Am J Transl Res 2021;13(11):12887-12896
www.ajtr.org /ISSN:1943-8141/AJTR0137612

Original Article

Effects of laparoscopic radical surgery in the treatment of colorectal cancer and correlations of VEGF and TGF-β1 with prognosis

Chuan-Peng Sun[1*], Yan Bai[2*], Jin-Qiang Jiang[3], Jian-Lin Wu[4]

[1]General Surgery, Yantai Zhifu Hospital, Yantai 264000, Shandong Province, China; [2]General Surgery, Tianjin Fifth Central Hospital, Tianjin 300450, China; [3]General Surgery One, Leling City People's Hospital, Leling 253600, Shandong Province, China; [4]Department of Gastrointestinal Surgery, Zibo Central Hospital, Zibo 255036, Shandong Province, China. [*]Equal contributors and co-first authors.

Received July 22, 2021; Accepted September 18, 2021; Epub November 15, 2021; Published November 30, 2021

Abstract: Objective: To investigate the effects of laparoscopic radical surgery on the treatment of colorectal cancer (CRC) and explore the correlations of vascular endothelial growth factor (VEGF) and transforming growth factor-β1 (TGF-β1) with prognosis. Methods: The clinical data of 210 patients with CRC admitted to the Yantai Zhifu Hospital from February 2015 to February 2018 were analyzed retrospectively. Among them, 110 patients were treated with laparoscopic radical surgery and assigned to the observation group, and the rest 100 patients were treated with routine open surgery and included in the open group. The two groups were compared in terms of operation time (OT), intraoperative blood loss (IBL), postoperative exhaust time (PET), length of hospital stays (LOS) and incidence of complications. Patients were also followed up for 3 years to count their survival rates. Serum expression levels of VEGF and TGF-β1, detected by enzyme-linked immunosorbent assays (ELISAs), were compared before and after treatment, and their correlations with patients' clinicopathological data and prognosis were analyzed. Results: Compared with the open group, patients in the observation group had longer OT, but lower IBL, PET, LOS, and overall incidence of complications. In the observation group, VEGF and TGF-β1 expression after treatment was remarkably lower than that before treatment and that in the open group. A 3-year survival rate of 80.0% was observed in the observation group. Univariate analysis showed that serum VEGF and TGF-β1 expression levels were closely related to Dukes staging and lymph node metastasis (LNM) (P<0.05). The Log-Rank test showed that the survival rate of patients with high VEGF and TGF-β1 expression was remarkably lower than that of those with low expression (P<0.05). According to Cox model multivariate analysis, Dukes staging, LNM, surgical methods and high VEGF and TGF-β1 expression were all independent risk factors for the prognosis of CRC patients (P<0.05). Conclusion: Laparoscopic radical surgery is effective and safe in treating CRC. VEGF and TGF-β1 are highly expressed in the serum of CRC patients, and are closely related to the tumor staging, LNM and prognosis of patients, which are of great significance for evaluating the condition and prognosis of CRC patients.

Keywords: Laparoscopic radical surgery, colorectal cancer, VEGF, TGF-β1, prognostic correlation

Introduction

As a common malignant tumor of the digestive tract, colorectal cancer (CRC) is one of the major cancers causing death in the world [1, 2]. According to relevant epidemiological data, there are 1.8 million new CRC cases and 881,000 deaths every year [3]. CRC has various pathogenic factors, with predisposing factors including internal and external factors such as high-fat diet, intestinal flora imbalance, genetic factors and inflammatory bowel disease [4]. At present, this disease is mainly treated by surgery, chemotherapy, radiotherapy and ablation [5]. Among them, laparoscopic radical surgery, the most commonly used standard radical method, is to insert a laparoscope through a puncture to explore the patient's abdominal cavity, further determining tumor location, removing the tumor and cleaning lymph nodes [6, 7]. Although the treatment of CRC is constantly updated and improved, the

efficacy for patients with advanced CRC is still unsatisfactory [8]. Therefore, exploring the treatment and prognosis of CRC is conducive to improving the prognosis of patients and is of practical significance for reducing the mortality rate of the disease.

Angiogenesis is a physiological process of developing new blood vessels from pre-existing vascular beds, which plays an important role in tumor growth and progression [9]. As a growth factor, vascular endothelial growth factor (VEGF) can initiate and regulate angiogenesis process [10]. Relevant reports have shown that high VEGF expression is related to tumor metastasis and poor survival in CRC patients [11, 12]. Through regulating cells' physiological processes such as growth, differentiation and apoptosis, transforming growth factor-β1 (TGF-β1) mediates the mechanism of tumor progression [13]. TGF-β1 is closely related to lymphangiogenesis in CRC, and targeted inhibitors against it may be helpful for treating CRC and other malignant tumors [14, 15]. There is a certain relationship between VEGF and TGF-β1 in tumor microenvironment. TGF-β1 in tumors promotes neutrophils to differentiate into a tumor-promoting phenotype, further making neutrophils express VEGF and other factors to support tumor expansion [16].

