

Analysis of outcomes of intra-operative rectal washout in patients with rectal cancer during anterior resection

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Abstract Local recurrence is a major setback for patients with rectal cancer after surgery. Implantation of exfoliated malignant cells has been considered as a possible mechanism of tumor recurrence. Although still controversial, intra-operative rectal washout has been described as a method to remove exfoliated malignant cells and reduce recurrence rates. The current study was designed to assess the differences in outcomes of patients with or without rectal washout. Data of 144 patients with rectal cancer undergoing anterior resection between 2006 and 2007 were reviewed in our study. 69 patients received rectal washout with approximately 1,500 ml physiological saline before anastomosis, and 75 patients received no-washout. The washout samples were sent for cytological examination. The incidence of recurrence and 5-year disease-free survival rates of the two groups were compared. Three patients had local recurrence in the washout group compared with 5 patients with no-washout during a median follow-up of 48 months ($p = 0.721$). The 5-year disease-free survival rate was 79.7 and 74.7 % in washout and no-washout groups, respectively ($p = 0.553$). Our results demonstrated that exfoliated malignant cells were ubiquitous in the rectal lumen during anterior resection. The difference of prognosis was not statistically significant, though trended toward being improved in the washout group. A large-scale research with longer follow-up time is required to draw a significant conclusion.

Keywords Rectal cancer · Rectal washout · Exfoliated malignant cells · Recurrence

Introduction

Colorectal cancer is one of the leading causes of cancer deaths worldwide. With changes of life patterns and dietary structures, the incidence of colorectal cancer, especially of rectal cancer, China is increasing in recent years. Local recurrence is the major setback for patients with rectal cancer after surgery in spite of adjuvant treatments such as chemotherapy, radiotherapy, or targeted therapy. Implantation of exfoliated malignant cells has been suggested as a possible mechanism of tumor recurrence [1, 2]. Consistent with this hypothesis, exfoliated malignant cells have been collected on circular stapling devices. In addition, there is evidence that malignant cells can shed into the lumen of the bowel, with the ability to implant and proliferate in the colorectal anastomosis [3, 4]. Therefore, it has been recommended to perform rectal washout before cross-stapling during anterior resection [5, 6]. However, to date, there is no direct evidence suggested that the prevention of implantation during surgery would reduce the recurrence of rectal cancer. In the current study, we evaluate the effect of rectal washout during anterior resection for rectal cancer on the recurrence of rectal cancer.

Methods

Patients

From July 2006 to June 2007, in Department of Gastrointestinal Cancer Surgery, Cancer Hospital, Chinese Academy

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of Medical Sciences, 144 patients with carcinoma of the rectum undergoing anterior resection were studied. The patients were divided into the washout group and the no-washout group. There were 69 and 75 patients in washout group and no-washout group, respectively. The patients in two groups were comparable with the respect to sex, age, and the distance of tumor to anal verge, and tumor size (Table 1).

Intra-operative rectal washout

All operations were completed by the same surgical team, and all patients received rectal cancer anterior resection. Following radical resection and total mesorectal excision (TME), a cross clamp was placed distal to the tumor after adequate mobilization of the rectum, and a soft bowel clamp was placed proximally to the tumor to ensure the segment bearing tumor was isolated. A Foley catheter linked with a ball-type flushing device was placed into the rectum in washout group; an average volume of 1,500 ml physiological saline was used to irrigate the rectal stump. About 70 ml physiological saline was used each time, and an average of 7 times was repeated. All the 1,500 ml physiological saline was collected in 3 bottles in sequence, and 10 ml Sodium Citrate was injected in each bottle for the purpose of anti-freezing. 3 bottles of sample were sent to pathology laboratory for cytological examination. Then, the transverse stapler was applied below the occluding clamp; the rectum was transected, and the anastomosis was performed using the circular stapler. Intra-operative rectal washout was not performed in no-washout group.

Follow-up

All patients were examined by computer tomography (CT), abdominal ultrasonography, CEA assessment, colonoscopy, and some other clinical examinations for local

recurrence every 3 months in the first 2 years after operation, then, received the examinations mentioned above once every 6 months. Patients were followed up to understand their situations one time per 3 months. All the 144 patients had the perfect follow-up results. The last follow-up was done in March 2012.

