (n =22)	p value	Control group (n =97)	Heparinization group (n =22)	p value
Sex, male/female (n)	194/167	19/10	0.221	13/9	15/7	0.530	58/39	15/7	0.466
Age, years (SD)	66.0 (11.7)	73.0 (8.9)	0.002	72.9 (8.7)	72.6 (9.3)	0.921	70.4(9.4)	72.6(9.3)	0.331
BMI, kg/m^2 (SD)	22.7 (3.3)	22.4 (2.1)	0.620	21.7 (2.8)	22.2 (1.8)	0.518	22.5(2.8)	22.2(1.8)	0.572
ASA score 1/2/3 (n)	173/179/9	3/14/12	< 0.0001	3/13/6	3/14/5	0.938	24/66/7	3/14/5	0.071
Site of disease (n)			0.005			0.741			0.885
Right-side colon	175	22		15	16		72	16	
Left-side colon	186	7		7	6		25	6	
Tumor size, mm (SD)	33.9 (20.6)	32.2 (23.2)	0.674	27.4 (19.8)	31.5 (24.3)	0.534	29.7 (17.5)	31.5 (24.3)	0.679
cT grade 1a/1b/2/3/4a/4b (n)	26/91/83/132/27/2	4/8/9/5/2/1	0.151	1/8/9/2/2/0	3/7/6/4/2/0	0.675	10/32/29/19/7/0	3/7/6/4/2/0	0.988
cStage 0/1/2/3a/3b/4 (n)	26/168/103/32/16/16	3/17/6/1/2/0	0.501	1/17/3/0/0/1	2/13/5/1/1/0	0.498	10/58/17/5/3/4	2/13/5/1/1/0	0.933
Previous abdominal surgery [n (%)]	116 (32.1)	9 (31.0)	0.903	9 (40.9)	6 (27.3)	0.340	34 (35.1)	6 (27.3)	0.486
Antithrombotic therapy Antiplatelet/anticoagulation/both (n)	32/5/0	17/10/2	< 0.0001	1/1/0	14/6/2	< 0.0001	11/3/0	14/6/2	< 0.0001

SD standard deviation, *BMI* body mass index, *ASA* American Society of Anesthesiologists

performed a propensity score (PS) analysis. The PS included 11 effective covariates, including age, sex, body mass index (BMI), history of previous abdominal surgery, smoking, alcohol, American Society of Anesthesiologists (ASA) score, tumor location, tumor size, clinical T stage, and lymphadenectomy. Each patient's PS was estimated using a logistic regression model, and we used the PS to match patients who received heparinization with corresponding control patients. For more plausible matching, we allowed duplicate matching (variable rate matching, maximum 7:1). The caliper width for PS matching was 0.2.

Statistical Analysis

Student's *t* test and Pearson's Chi square test were used for comparisons, as appropriate, and p values < 0.05 were considered significant. All statistical analyses were performed using JMP® Pro 13.1.0 (SAS Institute Inc, Cary, NC, USA).

RESULTS

Representative Case of Laparoscopic Surgery for Advanced Ascending Colon Cancer

Patients received a single, small (3 cm) laparotomy (electronic supplementary Fig. 1a). The surgeon confirmed that the CME was definitively completed (electronic supplementary Fig. 1b) and a CVL was performed at the root of the ileocolic artery and vein (electronic supplementary Fig. 1c). The operating time was 190 min and the estimated blood loss was 10 g. Resected specimens confirmed that the CME was properly completed (electronic supplementary Fig. 1d).

Patient Characteristics

Table 1 summarizes the clinical characteristics of the two groups. Among all 390 patients, age, ASA score, and disease site were significantly different between the control and heparinization groups. After variable-rate PS matching was performed to account for potential cohort biases, we analyzed a total of 119 patients (control: $n = 97$; heparinization: $n = 22$). The PS-matched groups showed no significant differences in sex, age, BMI, ASA score, disease site, tumor size, cT grade, cTNM stage, or abdominal surgery history.

Table 2 shows the characteristics of the 66 patients treated with antithrombotic agents. The indications for antithrombotic therapy were ischemic heart disease ($n = 20$), atrial fibrillation ($n = 14$), cerebral infarction ($n = 10$), internal carotid artery stenosis ($n = 9$), valvular heart disease ($n = 5$), arteriosclerosis obliterans ($n = 5$), deep vein thrombosis ($n = 3$), and lumbar spinal canal embolism ($n = 2$). Two patients in the heparinization group were treated with both antiplatelet and anticoagulant agents.