In this study, the effects of laparoscopic radical surgery on treating CRC and the correlations of VEGF and TGF-β1 with CRC patients' prognoses were mainly explored.

Materials and methods

General information

A total of 210 patients with CRC admitted to the Yantai Zhifu Hospital from February 2015 to February 2018 were enrolled in this study and their clinical data were retrospectively studied. Of them, 110 cases were treated by laparoscopic radical surgery and assigned to the observation group, and the rest 100 patients were treated by routine open surgery and included in the open group. Among them, 60 males and 50 females (average age 56.93±17.10 years) were in the observation group, whereas 59 males and 41 females (average age 54.61±13.58 years) were in the open group. This study was approved by the ethics committee of our hospital. The subjects and their guardians were informed of this study and signed the fully informed consent form.

Inclusion and exclusion criteria

Inclusion criteria: Those diagnosed with CRC by laboratory and pathological examinations [17]; those aged between 18 and 75 years; those with complete medical records; those with normal communication and cognitive abilities; those who could complete the 3-year follow-up; those eligible for Dukes staging.

Exclusion criteria: Those complicated with other malignant tumors; those with tumor rupture or metastasis of tumor cells during surgery; those with ascites and/or abdominal inflammation; those with a history of major abdominal surgery; those complicated with dysfunction of vital organs and/or immune system diseases; those with contraindications to laparoscopic radical surgery or routine open surgery; those with peritoneal and/or pelvic metastasis.

The inclusion criteria were applicable to both the open and observation groups.

Follow-ups

Through interviews, telephone interviews and medical records inquiry, 3-year follow-ups were conducted on patients in the observation group once every three months, to record their survival condition or disease progression. Overall survival (OS) was the period from diagnosis to death or the last follow-up date.

Therapeutic methods

Patients in both groups strictly followed the principle of tumor-free, and rectal cancer surgery followed the principle of total mesorectal excision.

Those in the open group were given routine open surgery. Endotracheal intubation and general anesthesia were conducted at first, and then a surgical incision was determined according to tumor location. After the abdominal cavity was probed, superior and inferior intestinal tubes of the tumor and the corresponding root of mesenteric vessels were ligated. Next, the intestinal tubes were freed, the mesenterium and intestinal tubes were ligated, and the surrounding lymph nodes were dissect-

ed. The bowel was severed 5 cm away from the tumor, and end-to-end or end-to-side anastomosis was performed. Finally, the abdominal cavity was rinsed, drained, and closed.

Those in the observation group were given laparoscopic radical surgery. At first, endotracheal intubation and general anesthesia were conducted to construct pneumoperitoneum. With the pressure kept at about 13 mmHg, the endoscopic probe and related instruments were placed. After the separation of the corresponding intestinal segments by radical surgical methods, the blood vessels were ligated, and the tumor-draining lymph nodes were cleaned. After that, a longitudinal incision with a length of about 4 cm was made on the diseased side to take out the diseased intestinal segments. Next, the drainage tube was placed, and the incision was closed. Different radical surgical methods were adopted according to the patients' conditions. Dixon operation was adopted if the tumor location was high and the anus could be preserved. Miles operation was adopted if the tumor was located below the peritoneal reflection and close to the anal margin, and the anus could not be preserved. Hartmann operation was adopted if general conditions were poor and the patients could not tolerate Miles operation, or if the patients suffered from acute intestinal obstruction and could not receive Dixon operation.

After surgery, the patients in both groups were given symptomatic treatment (analgesia, fluid infusion and anti-infection) and routine nursing.

Detection methods

Before and one month after treatment, elbow venous blood (5 mL) was collected from the subjects in the observation group after an 8-hour fasting in the early morning. Placed in coagulation promoting tubes, the blood was transferred to new test tubes and then centrifuged at 1500×*g* and 4°C for 10 min. After that, the supernatant was collected and placed at -80°C for subsequent detection. VEGF and TGF-β1 expression in serum was detected by enzyme-linked immunosorbent assays (ELISAs), with the operation process strictly following human VEGF ELISA kits and human TGF-β1 ELISA kits (Xuanke Biotechnology Co., Ltd., Shanghai, China, H-KMLJh311550, XK-SJH-1113) [18]. Finally, VEGF and TGF-β1 concentrations were analyzed by a spectrophotometer (ZEPING Bioscience & Technologies Co., Ltd., Beijing, China, UV5Nano).

Statistical analysis

GraphPad Prism 7 was used for data analysis and image rendering. The enumeration data were expressed as number of cases/percentage (n/%), and a chi-square test was used for comparison between groups. A chi-square test with correction for continuity was adopted when the theoretical frequency in the chi-square test was less than 5. The measurement data, recorded as mean ± SEM, were compared by an independent samples t test between groups. The survival of patients was analyzed with a Log-Rank test. Multivariate Cox regression analysis was adopted for analyzing the risk factors affecting the prognosis of CRC patients. When $P<0.05$, the difference is considered statistically significant.

