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Original Article

Indications of preventive ileostomy in sphincter-preserving surgery for patients with rectal cancer

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Abstract: Objective: This study aimed to investigate causes of anastomotic leakage following sphincter-preserving surgery, and explore indications of preventive ileostomy. Methods: 816 rectal cancer patients who underwent sphincter-preserving surgery in the Affiliated Hospital of Xuzhou Medical College between March 2004 and March 2014 were enrolled in the study. And the informations such as age, gender, underlying disease, nutritional status, smoking, alcohol abuse, along with records concerning blood loss, duration, and anastomotic height of the surgery, etc. were collected to conduct statistical analysis and investigate the relationship between these factors and post-operational anastomotic leakage. Results: Diabetic male patients that ≥ 65 years, with alcohol abuse, height of the anastomosis ≤ 5 cm, and surgical duration > 3 hours had higher incidence to develop anastomotic leakage in comparison to the control group, and the difference was of statistical significance. Conclusion: Risk factors of anastomotic leakage subsequent to sphincter-preserving surgery include indicators that are of clinical significance to assess whether an additional preventive ileostomy is needed, such as gender, age, diabetes, alcohol abuse, low anastomosis, surgical duration, etc.

Keywords: Rectal cancer, sphincter-preserving surgery, anastomotic leakage, risk factor

Introduction

The incidence of rectal cancer is in a gradually-increasing trend, which has made it a common clinical type of cancer. While radical surgery is still the major resort to treat rectal cancer, surgeons are continually harassed by post-operational anastomotic leakage. Although with continuous improvement of surgical techniques, the incidence of anastomotic leakage after lower-position sphincter-preserving surgery is not significantly reduced. Since total mesorectal excision (TME) was introduced by Heald et al. [1] in 1982, its clinical efficacy has been internationally accepted, and the treatment of rectal cancer has been revolutionized. After 30 years of clinical practice, TME has become the standard radical surgery to treat middle- and lower-position rectal cancer both at home and abroad. However, the incidence of anastomotic leakage after radical surgery has also increased dramatically, fluctuating between 4% and 26% according to Kong et al. [2-5]. And the incidence of anastomotic leakage subsequent to rectal cancer surgery out of 24, 288 patients based on MEDLINE database analysis was reported to be about 8.58% by Cong et al. [6]. Therefore, in order to reduce the incidence of anastomotic leakage as well as secondary operation, empirical preventive ileostomy is often adopted in clinical practice. And an effective pre-operational assessment system is in urgent need to solve the existing controversy over empirical prevention.

Anastomotic leakage, with an incidence of 5%-19.2% [7-9], is one of the most severe complications after sphincter-preserving surgery to treat rectal cancer. It seriously jeopardizes the post-operative recovery and even the life of the

Table 1. Single factor analysis on risk factors related to the incidence of anastomotic leakage

Variable	Anastomotic leakage (n = 90)		Total number of cases (n = 816)	X^2 value	*P* value
	Number of cases	Incidence (%)			
Age				6.394	0.013
< 65 years old	41	8.7	473		
≥ 65 years old	49	14.3	343		
Gender				7.068	0.009
Male	62	13.6	455		
Female	28	7.8	361		
Laparoscopic surgery				1.806	0.183
Yes	33	13.3	249		
No	57	10.1	567		
Diabetes				5.912	0.022
No	75	10.2	738		
Yes	15	19.2	78		
Hypertension				0.017	0.894
No	69	11.0	630		
Yes	21	11.3	186		
Pre-operational chemotherapy				0.073	0.772
No	86	11.0	784		
Yes	4	12.5	32		
Smoking				2.699	0.117
No	36	9.2	393		
Yes	54	12.8	423		
Alcohol abuse				16.391	0.000
No	51	8.4	606		
Yes	39	18.6	210		
Preventive ileostomy				3.710	0.060
No	63	10.0	633		
Yes	27	14.8	183		
Blood transfusion				2.260	0.154
No	72	10.3	696		
Yes	18	15	120		
BMI kg/m^2				2.846	0.097
< 28	81	11.8	684		
≥ 28	9	6.8	132		
Tumor staging				4.274	0.040
Stage I and II	63	12.9	489		
Stage III and IV	27	8.3	327		
Anastomotic height				5.109	0.029
≤ 5 cm	65	13.0	500		
> 5 cm	25	7.9	316		
Surgical duration				5.084	0.022
≤ 3 h	9	5.9	153		
> 3 h	81	12.2	663		
Tumor diameter				6.813	0.735
< 5 cm	54	11.5	471		
≥ 5 cm	36	10.4	345		
Surgical blood loss				1.716	0.210
< 300 ml	30	9.3	324		
≥ 300 ml	60	12.2	492		

