

# The effect of anti-adhesive agent on patients with low anterior resection syndrome

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ABSTRACT

**Objective:** This study aimed to evaluate the efficacy of the anti-adhesive agent in enhancing bowel function after a low anterior resection in patients diagnosed with rectal cancer.

**Methods:** From January 2006 to December 2020, we analyzed the prospective data of 112 patients with laparoscopic low anterior resection. The patients were divided into Anti-adhesive (n=54) and non-adhesive (n=58). The assessment of bowel function was conducted between 3 months to 24 months following surgery. It was evaluated by personal interviews (incontinence status), and by anorectal manometry.

**Results:** Of 112 patients, the mean age was 63.0 years. The mean frequency (p=0.041), urgency (p=0.036), and seepage (p=0.039) of bowel movements were significantly higher statistically in the study group in 3 months postoperatively. In 2 years, fecal incontinence score was significantly improved in in study group (p=0.025). In 24 months of follow-up, the study group showed a considerable increase in Maximum Anal Squeezing Pressure (MASP) from 146.3 mmHg to 178.9 mmHg (p=0.002), but no statistical differences were found between 2 groups during the follow-up period (p=0.838).

**Conclusion:** Applying an anti-adhesive agent to the pelvic cavity after laparoscopic low anterior resection in rectal cancer patients may reduce postoperative bowel movement dysfunction.

**Keywords:** anti-adhesive agent, low anterior resection syndrome, rectal resection

## INTRODUCTION

The most fundamental treatment strategy for rectal cancer is surgical radical resection. It is the standard surgical therapeutic principle of providing Total Mesorectal Excision (TME) composed of complete excision of the mesorectum with securing a safe resection margin and perioperative chemoradiotherapy as an additional treatment, depending on the stage of the malignant lesion. Nevertheless, surgical excision of the rectum might compromise its distinctive anatomical function, resulting in a range of functional side effects or problems.

From a functional standpoint, it is of utmost importance to give priority to the preservation of the anus in order to maintain a regular bowel function. Abdominoperineal resection, performed with adaptation, involves removing both the anus and rectum, resulting in a permanent stoma on the abdominal wall. This can lead to psychological problems and discomfort due to changes in the physical appearance for the patient. Preservation of anal function and autonomic nerves has become a crucial objective in radical surgery for rectal cancer. With advancements in molecular biology, oncological research, surgical techniques, and laparoscopic procedures, surgeons are now able to perform anal sphincter preservation surgery in the majority of patients [1, 2]. However, it is still reported that 25%-50% of patients who underwent anal preservation rectal resection complained of bowel dysfunction such as fecal incontinence, urgency, frequent bowel movements, tenesmus and clustering of stool [3-5].

The impairment of bowel function following rectal resection is referred to as Low Anterior Resection Syndrome (LARS). This condition is particularly noticeable when the rectum is separated and mobilized through TME, the left colon and the remaining rectum are severed at the level of the elevator ani muscle, and a linear anastomosis (straight end-to-end anastomosis) is performed. The causes can be attributed to several factors, such as reduced rectal compliance and volume resulting from rectal resection, impairment of the autonomic nervous system, damage to the anal sphincter caused by the insertion of the circular stapler through anus, and altered recto-anal reflex and sampling reflex that differentiate the characteristics of the stool [6, 7]. Various treatment methods, including pelvic floor muscle rehabilitation, bio-feedback therapy, and rectal balloon training, have been introduced to alleviate the symptoms of LARS. However, due to the participation of multiple factors, no particular effective treatment has been widely accepted [8, 9].

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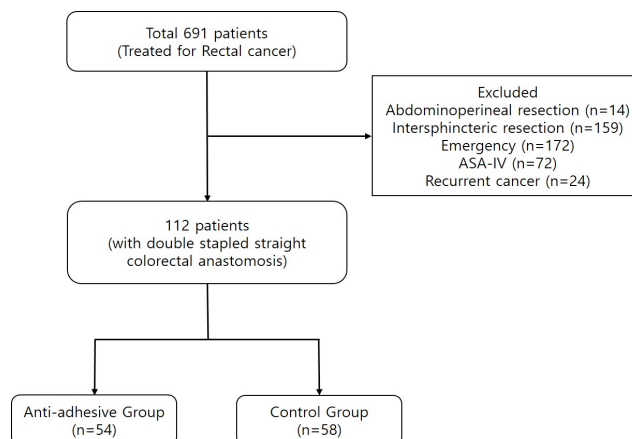
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Studies have shown that anti-adhesion agents are successful in decreasing the occurrence of postoperative adhesions that happen during abdominal and pelvic surgery [10, 11]. Anti-adhesion agents function by physically separating damaged and inflamed tissues and organs that display adhesion, while promoting the healing of normal tissues. Additionally, there have been findings indicating that anti-adhesion agents have shown improvement in peripheral nerve regeneration during experiments on animals [12].