Results

General information

The open group and observation group were not significantly different in age, gender, Dukes staging, lymph node metastasis (LNM), tumor sites, tumor size, degree of differentiation, tumor types, educational backgrounds, place of residence and types of surgery ($P>0.05$) (**Table 1**).

Surgical indicators

Surgical indicators in both groups were evaluated and recorded. The operation time (OT), intraoperative blood loss (IBL), postoperative exhaust time (PET) and length of hospital stays (LOS) in observation group were 177.29±26.54 min, 131.05±11.36 mL, 25.53±4.97 h and 10.10±2.43 d, respectively. The four indicators in the open group were 117.88±20.99 min, 153.85±10.88 mL, 38.41±7.33 h and 13.63±3.79 d, respectively. The OT was longer but the other three indicators were remarkably lower in the observation group as compared with the open group ($P<0.05$) (**Figure 1**).

Complications

The number of patients suffering from complications was recorded in both groups. In the

Table 1. Baseline data of open and observation groups [n (%), mean ± SD]

Factors	n	Open group (n=100)	Observation group (n=110)	χ^2/t	P
Age (Years)	210	54.61±13.58	56.93±17.10	1.082	0.281
Gender				0.651	0.515
Male	119	59 (59.00)	60 (54.55)		
Female	91	41 (41.00)	50 (45.45)		
Dukes staging				1.751	0.417
A	29	15 (15.00)	14 (12.73)		
B	87	45 (45.00)	42 (38.18)		
C	94	40 (40.00)	54 (49.09)		
Lymph node metastasis				0.782	0.377
Yes	97	43 (43.00)	54 (49.09)		
No	113	57 (57.00)	56 (50.91)		
Tumor sites				1.833	0.608
Right half colon	44	19 (19.00)	25 (22.73)		
Left half colon	13	5 (5.00)	8 (7.27)		
Transverse colon	46	25 (25.00)	21 (19.09)		
Rectum	107	51 (51.00)	56 (50.91)		
Tumor size (cm)	210	4.01±1.28	3.88±1.54	0.662	0.509
Degree of differentiation				1.259	0.533
High	2	1 (1.00)	1 (0.91)		
Moderate	184	85 (85.00)	99 (90.00)		
Poor	24	14 (14.00)	10 (9.09)		
Tumor types				2.147	0.342
Papillary adenocarcinoma	95	40 (40.00)	55 (50.00)		
Tubular adenocarcinoma	68	35 (35.00)	33 (30.00)		
Mucinous adenocarcinoma	47	25 (25.00)	22 (20.00)		
Educational backgrounds				3.375	0.185
Primary school	45	25 (25.00)	20 (18.18)		
Middle school	125	53 (53.00)	72 (65.45)		
University and above	40	22 (22.00)	18 (16.37)		
Place of residence				1.387	0.239
Countryside	94	49 (49.00)	45 (40.91)		
City	116	51 (51.00)	65 (59.09)		
Types of surgery				5.885	0.318
Radical surgery of right half colon	40	16 (16.00)	24 (21.82)		
Radical surgery of left half colon	19	11 (11.00)	8 (7.27)		
Radical surgery of transverse colon	44	24 (24.00)	20 (18.18)		
Dixon operation	61	25 (25.00)	36 (32.73)		
Miles operation	39	22 (22.00)	17 (15.45)		
Hartmann operation	7	2 (2.00)	5 (4.55)		

observation group, the number of cases suffering from incision infection, anastomotic bleeding, anastomotic fistula, intestinal obstruction and pulmonary infection was 1, 2, 3, 2 and 1, respectively, while that in the open group was 10, 5, 5, 3 and 5, respectively. The observation group had a significantly lower overall incidence of complications than the open group (8.19% vs. 28.00%) (**Table 2**).

VEGF and TGF-β1 expression before and after treatment

VEGF expression before and after treatment was 222.73±20.67 pg/mL and 119.3±16.21 pg/mL, respectively in the observation group, while that in the open group was 218.42± 20.31 pg/mL and 159.32±18.61 pg/mL, respectively. Before treatment, VEGF and TGF-