Statistical analysis

Statistical analyses were performed using statistical software package SPSS version 13.0. A p value <0.05 is considered to be statistically significant. Categorical variables were analyzed by chi-square test, and continuous variables were analyzed by the Student's t test. Survival analysis was performed by the Kaplan–Meier method with log-rank test.

Results

Cytological examination

Cytological examination of the first bottle of washing sample was positive for malignant cells in 55 patients (79.7 %) and negative in 14 patients, the positive rate was 20.3 % among the second bottle of washing sample, and all of the third bottles were negative for cytological examination.

Characteristics comparison of two groups

The two groups were well matched for patient characteristics in terms of age, sex, tumor localization, and tumor size (Table 1), and they were also identical for distal and radical clearance margins, gross appearance, pathological type, tumor differentiation, and tumor stage (Table 2). No patient in washout group received preoperative adjuvant therapy, and 51 patients received postoperative adjuvant therapy, whereas in no-washout group, 2 patients experienced preoperative adjuvant radiotherapy, and 54 patients received postoperative adjuvant therapy.

Prognoses of two groups

8 patients had local recurrence, and the total local recurrence rate was 5.6 %. 3 patients in washout group had anastomotic recurrence, while 4 patients had anastomotic recurrence, and 1 patient had pelvic recurrence in no-washout group. The local recurrence rate was 4.3 and 6.7 % in washout and no-washout groups, respectively.

26 patients had postoperative distant metastasis. There were 7 patients with liver metastasis and 5 patients with lung metastasis in washout group, but 8 patients with liver metastasis and 6 patients with lung metastasis in

Table 1 Comparison of two groups in patients and tumors

Parameters	Washout group <i>n</i> = 69	No-washout group <i>n</i> = 75	<i>p</i> value
Age, year (mean \pm SD)	56.3 \pm 11.7	59.0 \pm 10.6	0.139
Sex			0.867
Male	40	42	
Female	29	33	
Localization of tumor			0.212
Upper rectum	9	4	
Mid rectum	37	48	
Lower rectum	23	23	
Size of tumor, cm (mean \pm SD)	3.6 \pm 1.3	3.7 \pm 1.8	0.869

Table 2 comparison of specimens and adjuvant treatment

Parameters	Washout group <i>n</i> = 69	No-washout group <i>n</i> = 75	<i>p</i> value
Gross appearance of tumor			0.536
Bulky-exophytic	46	53	
Infiltrative-ulcerated	22	22	
Diffuse infiltrative	1	0	
Differentiation of tumor			0.040
Well	6	18	
Moderate	54	51	
Poor	9	6	
Pathological type of tumor			0.933
Adenocarcinoma	67	73	
Mucinous adenocarcinoma	2	2	
Distal resection margin, cm (mean \pm SD)	3.2 \pm 1.2	3.6 \pm 1.2	0.089
Radical margin			–
Negative	69	75	
Positive	0	0	
Stage of tumor			0.611
I	11	16	
II	25	28	
III	33	31	
Preoperative therapy			0.497
Yes	0	2	
No	69	73	
Postoperative therapy			0.468
Yes	51	51	
No	18	24	

no-washout group. The 5-year disease-free survival rate was 79.7 % for the washout group and 74.7 % for the no-washout group (Table 3) during a median follow-up of 48 months. Of the recurrences, 7 deaths (washout group = 3, no-washout group = 4) were directly attributed to carcinomatosis. The characteristics of recurrences were shown in Table 4; the possible factors which might be related to recurrence in washout group and no-washout group were identical.

Discussion

Local recurrence of rectal cancer is one of major obstacles for surgeons; the emergence of local recurrence will influence the prognosis of disease. Patients with local recurrence have poor quality of life and short survival time. Local recurrence has been attributed to several factors, for example, remaining solid tumor, stage of tumor, performance of a radical margin or not, reaction to adjuvant therapy, and so on. Implantation of exfoliated malignant cells has been suggested to explain the mechanism by which local recurrences occur. Exfoliated malignant cells

have been demonstrated in both rectal stump effluent and on circular stapling devices [7, 8]. In our study, exfoliated malignant cells had been found in washout samples of 79.7 % patients in washout group, and the result confirmed the ubiquity of exfoliated malignant cells in rectal lumen once again. In a previous research conducted by Maeda et al. [9] which included 30 patients, free malignant cells were found in 29 patients' washout sample. The ability of implantation and multiple fission in exfoliated malignant cells has concerned some researchers [3, 4]. These cells tend to implant on mucosal surface which is damaged by surgery, although exfoliated tumor cells do not have the ability of implanting on normal mucosa. Even these viable exfoliated malignant cells are able to cross an otherwise watertight anastomosis to cause locoregional recurrence [10].