Short-Term Surgical Outcomes

The control and heparinization groups did not differ significantly, before or after PS matching, in operation time, blood loss, blood transfusion, or conversion rate (Table 3). The postoperative major bleeding events of the control and heparinization groups were seven (1.9%) and two (6.9%) cases, respectively. Details for bleeding events are shown in electronic supplementary Table 1. After propensity matching, the postoperative bleeding events, including minor bleeding, of each group were 11 (11.4%) and four (18.2%) cases ($p = 0.646$), respectively. In addition, the groups were not significantly different in Clavien–Dindo Class III or higher complications. Of these other complications, thromboembolic events were observed in two patients in the heparinization group (a pulmonary

TABLE 2 Data regarding the indication for antithrombotic therapy of the two groups

	All patients (n =66)	
	Control group (n =37)	Heparinization group (n =29)
Indication for antithrombotic therapy		
Ischemic heart disease	12	8
Atrial fibrillation	6	8
Cerebral infarction	7	3
Internal carotid artery stenosis	8	1
Valvular heart disease	1	4
Arteriosclerosis obliterans	1	4
Deep vein thrombosis	1	2
Lumbar spinal canal stenosis	1	1

TABLE 3 Comparison of perioperative and postoperative data of the two groups

	All patients (n =390)			Patient propensity matching (n =44)			Variable rate matching (n =119)		
	Control group (n =361)	Heparinization group (n =29)	p value	Control group (n =22)	Heparinization group (n =22)	p value	Control group (n =97)	Heparinization group (n =22)	p value
Operation time, min (SD)	207.1 (61.1)	203.3 (44.3)	0.742	191.1 (51.1)	204.4 (43.8)	0.359	199.6 (60.2)	204.4 (43.8)	0.727
Blood loss, mL (SD)	64.2 (137.1)	115.7 (338.0)	0.097	87.0 (166.6)	58.4 (61.4)	0.454	96.6 (222.1)	58.4 (61.4)	0.427
Blood transfusion [n (%)]	4 (1.1)	1 (3.5)	0.281	1 (4.6)	0 (0)	0.312	2 (2.1)	0 (0)	0.497
Conversion [n (%)]			0.834			0.635			0.864
Add port	33 (9.1)	3 (10.3)		3 (13.6)	2 (9.1)		10 (10.3)	2 (9.1)	
Open	4 (1.1)	0 (0.0)		0 (0)	0 (0)		0 (0)	0 (0)	
Postoperative stay, days (SD)	9.7 (7.1)	16.5 (32.4)	0.002	8.7 (3.0)	17.9 (37.1)	0.252	9.5 (5.8)	17.9 (37.1)	0.034
Postoperative bleeding events [n (%)]			0.120			0.199			0.646
Major bleeding	7 (1.9)	2 (6.9)		1 (4.6)	1 (4.6)		2 (2.1)	1 (4.6)	
Minor bleeding	39 (10.8)	5 (17.2)		0 (0)	3 (13.6)		9 (9.3)	3 (13.6)	
Comorbidities (Clavien–Dindo ≥ III) [n (%)]	11 (3.1)	2 (6.9)	0.267	1 (4.6)	1 (4.6)	1.000	2 (2.1)	1 (4.6)	0.502

SD standard deviation

embolism and a myocardial infarction) and one patient in the control group (a deep vein thrombosis). Only postoperative stay differed significantly between the two groups, both before and after propensity matching (before matching: 9.7 vs. 16.5 days, $p = 0.002$; after matching: 9.5 vs. 17.9 days, $p = 0.034$).

Long-Term Outcomes

The median follow-up period was 1308 days (range 28–3095). The 5-year cumulative survival rates of the heparinization and control groups were 82.0% and 88.3% ($p = 0.144$), respectively, before propensity matching, and 95.5% and 89.4% ($p = 0.651$), respectively, after propensity matching (Fig. 1). The 5-year cumulative recurrence-free survival rates of the heparinization and control groups were 85.2% and 81.9% ($p = 0.835$), respectively, before propensity matching, and 95.5% and 90.0% ($p = 0.694$), respectively, after propensity matching (Fig. 1). Thus, both before and after PS matching, the cumulative overall and recurrence-free survival curves did not show any significant effect of heparinization.

