Exploration of Treatment in Patients with T3 Rectal Cancer with EMVI

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Abstract: To explore the clinical efficacy of neoadjuvant chemoradiotherapy, combined with surgery and direct surgery in patients with stage T3 rectal cancer combined with EMVI. **Method:** The clinical data of patients with extragastrointestinal middle and low rectal cancer in the First Affiliated Hospital of Chongqing Medical University from January 2015 to May 2019 were retrospective reviewed, including 59 patients in the neoadjuvant treatment group (neoadjuvant chemoradiotherapy +surgical treatment) and 71 patients in the direct surgery group. Both groups underwent total rectal total membrane resection. **Data and Methods:**The concurrent chemotherapy regimens were all included in the XELOX regimen. The RT was performed by IMRT with D T 45 to 50.4 G y, from 1.8 to 2.0 G y each, for 25 to 28 sessions. Perioperative conditions, postoperative pathology and follow-up of the two groups were observed. **Results:** There was no significant difference in postoperative conditions (gastrointestinal function recovery time, postoperative drainage drainage, postoperative time of drainage removal) between the neoadjuvant treatment group and the direct surgery group (P> 0. 05); The length of postoperative hospital stay was significantly different (P <0.05); No significant operation time occurred between the neoadjuvant treatment group (264 min vs. 239 min) and the surgical group, (P> 0. 05)； The amount of intraoperative bleeding (85.7ml vs.110.0 ml), the number of lymph node dissection (11 vs. 13), the lymph node positive rate (27.12% vs.43.6%) betweenthe neoadjuvant treatment group and the direct surgery group had statistical significant (P＜0. 05); The 3-yearrecurrence-free survival (93.2 %) rate was higher in the neoadjuvant treatment group than in the direct surgery group (74.6 %), which was significant (P <0.05); The 3-year survival rate (98.30,% vs. 85.9 %) was significantly significant (P <0.05); There was no significant difference in the anal preservation rate (71.19% vs. 80.28%) (P> 0. 05). **Conclusion:** The neoadjuvant chemoradiotherapy improves the recurrence-free survival rate of locally advanced rectal cancer, and has no obvious effect on the postoperative complications rate, anal preservation rate and gastrointestinal function recovery.

Keywords: Rectal Cancer; Neoadjuvant Chemoradiotherapy; EMVI; Long-Term Efficacy

Introduction

At present, there are different controversies at home and abroad about the treatment of T3 patients with low rectal cancer. The American Association for Clinical Oncology for Treatment The treatment guidelines (NCCN) believe that patients with stage T3 rectal cancer (regardless of the presence of positive lymph nodes) will need preoperative new supplementation Aid, chemoradiotherapy, [1]. And the European Annual Cancer Conference believes that according to the patient risk grade, the risk grade is medium risk, can be directly advanced The surgical [2] was performed. Meanwhile, multiple studies suggest that MR suggests that positive EMVI may be considered a risk for rectal cancer metastasis One of the factors, the [3,4]. The latest version of the Society of Medical Oncology (ESMO) guidelines also see the mr-EMVI as an important one Risk factor, [2]. Therefore, 130 patients of medium and low rectal cancer with EMVI positive patients were

retrospectively studied Analysis, now the results are reported as follows.

1. Data and methods

1.1 General Information:

Inclusion criteria:(1) Preoperative colonoscopy biopsy suggested rectalcancer.; (2) Pre-hospital examination is excluded Tumors originating elsewhere outside the rectum;(3) Colonoscopy indicated that the tumor location was 10cm (4) with perfect rectal MR examination, and the stage was T3 / EMVI + / CRM-. Exclusion criteria:(1) Unable to tolerate surgery or neoadjuvant treatment for their own reasons; (2) the preoperative examination indicates distant metastasis or tumors at other sites, and it is

impossible to judge where the primary lesion is;(3) No rectal MR examination before surgery; (4) Hartmann surgery or palliative surgery. The Gastroenterology and intestinal Surgery Department of the First Affiliated Hospital of Chongqing Medical University was collected from January 2015 to May 2019 .according to the NCCN guidelines and the CSCO guidelines Patients underwent preoperative neoadjuvant therapy, requiring 71 direct surgical treatment and preoperative chemotherapy patients 59 human being,Sex, age, body mass index (BMI), history of abdominal surgery, and underlying disease and surgery None of the pre-stages were statistically different.