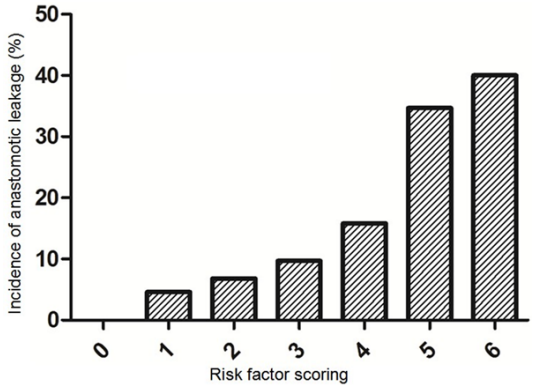

Figure 1. Relationship between risk factor scoring and the incidence of anastomotic leakage.

patient. And rational risk assessment of anastomotic leakage and timely prevention are of great importance. Clinical data of 816 rectal cancer patients that were treated by sphincter-preserving surgery in our hospital from March 2004 to March 2014 were collected and analyzed to explore risk factors of post-operational anastomotic leakage and indications of preventive ileostomy.

Materials and methods

Subjects

This study included 816 patients that underwent sphincter-preserving surgery for rectal cancer in the Affiliated Hospital of Xuzhou Medical College between March 2004 and March 2014. And retrospective statistical analysis on clinical data of all the subjects was carried out. All patients were pathologically diagnosed as rectal cancer, and the distance between the tumor's lower edge and the anal verge ranged from 4 to 16 cm (confirmed by colonoscopy). Patients' general information is shown in **Table 1**.

Methods

All surgeries were performed by specialized doctors with at least senior professional titles as per TME principles [1]. The surgical doctor decided if a preventive ileostomy was needed according to the location and size of the tumor, difficulty of the operation, present obstruction, recent radiotherapy and chemotherapy, as well as his or her own assessment on the condition of the patient. Among the 816 patients, 249 accepted laparoscopic surgery, including 7 who were converted to open surgery and thus included in the open group. Preventive proximal ileostomy was performed on 183 patients, and secondary operations were given to return the ileostomy in 3-6 months. If the diagnosis of anastomotic leakage was determined, fasting and intravenous nutrition were required to maintain water-electrolyte balance. Meanwhile, patients were also prescribed antibiotics and daily rinsing with normal saline (NS) and metronidazole solution through the drainage tube.

Potential relevant factors before and during the surgery were recorded to determine their influence on anastomotic leakage. The eight before-surgery factors included gender, age, body mass index (BMI), diabetes, hypertension, smoking and alcohol abuse, as well as recent adjuvant radiotherapy and chemotherapy. And the six intraoperative factors were laparoscopic surgery, tumor diameter, blood loss in surgery, surgical duration, height of the anastomosis, and blood transfusion.

Parameter selection and definition

Surgical duration: The time period from skin incision to suture completion.

Blood loss in surgery: The volume of liquid in the suction unit plus the weight gained by auxiliary materials, and minus the total volume of rinsing water.

Anastomotic leakage: It referred to purulence, feces and gas discharged from the drainage tube after surgery, and peritonitis manifestations may be present, such as lower abdominal pain, fever, leukocytosis, etc. Special forms of anastomotic leakage like rectovaginal fistula and rectovesicular fistula were also included in the study, and contrast enema X-ray examination may help diagnose.

Statistical analysis

Statistical analysis was conducted using SPSS 16.0. Measurement data were presented in $\overline{x} \pm s$. The t-test was adopted for intergroup comparison, and X^2 test was employed for enumeration data comparison. And logistic regression was applied in multivariate analysis. $P \leq 0.05$ indicated significant difference.

Table 2. Logistic regression analysis on risk factors of anastomotic leakage

Parameter	B	Standard error	Wald value	P	OR (95% CI)
Diabetes	0.871	0.332	6.902	0.009	2.390 (1.124-40221)
Age ≥ 65 years	0.640	0.234	7.477	0.006	1.897 (1.157-3.256)
Surgical duration > 3 hours	0.776	0.370	4.414	0.036	2.174 (1.524-4.125)
Alcohol abuse	1.169	0.245	22.789	0.000	3.217 (1.213-5.269)

Table 3. Comparison between risk factors of the preventive ileostomy group and the control group