DISCUSSION

In this study, we evaluated how heparinization affected single-site laparoscopic surgery for colorectal cancer. We mainly assessed postoperative bleeding because recent reports that evaluated antiplatelet and anticoagulant therapy effects perioperatively in abdominal surgery demonstrated that the rates of stent/vessel thrombosis by heparinization were not significantly different.

In the present study, heparinization did not affect the operation time, blood loss, blood transfusion rate, or conversion rate. Although we observed a tendency toward more frequent postoperative bleeding and postoperative complications in the heparinization group, the differences between groups were not statistically significant. Moreover, after PS matching, these trends disappeared. The rate of major bleeding events of all patients was 2.3%, which is higher than the 0.95% in JCOG 0404.[15] This is because our study enrolled consecutive cases, which is considered to be different from JCOG 0404, which registered only healthy patients. In addition, ASA and PS were matched by PS, and those with worse general condition were compared with each other (the rate of patients with an ASA score of 1 before and after matching was 45.1% and 22.7%, respectively). Therefore, it is presumed that the major bleeding event was more observed in 3 of 119 patients (2.5%) after matching. Overall, among 66 patients who received antithrombotic therapy, one developed a pulmonary embolism and one developed a myocardial infarction

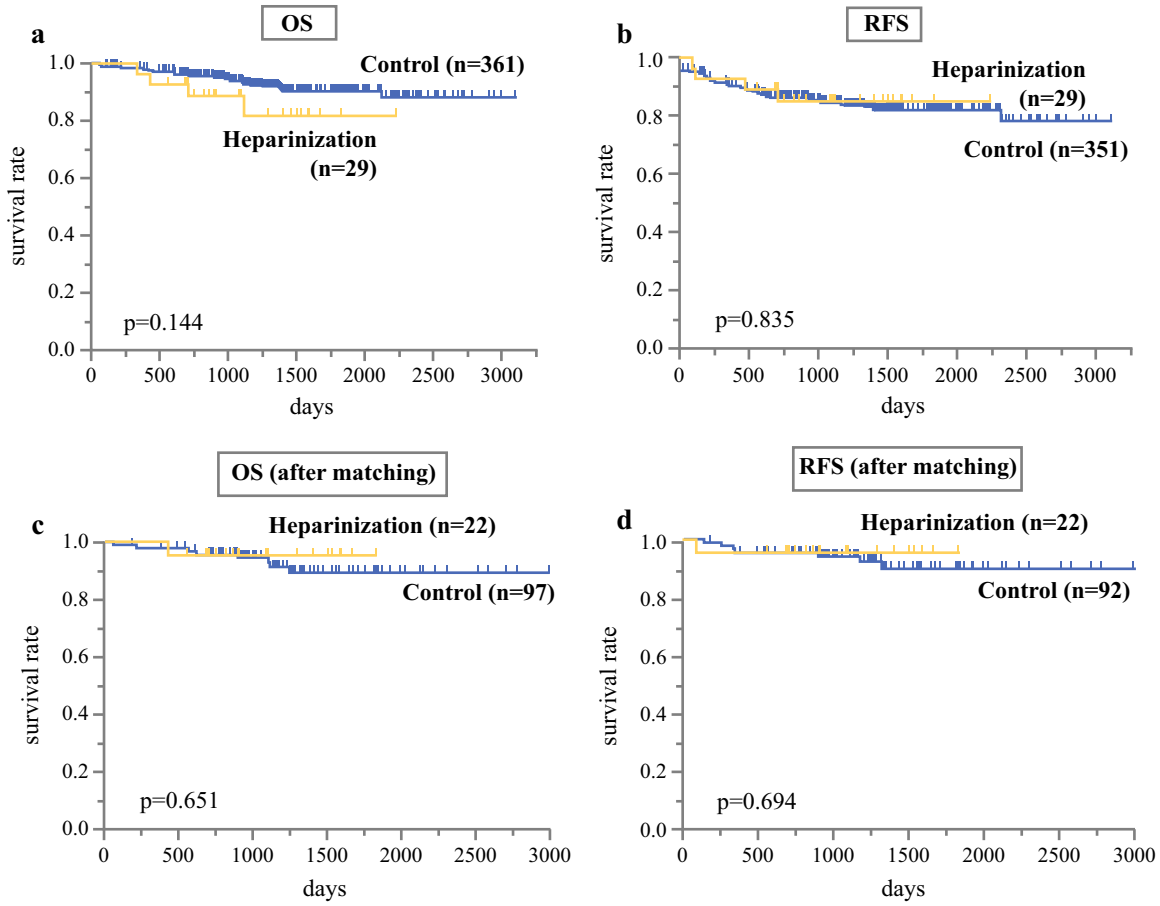

FIG. 1 Comparison of survival rates between the heparinization and control groups. (**a, c**) Cumulative OS and (**b, d**) RFS, measured (**a, b**) before propensity matching and (**c, d**) after propensity matching. *OS* overall survival, *RFS* recurrence-free survival

postoperatively; both these patients had received heparin treatment. After PS matching, postoperative hospital stay was prolonged in the heparinization group compared with controls.

Some previous reports have shown that patients who received heparinization therapy perioperatively for abdominal surgery had higher risks of postoperative bleeding and prolonged postoperative stay (electronic supplementary Table 2). In the present study, after PS matching, we observed no difference in postoperative bleeding, but the heparinization group had a longer median postoperative hospital stay than the control group. The prolonged hospitalization was thought to be due to the continuation of hospitalization until postoperative warfarin efficacy improved, a unique strategy widely practiced in Japan. Since there were no factors that caused prolonged hospitalization other than warfarin, we only considered warfarin as the cause, from the results of this study.