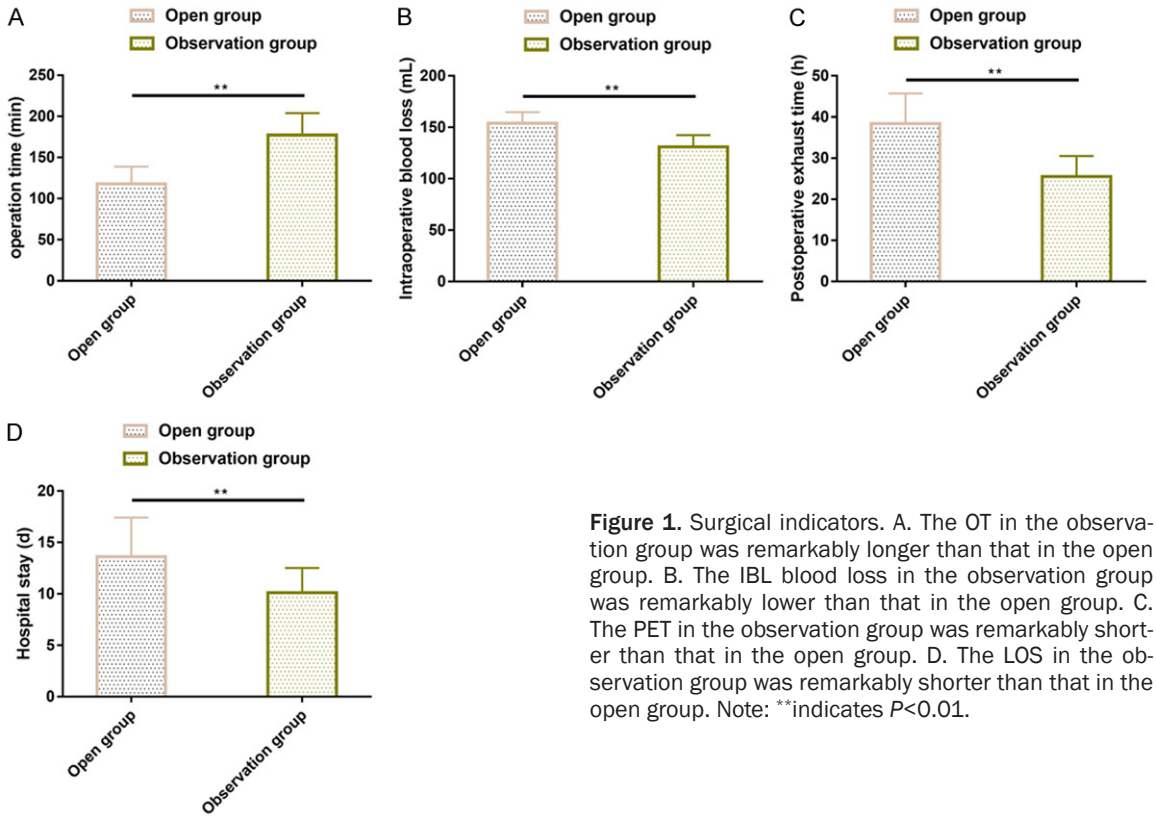

Figure 1. Surgical indicators. A. The OT in the observation group was remarkably longer than that in the open group. B. The IBL blood loss in the observation group was remarkably lower than that in the open group. C. The PET in the observation group was remarkably shorter than that in the open group. D. The LOS in the observation group was remarkably shorter than that in the open group. Note: **indicates $P<0.01$.

Table 2. Complications [n (%)]

Categories	Open group (n=100)	Observation group (n=110)	χ^2 value	*P* value
Incision infection	10 (10.00)	1 (0.91)	-	-
Anastomotic bleeding	5 (5.00)	2 (1.82)	-	-
Anastomotic fistula	5 (5.00)	3 (2.73)	-	-
Intestinal obstruction	3 (3.00)	2 (1.82)	-	-
Pulmonary infection	5 (5.00)	1 (0.91)	-	-
Total	28 (28.00)	9 (8.19)	14.174	<0.001

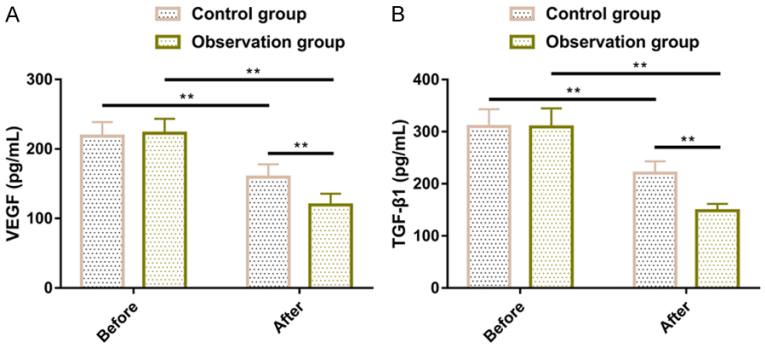

Figure 2. VEGF and TGF-β1 expression before and after treatment. A. In the observation group, VEGF expression after treatment was remarkably lower than that before treatment and that in the open group. B. In the observation group, TGF-β1 expression after treatment was remarkably lower than that before treatment and that in the open group. Note: **indicates $P<0.01$.

β1 were not significantly different between the two groups ($P>0.05$). In both groups, the expression of VEGF and TGF-β1 was reduced significantly after treatment ($P<0.05$). After treatment, VEGF and TGF-β1 expression was remarkably lower in the observation group compared with that in the open group ($P<0.05$) (**Figure 2**).