Intra-operative rectal washout has been applied on clinical practice by some surgeons. Rectal washout is considered safe by most surgeons, although there are a few case reports concerning the serious side effects after instilling commonly used solutions such as ceterimide [11] and chlorhexidine [12]. Proponents of intra-operative rectal washout state that exfoliated malignant cells can be

Table 3 Prognoses of patients in two groups

Parameters	Washout group <i>n</i> = 69	No-washout group <i>n</i> = 75	<i>p</i> value
Local recurrence			0.721
Yes	3	5	
No	65	70	
Distant metastasis			0.842
Yes	12	14	
No	57	61	
5-year disease-free survival			0.553
Yes	55	56	
No	14	19	

Table 4 Comparison of patients with recurrence in two groups

Characteristics	Washout group <i>n</i> = 3	No-washout group <i>n</i> = 5	<i>p</i> value
TNM stage			0.347
I	0	2	
II	0	1	
III	3	2	
Mean tumor size (cm)	4.0 ± 2.4	3.2 ± 1.3	0.542
Mean distal resection margin (cm)	3.3 ± 2.1	2.8 ± 0.4	0.644
Distance to anal verge (cm)	8.8 ± 4.6	7.0 ± 3.2	0.518
Intra-operative spillage	0	0	–
Postoperative therapy	3	3	0.444

removed by this method, reducing local recurrence rate and improving prognosis. Meanwhile Church et al. [6] stated that eliminating exfoliated malignant cells thorough rectal irrigation mainly by mechanical cleansing, rather than by any cytotoxic effect of the irrigant, saline alone should be considered firstly. Some professors put forward the opposite viewpoint; they cast doubt on the merit of intra-operative rectal washout. In the study of Agaba et al. [10], 90 patients with rectal cancer received rectal irrigation with cetrimide before anastomosis, 51 patients did not undergo rectal washout, and there was no significant difference in local recurrence rates between the two groups (4.4 vs. 5.9 %, $p = 0.0653$). The American Society of colon and rectal surgeons concluded that there was insufficient evidence to recommend intra-operative rectal washout [13]. Whether the intra-operative rectal washout should be used on clinical practice routinely or not is still uncertain. And it is still unclear whether this can translate into a reduction in the incidence of local recurrence. Despite the ubiquity of exfoliated malignant cells, recurrence rates are very low, for example, the 5-year rate of local recurrence of rectal

cancer was 4.3 % in the study of Mathis et al. [14], and the total recurrence rate was 5.6 % in our study. All this evidence testifies that more factors and mechanisms should be considered for the recurrence of rectal cancer, and the existence of free malignant cells was not as important as we thought. In our study, the recurrence rates were 4.3 and 6.7 % in washout group and no-washout group, respectively, the difference was not significant ($p = 0.721$), and the 5-year disease-free survival rates were 79.7 and 74.7 % in washout group and no-washout group, respectively, which were similar to the results of the study of Agaba et al. [10].

When interpreting our results, some reasons should be taken into account. First, the proportion of well-differentiated adenocarcinoma was obviously higher in non-washout group, and well-differentiated adenocarcinoma was associated with good prognosis as is known to all. This may be the key factor which influenced outcome analysis and led to the deviation of result. Second, the size of our study was not sufficient to detect the difference of the local recurrence and the 5-year disease-free survival rate. Third, the follow-up time of our study was not long enough to make sure that all of local recurrences were tracked down, and some potential recurrences may become apparent and new recurrences maybe emerge as the extending of follow-up time.

Conclusions

There is a trend of better prognosis in washout group but there is not statistically significant. A more large-scale study is required to draw a conclusion on the effect of rectal washout on the local recurrence of rectal carcinoma after surgery.

Conflict of interest None.

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