In this study, we controlled for covariates using PS matching to obtain a reliable evaluation of perioperative heparinization. Although the most common adjustment method in studies with a dichotomous outcome is logistic regression,[16] studies have shown that the PS was more robust, more precise, and more statistically powerful than logistic regression.[17] Moreover, the variable rate-matching method that we adopted was considered effective for removing biases, when the size of the treatment group is much smaller than the control group, as in this study.[18]

A previous meta-analysis on CME indicated that CME increased the risk of blood loss.[19] However, the results of this study indicated that, even with heparinization, a well–trained surgeon could safely perform single-site laparoscopic surgery with a good oncological outcome and reduced complications, including bleeding.

The present study had some limitations. First, it was a retrospective study carried out in a single institution, and, second, the heparinization group was rather small. However, PS matching was performed to reduce the effects of these limitations. Therefore, the present analysis demonstrated that single-site laparoscopic colectomy with CME for colorectal cancer and bridging heparin therapy could be safe and feasible. Third, this study examined the safety and feasibility between cases of single-site laparoscopic colectomy with and without heparinization. We were not

able to compare single-site laparoscopic surgery with standard multiport colectomy because we conducted single-site laparoscopic surgeries for colectomy as a standard strategy. In addition, standard multiport laparoscopic surgeries were rarely conducted in the study period because we hypothesized that a single-site colectomy performed by a single surgeon should reduce the unexpected bleeding due to manipulation of the assistants. However, the results of this study demonstrated that patients who require heparinization benefit from the less invasive nature of single-site laparoscopic surgery. We agree that since similar research in conventional laparoscopic surgery for colon cancer has not been performed to date, it is also considered that examination of the safety of laparoscopic surgery with heparinization, and comparative examination between conventional and single-site laparoscopic surgery, should be conducted in the future.

CONCLUSIONS

This report demonstrates that single-site laparoscopic surgery for colorectal cancer was feasible and safe, even when heparinization was performed, without increasing the risk of postoperative bleeding complications. However, the heparinization group had longer postoperative hospital stays than the control group due to the need for medication adjustments after heparinization.

FUNDING None.

DISCLOSURE Kazuya Iwamoto, Hidekazu Takahashi, Makoto Fujii, Naotsugu Haraguchi, Taishi Hata, Chu Matsuda, Hirofumi Yamamoto, Tsunekazu Mizushima, Masaki Mori, and Doki Yuichiro declare no conflicts of interest.