Correlations of VEGF and TGF-β1 with clinical parameters of patients undergoing laparoscopic radical surgery

With the median value of serum VEGF and TGF-β1 expression of patients undergoing laparoscopic radical surgery as the critical value (VEGF: 217.28 pg/mL, TGF-β1: 298.51 pg/mL), the patients were divided into high and low expression groups, to evaluate the correlation of

Table 3. Correlation of VEGF with pathological data [n (%)]

Factors	n	Low VEGF expression (n=55)	High VEGF expression (n=55)	χ^2 value	*P* value
Age (Years)				2.465	0.116
<60	68	38 (69.09)	30 (54.55)		
≥60	42	17 (30.91)	25 (45.45)		
Gender				1.320	0.251
Male	60	27 (49.09)	33 (60.00)		
Female	50	28 (50.91)	22 (40.00)		
Dukes staging				10.836	0.004
A	14	7 (12.73)	7 (12.73)		
B	42	29 (52.73)	13 (23.64)		
C	54	19 (34.54)	35 (63.63)		
Lymph node metastasis				11.786	<0.001
Yes	54	18 (32.73)	36 (65.45)		
No	56	37 (67.27)	19 (34.55)		
Tumor sites				1.471	0.689
Low rectum	22	9 (16.36)	13 (23.64)		
Middle rectum	55	30 (54.55)	25 (45.45)		
High rectum	15	8 (14.55)	7 (12.73)		
Sigmoid colon	18	8 (14.54)	10 (18.18)		
Tumor size (cm)				1.533	0.216
<5	76	41 (74.55)	35 (63.64)		
≥5	34	14 (25.45)	20 (36.36)		
Degree of differentiation				1.491	0.475
High	1	0 (0.00)	1 (1.82)		
Moderate	99	51 (92.73)	48 (87.27)		
Poor	10	4 (7.27)	6 (10.91)		
Tumor types				1.212	0.546
Papillary adenocarcinoma	55	25 (45.45)	30 (54.55)		
Tubular adenocarcinoma	33	17 (30.91)	16 (29.09)		
Mucinous adenocarcinoma	22	13 (23.64)	9 (16.36)		

their high and low expression with the patients' clinical parameters. According to the univariate analysis, serum VEGF and TGF-β1 expression was closely related to Dukes staging and LNM (*P*<0.05), but not to age, gender, tumor sites, tumor size, degree of differentiation and tumor types (*P*<0.05) (**Tables 3**, **4**).

Survival analysis of patients undergoing laparoscopic radical surgery

All the 110 cases in the observation group were followed up for 3 years, and all of them successfully completed the follow-ups. The overall survival rate was 80.0% (88/110). The median value of serum VEGF and TGF-β1 expression was taken as the critical value (VEGF: 217.28 pg/mL, TGF-β1: 298.51 pg/mL), to evaluate the correlation of their high and low expression with the patients' 3-year survival. The data showed that the survival rate of patients with high expression of VEGF and TGF-β1 was significantly lower than that of patients with low expression (*P*<0.05). According to the Multivariate Cox regression analysis, Dukes staging (*P*=0.007), LNM (*P*=0.039), surgical methods (*P*=0.035) and high VEGF (*P*<0.001) and TGF-β1 (*P*<0.001) expression were independent risk factors for the prognosis of CRC patients (**Figure 3** and **Table 5**).

Discussion

CRC is the third most common malignant tumor around the world, with a mortality rate of approximately 10% of all cancer-related death

Table 4. Correlation of TGF-β1 with pathological data [n (%)]

Factors	n	Low TGF-β1 expression (n=55)	High TGF-β1 expression (n=55)	χ^2 value	*P* value
Age (Years)				0.154	0.695
<60	68	35 (63.64)	33 (60.00)		
≥60	42	20 (36.36)	22 (40.00)		
Gender				3.667	0.056
Male	60	25 (45.45)	35 (63.64)		
Female	50	30 (54.55)	20 (36.36)		
Dukes staging				20.952	<0.001
A	14	10 (18.18)	4 (7.27)		
B	42	30 (54.55)	12 (21.82)		
C	54	15 (27.27)	39 (70.91)		
Lymph node metastasis				24.590	<0.001
Yes	54	14 (25.45)	40 (72.73)		
No	56	41 (74.55)	15 (27.27)		
Tumor sites				15.758	0.001
Low rectum	22	19 (34.55)	3 (5.45)		
Middle rectum	55	25 (45.45)	30 (54.55)		
High rectum	15	5 (9.09)	10 (18.18)		
Sigmoid colon	18	6 (10.91)	12 (21.82)		
Tumor size (cm)				1.533	0.216
<5	76	41 (74.55)	35 (63.64)		
≥5	34	14 (25.45)	20 (36.36)		
Degree of differentiation				1.410	0.494
High	1	0 (0.00)	1 (1.82)		
Moderate	99	49 (89.09)	50 (90.91)		
Poor	10	6 (10.91)	4 (7.27)		
Tumor types				3.382	0.184
Papillary adenocarcinoma	55	32 (58.18)	23 (41.82)		
Tubular adenocarcinoma	33	15 (27.27)	18 (32.73)		
Mucinous adenocarcinoma	22	8 (14.55)	14 (25.45)		