Parameter	Preventive ileostomy		Control group		X^2 value	*P* value
	N	%	N	%		
Surgical duration (h)						
< 3	0	0	153.0	100.0	53.295	0.000
≥ 3	180	27.1	483.0	72.9		
Anastomotic height (cm)						
≤ 5	147	29.4	353.0	70.6	40.472	0.000
> 5	33	10.4	283.0	89.6		
Age (years)						
≤ 65	76	22.2	267.0	77.8	0.025	0.932
> 65	107	22.6	366.0	77.4		
Diabetes						
Yes	30	38.5	48.0	61.5	14.747	0.001
No	153	20.7	585.0	79.3		
Alcohol abuse						
Yes	51	24.3	159.0	75.7	0.562	0.444
No	132	21.8	474.0	78.2		

Results

Single factor analysis revealed that the risks of anastomotic leakage included age ≥ 65 years, male, surgical duration > 3 hours, diabetes, alcohol abuse, and anastomotic height ≤ 5 cm (**Table 1**). Each of these risk factors listed above was scored as 1 point to analyze its relationship with anastomotic leakage (**Figure 1**). And the total score was found to be positively correlated with the probability to develop anastomotic leakage, with significant difference.

Binary Logistic regression multivariate analysis indicated that independent risk factors of anastomotic leakage included diabetes, alcohol abuse, age ≥ 65 years, and surgical duration > 3 hours (**Table 2**). The surgical duration was longer while the anastomotic height was lower in patients that underwent preventive ileostomy compared to those that did not (**Table 3**).

After receiving systematic therapy following the sphincter-preserving surgery, 811 out of 816 patients were discharged from hospital, and 5 patients died (1 due to pulmonary embolism, 2 due to severe post-operational infection which led to multiple organ failure, 1 due to heart failure, and 1 due to pulmonary infection followed by respiratory failure). A total of 258 patients (31.6%) suffered from anastomotic leakage, incision infection, and hypostatic pneumonia; 90 cases had anastomotic leakage (11.0%), and secondary operations were required in 39 cases (43.3%). Anastomotic leakage was observed in 27 out of the 183 patients (14.8%) that received preventive ileostomy, and secondary operations were performed on 3 patients for post-operative hemorrhage and pelvic abscess. Terminal ileum feces diversion enterostomy was performed on 36 out of the 63 patients that received no preventive ileostomy and developed anastomotic leakage, due to worsened post-operational general condition, inadequate pelvic drainage, fever and severe symptoms of peritonitis, or the fact that abnormal drainage volume and content were not significantly improved after 3-4 weeks of active rinsing.

The study showed that the anastomotic leakage appeared 4-17 days (average, 8.03 ± 2.55 days) after surgery. Anastomotic leakage was presented in 27 cases 4-6 days after surgery, in 60 patients 7-14 days after surgery and in 3 patients 14 days later after surgery.

Discussion

This retrospective study on 816 patients treated in our hospital revealed that risk factors of anastomotic leakage following sphincter-preserving surgery were low anastomosis (≤ 5 cm), age ≥ 65 years, male, alcohol abuse, diabetes and surgical duration > 3 hours.

Age and gender

The incidence of anastomotic leakage in patients over 65 years was relatively higher (14.3% vs. 8.7%), because elderly patients had worse nutritional condition compared to younger ones, and alos had underlying diseases (such as diabetes, etc.) which were also risk factors of anastomotic leakage [10-12]. Moreover, function capacities of vital organs (heart, lungs, kidneys etc.) among aged patients were not sufficient enough to bear the impact of surgical procedures, and thus anastomotic leakage tended to be developed. Additionally, male patients were more likely to suffer from anastomotic leakage than females (13.6% vs. 7.8%). And the reason may be that it's hard to expose the operational field while separating the rectum, due to the narrower male pelvis, thereby contributing to the incidence of injuring remnant distal rectum and adjacent vessels [13].

Surgical factors

Prolonged surgical duration has already been proved by scholars as the risk factor of anastomotic leakage [14, 15]. In this study, it was found that patients presented a higher incidence (12.2% vs. 5.9%) to develop anastomotic leakage if surgical duration was longer than 3 hours, consistent with the findings of Park et al. [16]. Prolonged duration of the surgery was usually attributed to difficulties of operational procedures, tumor disposal, and hemorrhagic incidents, etc. that added up the probability of operative complications and abdominal infection [15]. Excessive surgical blood loss (≥ 300 ml) and blood transfusion during surgery were also reported as risk factors of anastomotic leakage [17-19]. Several studies [18, 19] have revealed that blood transfusion during surgery may suppress patient's immune mechanism, and increase the incidence of postoperative infection that results in anastomotic leakage. In this study, the incidence of anastomotic leakage was higher in the transfusion group than the non-transfusion group, but the difference was of no statistical significance, which was probably due to statistical results affected by the insufficient cases selected for the transfusion group. Excessive blood loss during surgery will cause tissue hypoperfusion, anastomotic ischemia and eventually the leakage. As shown in **Table 1**, a higher incidence of anastomotic leakage was observed in the transfusion group as well as patients with blood loss volume more than 300 ml. However, the difference had no statistical significance. The recorded volume of blood loss of the two groups was (403.96 ± 150.25) ml and (167.69 ± 50.35) ml, respectively; allowing for the compensatory capacity, the blood loss above 300 ml of the first group would not significantly influence blood supply to the anastomotic area.