Table 1 Comparison of general data for one or two groups of rectal cancer patients [Case (%)]

Clinical parameters	The Direct Surgery Group（71）	New Auxiliary Group (59)	P
Age	59	57	0.925
Sex			0.413
Male	55	42	
Female	16	17	
BMI	23.7±3. 5	24. 4±3. 6	0. 595
History of abdominal surgery	17(23.9%)	13(22.1%)	0.797
Preoperative staging			0.872
II(cT3N0M0)	16	14	
III($cT_3N_{1-2}M0$)	55	45	

The tumor target area (GTV) is the primary lesion and metastatic lymph node determined on imaging, the clinical target area (CTV) is GTV + selective lymphatic drainage area, and the planned target area (PTV) is CTV expansion of 0. 5~1. 0 cm. All patients underwent surgery at 8-12 weeks after the completion of the neoadjuvant therapy.

1.2 Modus operandi:

The procedure was performed according to standard TME principles with routine lymph node dissection. According to the results of preoperative anal finger examination and colonoscopy, the patients with the distance from the lower edge of the tumor to the anal edge is within 4-10cm will undergo anal preservation surgery. For patients with tumors located at the lower edge of the anus, miles surgery is performed.

1.3 Follow-up visit:

To consult the inpatient medical records, outpatient review and regular telephone inquiry. If CT indicated recurrence, gastroenteroscopy or magnetic resonance examination was improved. The first postoperative year and once every 6 months from the second to the third postoperative year. Recurrence-free survival was defined as the time from surgery to the onset of local recurrence. Overall survival was defined as the deadline from surgery to patient death or follow-up.

1.4 Statistical method:

Data was processed with the SPSS 22 version. 0 software.χ 2 test is used for comparing count data, T test for normal distribution data and Mann-Whitney U test. Survival analysis was performed with the Kaplan parallel Log-r-rank method.

Table 2 Perioperative condition comparison of the patients in the two groups [Case (%)]

Clinical parameters	The Direct Surgery Group（71）	New Auxiliary Group (59)	P
Modus operandi			
Dixon	57	42	
Miles	14	17	
Protected ileostomy	12	27	0
Operation time	202 （201-209）	208（200-210）	0.021
Intraoperative bleeding volume (ml)	110 (79.5～ 200. 0)	85.7 0(50. 0～ 116. 3)	0. 013
Gastrointestinal function recovery time (D)	3	3	0. 988
Extubation time	7.0(6.3～8.9)	8.0 (6.8～ 9.4)	0. 312
length of stay (D)	18.0(10.5～ 24.3)	11.0(8.7 ～ 13.4)	0. 000

Dixon=anterior rectal resection; Miles=abdominoperineal resection；D=Day

2. Result

Perioperative and post-operative pathology conditions: an R0 resection was obtained in both groups. The intraoperative bleeding volume, and the proportion of protective ileostomy in the neoadjuvant treatment group were all significantly higher than that in the direct surgery group (P＜0.05); There was no significant difference in the postoperative recovery situation (postoperative drainage rate, gastrointestinal function recovery time, and extubation time between the two groups (P＞0. 05) ;

For 130 patients with low rectal cancer (tumor was 10 cm from the anal margin), dixon was performed in 42 out of 59 patients (71.19%) in the neoadjuvant treatment group,Dixon was performed in 57 (80.28%) of the direct surgery group.

The incidence of postoperative complications was significantly higher in the neoadjuvant treatment group than in the direct surgery group (46.3% vs. 25.3%, P = 0. 001). Perineal incision complications (including infection, dehiscence, delayed incision healing, etc.) in the neoadjuvant group (25.4% vs 5.6% P=0.006) were significantly higher than those in the direct surgery group.