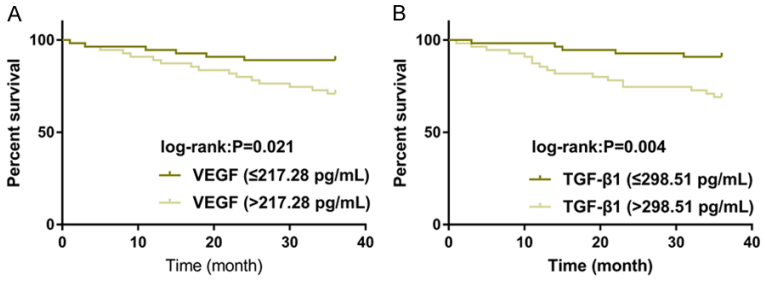

Figure 3. Correlation of serum VEGF and TGF-β1 expression with 3-year OS. A. The survival rate of patients with high expression of VEGF was significantly lower than that of patients with low expression. B. The survival rate of patients with high TGF-β1 expression was significantly lower than that of patients with low expression.

worldwide [19, 20]. With unsatisfactory prognosis, its incidence and mortality rate are still rising even in developed countries [21, 22]. Therefore, it is of great value to study the treatment and prognosis of CRC for improving CRC patients' survival outcomes.

First, we evaluated the efficacy of laparoscopic radical surgery in the treatment of CRC. The observation group had significantly longer operation time but lower values of intraoperative blood loss, postoperative exhaust time and length of hospital stays than the open group, indicating that laparoscopic radical surgery takes relatively long time, but it

Table 5. Univariate and multivariate Cox regression analysis

Indicators	Univariate		Multivariate	
	HR (95% CI)	P	HR (95% CI)	P
Age	0.974 (0.935-1.022)	0.289		
Gender	0.989 (0.960-1.004)	0.150		
Dukes staging	7.512 (1.935-29.318)	0.005	1.889 (0.341-11.256)	0.007
Lymph node metastasis	4.846 (1.462-16.574)	0.013	1.265 (0.109-9.054)	0.039
Tumor sites	1.455 (0.775-2.612)	0.264		
Tumor size	3.081 (0.915-10.456)	0.073		
Degree of differentiation	0.422 (0.147-1.122)	0.104		
Tumor types	0.654 (0.347-1.269)	0.218		
Surgical methods	3.945 (1.032-15.241)	0.044	3.652 (1.087-12.335)	0.035
VEGF	1.845 (1.301-1.766)	0.031	2.610 (1.575-4.226)	<0.001
TGF-β1	4.844 (1.467-16.351)	0.012	4.039 (1.668-9.783)	<0.001

has a significant advantage in promoting the recovery of patients. Similarly, the study by Tan and others [23] shows that, for patients with stage IV CRC, laparoscopic radical surgery takes remarkably longer time than open surgery, but the indicators of the former, such as intraoperative blood loss, exhaust time and LOS, are significantly lower. Reasons for the above advantages are that compared with traditional open surgery, laparoscopic radical surgery has a clearer visual field (which is effective in protecting blood vessels) and smaller incision (which is conducive to postoperative recovery) [24]. In terms of safety, the observation group had a significantly lower overall incidence of complications (8.19%). This suggests that laparoscopic radical surgery is remarkably safer than routine open surgery. Based on the above data, laparoscopic radical surgery is remarkably superior to routine open surgery in efficacy and safety.

Besides, VEGF and TGF-β1 expression before and after treatment in both groups as well as its correlation with the prognosis of CRC patients were evaluated. After treatment, VEGF and TGF-β1 expression decreased significantly in both groups, and the expression was remarkably lower in patients undergoing laparoscopic radical surgery than those undergoing routine open surgery. This demonstrates that laparoscopic radical surgery is more conducive to reducing their expression in patients. After that, their clinical significance for the prognosis of patients undergoing laparoscopic radical surgery was studied. Serum VEGF and TGF-β1 expression was closely related to the Dukes staging and LNM of CRC patients, but not remarkably correlated with age, gender, tumor sites, tumor size and degree of differentiation. According to Xu and others [25], serum VEGF expression in CRC patients is related to Dukes staging and LNM, which is consistent with our research results. And the study by Zhu and others [26] shows that high TGF-β1 expression in CRC cytoplasm and matrix is closely related to Dukes staging and LNM, which is also similar to our research results. All the above studies indicate that VEGF and TGF-β1 may be prognostic indicators of CRC patients, but further verification is warranted. In terms of prognosis, the observation group had a 3-year survival rate of 80.0%, similar to the findings of Nowakowski and others [27]. The Log-Rank test showed that compared with those with low VEGF and TGF-β1 expression, the survival rate of patients with high expression was remarkably lower. This indicates that high VEGF and TGF-β1 expression signifies the poor prognosis of CRC. Mohamed and others [28] have also pointed out that high VEGF expression is related to the poor prognosis of CRC patients. Wang and others [29] have confirmed that TGF-β1 can be activated by E26 transformation specific (ETS) homologous factors, thus promoting the malignant development of CRC. Finally, Cox model multivariate analysis was conducted for further evaluation. The results showed that Dukes staging, LNM, surgical methods and high VEGF and TGF-β1 expression were independent risk factors affecting the prognosis of CRC patients.