Underlying disease

The study of Zaharie and Vignali et al. [10, 20] has indicated that rectal cancer patients are more likely to develop anastomotic leakage if they have underlying diseases such as diabetes, hypoproteinemia, anemia, etc. Diabetic patients in this study presented with a higher incidence of anastomotic leakage (19.2% vs. 9.0%), consistent with the results of Vignali et al. Because of systematic metabolic disorder, diabetic patients have inferior healing and anti-infection capacities, and slower healing will cause infection and inflammation that result in anastomotic leakage.

Recent radiotherapy and chemotherapy before surgery

Literature review has shown that the incidence of anastomotic leakage remarkably increases (from 9.7% to 26.6%) in patients that have received radiotherapy and chemotherapy before surgery [21-24]. And this is because such therapies will influence cell metabolism and tissue repair, which in turn will cause anastomotic leakage. Only 32 patients in this study received recent adjuvant chemotherapy before surgery, and 4 presented with post-operative anastomotic leakage. The difference in comparison to the control group (12.5% vs. 11.0%) had no statistical significance, probably relevant to insufficient cases of the chemotherapy group.

Smoking and alcohol abuse

Other studies have proved that smoking and alcohol abuse will increase the risk to develop anastomotic leakage [10, 25, 26]. And this is also confirmed in our study. Smoking causes vasoconstriction, and slows down circulation, which reduces blood supply to the anastomotic area. Long-term alcohol abuse incurs subclinical cardiac insufficiency, suppressed immune system, reduced blood coagulation, reduced

tissue repair, influencing healing of the anastomotic area [27, 28].

Tumor

Chen et al. [28] have listed tumor size as a possible risk factor of anastomotic leakage. Allowing for the lengthy growing period of the tumor, the larger the tumor size, the greater the systematic influence and the more extensive the excision. In our study, the difference between incidences of anastomotic leakage in patients with tumor diameters < 5 cm and ≥ 5 cm was significant, consistent with the finding of Chen WR et al. Therefore, tumor diameter was not the risk factor of anastomotic leakage. Middle and lower anastomosis (≤ 5 cm) presented a higher incidence of anastomotic leakage in this study, conforming to various other researches [8, 29]. And possible reasons may be that low anastomosis increases the tension in the anastomotic area and the difficulty of the operation on distal rectum. Also, the blood supply of proximal bowel segment in low anastomosis is worse than that of anastomosis conducted on an elevated position.

Preventive ileostomy

The advantages of preventive ileostomy: Shortened gas passage by anus after surgery, earlier food intake, and earlier removal of pelvic drainage tube; Lower incidence of complications and anastomotic leakage; Shorter postoperative hospital stay and remarkably-reduced treatment costs [30]. The disadvantages: Anastomotic infection, necrosis, skin irritation, etc.; Severe complications, such as anastomotic prolapse, retraction and stenosis, parastomal hernia and fistula, etc.; Prolonged hospital stay and difficulty in recovery; 4. Secondary operation needed to return anastomosis, and extra costs for inpatient treatment [31]. The incidence of patients that received preventive ileostomy was higher compared to those that did not. This is considered as a result of the selection bias when performing preventive ileostomy in anastomosis. The risk of anastomotic leakage was remarkably higher in the preventive ileostomy group than the control group (the difference was of statistical significance), which was proved by the inter-group comparison in surgical duration and anastomotic height (**Table 3**).

In conclusion, the incidence of anastomotic leakage after sphincter-preserving surgery for rectal cancer is closely related to low anastomosis (≤ 5 cm), age ≥ 65 years, male, alcohol abuse, diabetes, and prolonged surgical duration. Each of these listed factors has been scored as 1 point in this study, and the results reveal that such score is in positive correlation with the incidence of anastomotic leakage. Therefore, preventive ileostomy should be considered if patient scores > 3 points in the risk factor assessment stated above. This is in accordance with results of the research conducted by Telem et al. [32]. At present, empirical preventive ileostomy is often carried out in clinical practice, which has inflicted unnecessary pain and treatment costs on many patients. The establishment of this scoring system can effectively reduce the incidence of anastomotic leakage and alleviate the suffering of patients.

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Disclosure of conflict of interest

None.

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