Comparison of postoperative efficacy:The 3-year relapse survival period in the neoadjuvant chemoradiotherapy group was (11.3 ± 9.3) months in the direct surgery chemoradiotherapy group, and the 3-year relapse survival period was (22.7 ± 12.1),no significant difference between the two groups (P=0.095).Neoadjuvant recurrence-free survival rate (93.2%) was higher than that in the direct surgery group (74.6%),The difference was statistically significant (P＜0. 05) ,recurrence curves between the two groups are seen in Figure 1.The median time to death in the surgical group was 18 months, and the 3-year overall survival rate in the neoadjuvant chemoradiotherapy group was 98.30%,the 3-year overall survival rate in the direct surgery group was 85.9%,there were significant differences between the two groups (P＜0. 05),The survival curves between the two are shown in Figure 2.

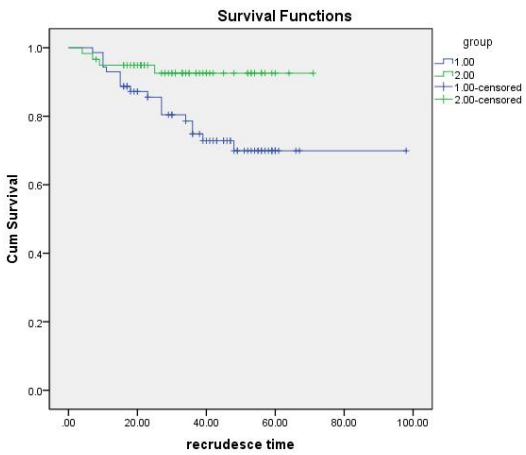
Table 3 Postoperative pathological data of both groups [case (%)]

Clinical parameters	The Direct Surgery Group（71）	New Auxiliary Group (59)	P
Number of lymph node dissection	13	11	0

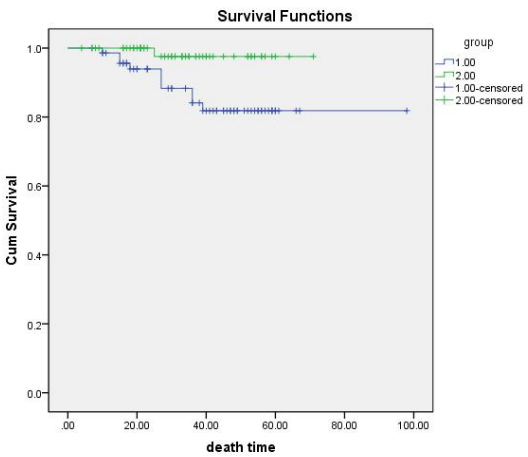
Number of positive lymph nodes	31 （43.6）	16（27.12）	0.037
Postoperative stage			0.002
0	0(0.00)	9(15.25)	
I pT1-2N0M0	4(5.60)	18(30.51)	
II pT3-4N0M0	57(80.28)	26(44.07)	
III pT2-4N1-2M0	10(14.08)	6(10.17)	

Table 4 Comparison of postoperative complications between the two groups [Case (%)]

Complication	The Direct Surgery Group（71）	New Auxiliary Group (59)	P
Anastomotic fistula	8 （11.27）	4（6.78）	0.375
Pneumonia	6 （8.45）	3（5.09）	0.685
Abdominal incision infection	5 （7.04）	2（3.39）	0.597
Abdominal infection	9 （12.68）	7（11.86）	0.888
Complications associated with the perineal incision	4 （5.6）	13 (22.0)	0.006



(Figure 1)



(Figure 2)

1= Direct surgery group ; 2= neoadjuvant chemotherapy group

3. Discussion

For patients with stage T3N0M0 intermediate and low rectal cancer, it is still controversial whether all such patients should receive neoadjuvant chemoradiotherapy or not in [5,6].Histopathological extrtramural vascular invasion (EMVI) is defined as tumor cell invasion of veins beyond the muscularis propria, suggesting a poor prognosis for patients with rectal cancer and attracting widespread attention to [7,8] in pathological reports of colorectal cancer.External vascular invasion in rectal cancer is a poor prognostic factor, with a 5-fold increase in the rate of synchronous metastasis and a nearly 4-fold increase in the persistent risk of developing metastasis during postoperative follow-up with [9]. Lack of confidence in the accurate detection of EMVI may be the reason not considered a mandatory treatment factor [10],meanwhile, because the prevalence of EMVI varies widely and the value is underestimated in histopathological specimens is used, [11] is also one of the clinical reasons for not treating EMVI as a therapeutic factor.Therefore, this study included low-grade rectal cancer, with

a stage of T3 / EMVI + / CRM-in patients.