The innovation of this study is that the effects of laparoscopic radical surgery on treating CRC have been evaluated, and that the correlations

of VEGF and TGF-β1 with CRC patients' prognoses have been analyzed. Our study has confirmed that laparoscopic radical surgery is markedly effective in treating CRC, and that high VEGF and TGF-β1 expression signifies the poor prognosis of CRC. However, this study still needs to be improved. First, the effect of laparoscopic radical surgery on the long-term outcome of CRC patients can be supplemented. Second, the underlying mechanisms of VEGF and TGF-β1 affecting the patients' prognoses can be explored. Finally, the sample size can be enlarged to further improve the accuracy of experimental results.

In summary, laparoscopic radical surgery is effective and safe in treating CRC. Additionally, with high expression profiles in patients with CRC, VEGF and TGF-β1 can predict the tumor staging, LNM and prognosis of patients to a certain extent, which is conducive to evaluating the condition and prognosis of patients.

Disclosure of conflict of interest

None.

Address correspondence to: Jian-Lin Wu, Department of Gastrointestinal Surgery, Zibo Central Hospital, No. 54, Gongqingtuan West Road, Zibo 255036, Shandong Province, China. Tel: +86-0533-2360700; E-mail: jianlin1127@163.com

References

[1] Jacobs BA, Prince S and Smith KA. Gastrointestinal nematode-derived antigens alter colorectal cancer cell proliferation and migration through regulation of cell cycle and epithelial-mesenchymal transition proteins. Int J Mol Sci 2020; 21: 7845.

[2] Hsieh MH, Kung PT, Kuo WY, Ke TW and Tsai WC. Recurrence, death risk, and related factors in patients with stage 0 colorectal cancer: a nationwide population-based study. Medicine (Baltimore) 2020; 99: e21688.

[3] Zhang Q, Ding Z, Wan L, Tong W, Mao J, Li L, Hu J, Yang M, Liu B and Qian X. Comprehensive analysis of the long noncoding RNA expression profile and construction of the lncRNA-mRNA co-expression network in colorectal cancer. Cancer Biol Ther 2020; 21: 157-169.

[4] Jin XH, Lu S and Wang AF. Expression and clinical significance of miR-4516 and miR-21-5p in serum of patients with colorectal cancer. BMC Cancer 2020; 20: 241.

[5] Huang L, Zhang Y, Li Z, Zhao X, Xi Z, Chen H, Shi H, Xin T, Shen R and Wang T. MiR-4319 suppresses colorectal cancer progression by targeting ABTB1. United European Gastroenterol J 2019; 7: 517-528.

[6] Ye SP, Zhu WQ, Liu DN, Lei X, Jiang QG, Hu HM, Tang B, He PH, Gao GM, Tang HC, Shi J and Li TY. Robotic-vs laparoscopic-assisted proctectomy for locally advanced rectal cancer based on propensity score matching: short-term outcomes at a colorectal center in China. World J Gastrointest Oncol 2020; 12: 424-434.

[7] Lupinacci RM, Andraus W, De Paiva Haddad LB, Carneiro D' Albuquerque LA and Herman P. Simultaneous laparoscopic resection of primary colorectal cancer and associated liver metastases: a systematic review. Tech Coloproctol 2014; 18: 129-135.

[8] Li K, Zhang J, Zhang M, Wu Y, Lu X and Zhu Y. miR-378a-5p inhibits the proliferation of colorectal cancer cells by downregulating CDK1. World J Surg Oncol 2021; 19: 54.

[9] Dan LA, Werdyani S, Xu J, Shestopaloff K, Hyde A, Dicks E, Younghusband B, Green J, Parfrey P, Xu W and Savas S. No associations of a set of SNPs in the vascular endothelial growth factor (VEGF) and matrix metalloproteinase (MMP) genes with survival of colorectal cancer patients. Cancer Med 2016; 5: 2221-2231.

[10] Dos Santos E, Ramos JC, Normando AG and Leme AF. Prognostic value of the immunohistochemical expression of vascular endothelial growth factors in malignant salivary gland neoplasms: a systematic review and meta-analysis. Med Oral Patol Oral Cir Bucal 2021; 26: e126-e135.

[11] Kocael A, Vatankulu B, Simsek O, Cengiz M, Kemik A, Kocael P, Halac M, Sonmezoglu K and Ulualp K. Comparison of (18)F-fluorodeoxyglucose PET/CT findings with vascular endothelial growth factors and receptors in colorectal cancer. Tumour Biol 2016; 37: 3871-3877.