REFERENCES

1. Colvin H, Mizushima T, Eguchi H, et al. Gastroenterological surgery in Japan: the past, the present and the future. *Ann Gastroenterol Surg*. 2017;1:5–10.
2. Takemasa I, Doki Y, Mori M, et al. Feasibility of single-site laparoscopic colectomy with complete mesocolic excision for colon cancer: a prospective case-control comparison. *Surg Endosc*. 2014;28:1110–8.
3. Hiraki M, Takemasa I, Mori M, et al. Evaluation of invasiveness in single-site laparoscopic colectomy, using "the PainVision™ system" for quantitative analysis of pain sensation. *Surg Endosc*. 2014;28:3216–23.
4. Miyo M, Takemasa I, Mori M, et al. Long-term outcomes of single-site laparoscopic colectomy with complete mesocolic excision for colon cancer: comparison with conventional multiport laparoscopic colectomy using propensity score matching. *Dis Colon Rectum*. 2017;60:664–73.
5. Nishizawa Y, Hata T, Mori M, et al. Clinical benefits of single-incision laparoscopic surgery for postoperative delirium in elderly colon cancer patients. *Surg Endosc*. 2018;32:1434–40.
6. West NP, Hohenberger W, Weber K, et al. Complete mesocolic excision with central vascular ligation produces an oncologically superior specimen compared with standard surgery for carcinoma of the colon. *J Clin Oncol*. 2010;28:272–8.
7. Bertelsen CA, Neuenschwander AU, Jansen JE, et al. Disease-free survival after complete mesocolic excision compared with conventional colon cancer surgery: a retrospective, population-based study. *Lancet Oncol*. 2015;16:161–8.
8. Hohenberger W, Weber K, Matzel K, et al. Standardized surgery for colonic cancer: complete mesocolic excision and central ligation—technical notes and outcome. *Colorectal Dis*. 2009;11:354–64.
9. Takahashi H, Takemasa I, Mori M, et al. The single-center experience with the standardization of single-site laparoscopic colectomy for right-sided colon cancer. *Surg Today*. 2017;47:966–72.
10. Varkarakis IM, Rais-Bahrami S, Allaf ME, et al. Laparoscopic renal-adrenal surgery in patients on oral anticoagulant therapy. *J Urol*. 2005;174:1020–3.
11. Ercan M, Bostanci EB, Ozer I, et al. Postoperative hemorrhagic complications after elective laparoscopic cholecystectomy in patients receiving long-term anticoagulant therapy. *Langenbecks Arch Surg*. 2010;395:247–53.
12. Mita K, Ito H, Murabayashi R, et al. Postoperative bleeding complications after gastric cancer surgery in patients receiving anticoagulation and/or antiplatelet agents. *Ann Surg Oncol*. 2012;19:3745–52.
13. Fujikawa T, Tanaka A, Abe T, et al. Effect of antiplatelet therapy on patients undergoing gastroenterological surgery: thromboembolic risks versus bleeding risks during its perioperative withdrawal. *World J Surg*. 2015;39:139–49.
14. Wakasugi M, Tei M, Suzuki Y, et al. Single-incision totally extraperitoneal inguinal hernia repair is feasible and safe in patients on antithrombotic therapy: a single-center experience of 92 procedures. *Asian J Endosc Surg*. 2017;10:301–7.
15. Yamamoto S, Inomata M, Katayama H, et al. Short-term surgical outcomes from a randomized controlled trial to evaluate laparoscopic and open D3 dissection for stage II/III colon cancer: Japan Clinical Oncology Group Study JCOG 0404. *Ann Surg*. 2014;260:23–30.
16. Kurth T, Walker AM, Glynn RJ, et al. Results of multivariable logistic regression, propensity matching, propensity adjustment, and propensity-based weighting under conditions of nonuniform effect. Am J Epidemiol. 2006;163:262–70.
17. Cepeda MS, Boston R, Farrar JT, et al. Comparison of logistic regression versus propensity score when the number of events is low and there are multiple confounders. *Am J Epidemiol*. 2003;158:280–7
18. Leite W. Practical propensity score methods using R. Thousand Oaks, CA: Sage Publishing; 2017
19. Wang C, Gao Z, Shen K, et al. Safety, quality and effect of complete mesocolic excision vs non-complete mesocolic excision in patients with colon cancer: a systemic review and meta-analysis. *Colorectal Dis*. 2017;19:962–72