In this study, 9 out of the 59 patients in the neoadjuvant chemotherapy group achieved pathological remission, with a PCR rate (15.2%), which basically matched the [12] with 16.5% to 22.8% in the NSABP R-04 clinical trials.At the same time, relevant studies showed that the diagnosis accuracy of T3 stage rectal cancer was 82.4% [13]. The postoperative pathological results of the surgical group in this study suggested that the proportion of patients with T3 rectal cancer was 80.28%, which was consistent with relevant studies.

The number of lymph node clearance and lymph node positive rate in the neoadjuvant group were lower than that in the surgical group.The neoadjuvant group can reduce the number of positive lymph nodes (on average of 3) and reduce the rate of positive lymph nodes, which is consistent with the results of relevant foreign studies: [14,15].The duration of surgery in the neoadjuvant group was not significant compared with the surgical group (264 min vs 239 min P=0.131), but the intraoperative bleeding volume was less than that in the surgical group (85.7 ml vs 110 ml P=0.013).The possible reason is that the pelvic tissue edema and fibrosis caused by preoperative radiotherapy make it difficult to judge the correct free level during the operation, which increases the difficulty of the operation. Therefore, it leads to more care during the main knife operation and more caution about intraoperative bleeding and other related problems, thus reducing the amount of intraoperative bleeding.

However, there are many studies on adverse reactions of neoadjuvant chemoradiotherapy, but there are few studies on neoadjuvant perioperative complications. It has been controversial whether preoperative neoadjuvant chemoradiotherapy can increase postoperative complications in [16]. The results of this study suggest that the postoperative complications (including: anastomotic fistula, incision infection, pneumonia, and abdominal cavity infection) in the neoadjuvant chemotherapy group were not statistically significant compared with the surgical group (P>0.05). However, perineal incision-related complications increased significantly compared with the surgical group, which was consistent with the findings of Hoare's et al.[17]. The results of this study suggest that the neoadjuvant chemoradiotherapy could not improve the anal preservation rate for the patients with low rectal cancer, and it was different from the relevant domestic research results in [18]. Large research institutions need to further improve the relevant research.

The relevant study results suggest that distant metastasis is the main cause of death in patients with colorectal tumors, [19], Liver metastasis is a common site of metastasis in such patients, and about one-third of CRC patients developed within three years [20,21], Even after radical resection of the primary lesion, the patient's liver metastasis rate was approximately 10–25% [22].In this study, the rate of postoperative liver metastasis in direct surgery within three years was 19.71%, which is consistent with the relevant study.However, the postoperative liver metastasis rate of the neoadjuvant chemotherapy group was 6.8%, which was statistically significant (P= 0.033), suggesting that the neoadjuvant chemoradiotherapy could improve the prognosis of such patients;At the same time, relevant foreign studies suggest that venous invasion can lead to a poor survival rate, [23],the results of this study suggest that there was a statistical significant difference between the three-year overall survival rate of 98.30% in the neoadjuvant group and 85.9% in the direct surgery group (P＜0. 05).It suggests that the neoadjuvant chemoradiotherapy has some effect on improving the long-term survival rate of such patients.

In conclusion, for patients with T3 medium and low rectal cancer combined with EMVI positive patients, preoperative neoadjuvant can reduce intraoperative bleeding and shorten the length of hospital stay, with no significant effect on postoperative complications.In terms of long-term efficacy, neoadjuvant chemotherapy can significantly improve the recurrence-free survival rate and the three-year overall survival rate of patients.Therefore, preoperative neoadjuvant chemoradiotherapy is recommended for such patients.

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