[12] Yeh CC, Shih LJ, Chang JL, Tsuei YW, Wu CC, Hsiao CW, Chuu CP and Kao YH. Synchronous vascular endothelial growth factor protein profiles in both tissue and serum identify metastasis and poor survival in colorectal cancer. Sci Rep 2019; 9: 4228.

[13] Itatani Y, Kawada K and Sakai Y. Transforming growth factor-beta signaling pathway in colorectal cancer and its tumor microenvironment. Int J Mol Sci 2019; 20: 5822.

[14] Liu Y, Sheng J, Dai D, Liu T and Qi F. Smad4 acts as tumor suppressor by antagonizing lymphangiogenesis in colorectal cancer. Pathol Res Pract 2015; 211: 286-292.

[15] Gachpazan M, Kashani H, Hassanian SM, Khazaei M, Khorrami S, Ferns GA and Avan A. Therapeutic potential of targeting transforming

growth factor-beta in colorectal cancer: rational and progress. Curr Pharm Des 2019; 25: 4085-4089.
[16] Mizuno R, Kawada K, Itatani Y, Ogawa R, Kiyasu Y and Sakai Y. The role of tumor-associated neutrophils in colorectal cancer. Int J Mol Sci 2019; 20: 529.
[17] Gao ZY, Li M and Gu J. Sampling survey report on Chinese physicians' cognition of the guidelines on diagnosis and treatment of colorectal cancer. Zhonghua Wei Chang Wai Ke Za Zhi 2020; 23: 1067-1073.
[18] Chen Y, Harrington BS, Lau KCN, Burke LJ, He Y, Iconomou M, Palmer JS, Meade B, Lumley JW and Hooper JD. Development of an enzyme-linked immunosorbent assay for detection of CDCP1 shed from the cell surface and present in colorectal cancer serum specimens. J Pharm Biomed Anal 2017; 139: 65-72.
[19] Liu Q, Zhang W, Luo L, Han K, Liu R, Wei S and Guo X. Long noncoding RNA TUG1 regulates the progression of colorectal cancer through miR-542-3p/TRIB2 axis and Wnt/beta-catenin pathway. Diagn Pathol 2021; 16: 47.
[20] Dekker E, Tanis PJ, Vleugels JLA, Kasi PM and Wallace MB. Colorectal cancer. Lancet 2019; 394: 1467-1480.
[21] Jiang X, Zhu Q, Wu P, Zhou F and Chen J. Up-regulated long noncoding RNA LINC01234 predicts unfavorable prognosis for colorectal cancer and negatively correlates with KLF6 expression. Ann Lab Med 2020; 40: 155-163.
[22] Wang L, Cho KB, Li Y, Tao G, Xie Z and Guo B. Long noncoding RNA (lncRNA)-mediated competing endogenous RNA networks provide novel potential biomarkers and therapeutic targets for colorectal cancer. Int J Mol Sci 2019; 20: 5758.
[23] Tan SJ, Jiang Y, Xi QL, Meng QY, Zhuang QL, Han YS and Wu GH. Meta-analysis of laparoscopic versus open surgery for palliative resection of the primary tumor in stage IV colorectal cancer. Zhonghua Wei Chang Wai Ke Za Zhi 2020; 23: 589-596.
[24] Yang SX, Sun ZQ, Zhou QB, Xu JZ, Chang Y, Xia KK, Wang GX, Li Z, Song JM, Zhang ZY, Yuan WT and Liu JB. Security and radical assessment in open, laparoscopic, robotic colorectal cancer surgery: a comparative study. Technol Cancer Res Treat 2018; 17: 1533033818794160.
[25] Xu H, Ren YJ, Liu K, Min XL, Yang L, Zhou Y, Zheng J and Yang C. Correlations of serum VEGF and MMP-2 levels with CLM in CRC patients and effects of TACE on their expressions. Eur Rev Med Pharmacol Sci 2018; 22: 3394-3401.
[26] Zhu J, Chen X, Liao Z, He C and Hu X. TGFBI protein high expression predicts poor prognosis in colorectal cancer patients. Int J Clin Exp Pathol 2015; 8: 702-710.
[27] Nowakowski M, Pisarska M, Rubinkiewicz M, Torbicz G, Gajewska N, Mizera M, Major P, Potocki P, Radkowiak D and Pedziwiatr M. Postoperative complications are associated with worse survival after laparoscopic surgery for non-metastatic colorectal cancer-interim analysis of 3-year overall survival. Wideochir Inne Tech Maloinwazyjne 2018; 13: 326-332.
[28] Mohamed SY, Mohammed HL, Ibrahim HM, Mohamed EM and Salah M. Role of VEGF, CD105, and CD31 in the prognosis of colorectal cancer cases. J Gastrointest Cancer 2019; 50: 23-34.
[29] Wang L, Ai M, Nie M, Zhao L, Deng G, Hu S, Han Y, Zeng W, Wang Y, Yang M and Wang S. EHF promotes colorectal carcinoma progression by activating TGF-beta1 transcription and canonical TGF-beta signaling. Cancer Sci 2020; 111: 2310-2324.