Therefore, the authors hypothesized that administering an anti-adhesion agent in the pelvic cavity after low anterior resection would restrict the local inflammatory response, diminish fibrosis, and expedite the restoration of nerve activity and effectiveness, thereby improving the mobility and storage of the large intestine and facilitating smooth evacuation of stool. Consequently, the authors conducted a subsequent investigation on the gastrointestinal symptoms experienced by patients who utilized an anti-adhesion agent in the pelvic cavity following rectal resection.

## METHODS

Between January 2006 and December 2020, the authors



**Fig. 1.** Flowchart for inclusion and exclusion

In 2011, Hanmi Medicare in Seoul, Korea released a product called Guardix-sol<sup>®</sup>. The study selected patients who had not used anti-adhesion agents before this release (referred to as the control group) and patients who started using anti-adhesion agents after the release (referred to as the study group). The purpose was to analyze the difference in bowel function between these two groups.

During laparoscopic surgery, the inferior mesenteric artery was ligated at its origin from the abdominal aorta in all patients. The splenic flexure was completely mobilized to mandate tension-free coloanal anastomosis and pelvic dissection was performed while preserving the superior hypogastric plexus. Total mesorectal excision was conducted in all cases, ensuring preservation of the autonomic nerves and ureter, unless they were immediately affected by the tumor. Following the full detachment of the rectum from the pelvic floor muscle, an automatic linear stapler was used to cut the rectum. Subsequently, a straight colo-rectal anastomosis was carried out by utilizing an automatic circular stapler. After the completion of the anastomosis, an anti-adhesion agent was applied in the pelvic cavity for the study group. The anti-adhesion agent used was a mixed solution of Hyaluronic Acid (HA) and Carboxymethyl Cellulose (CMC), specifically known as HA-CMC and marketed as Guardix-sol<sup>®</sup> by Hanmi Medicare in Seoul, Korea.

conducted a study on patients who had laparoscopic low anterior resection following a diagnosis of rectal cancer at Pusan National University Hospital and Yangsan Pusan National University Hospital. The patient data were prospectively recorded in our hospital's colorectal surgical database, and the postoperative follow-up and analysis was performed retrospectively. The main inclusion criteria for the patients in the study were individuals who had entirely intact anatomical structure of the anal sphincter and had their natural bowel passage restored through colon-rectal anastomosis following low anterior resection. The patients who were excluded from the study were those who had undergone abdominoperineal resection (n=14) and intersphincteric resection (n=159). Furthermore, the study excluded individuals (n=127) who had previously undergone preoperative chemoradiotherapy, a treatment known to potentially cause impaired bowel function following surgery. Furthermore, patients who had emergency surgery (n=172), American Society of Anesthesiologists (ASA) grade IV body classification (n=72), as well as patients with recurring cancer (n=24) and concurrent cancer (n=11) were also not included. By applying these inclusion and exclusion criteria, a total of 112 patients were included in the study (Figure 1).

The primary components of Guardix-sol<sup>®</sup> are sodium Hyaluronate (HA) and Carboxymethyl Cellulose (CMC). HA is a negatively charged polysaccharide that is found in synovial fluid, vitreous fluid, and extracellular matrix. It is composed of D-glucuronic acid and N-acetyl-D-glucosamine, and it forms a linear polymer with exceptional biocompatibility and biocompatibility. The material's properties prevent sticking by coating the tissue surface during surgery and inhibiting the production of fibers. Nevertheless, its anti-adhesion function is restricted due to its rapid decomposition, with a half-life of merely 3 days. CMC is a hydrophilic polymer derived from plant cellulose. It has a low molecular weight and is resistant to decomposition in the human body due to the absence of decomposing enzymes. During the recovery of the mucosa, this substance remains on the tissue surface due to its delayed absorption in the body. Subsequently, it is transported to the liver, where it is broken down, absorbed, and eliminated through the metabolic pathway of carbohydrates. It possesses a prolonged residual duration and can function well as a physical barrier. Guardix-sol<sup>®</sup>, formulated by leveraging the benefits and drawbacks of its constituent elements, undergoes natural decomposition in the body during a span of two weeks post-surgery. It is thereafter absorbed and eliminated within a month. While previous studies have demonstrated that the HA-CMC mixed component does not have an

impact on the healing of anastomosis, it was used cautiously to avoid direct contact with the anastomosis while applying an anti-adhesion agent in order to maintain the stability of the clinical outcomes [13, 14]. The creation of the temporary loop ileostomy was carried out when it was in an unstable state, determined by the presence of positive anastomotic tension and air leakage during testing. The restoration of the intestinal fistula took place around 4 months following the surgery. The investigation focused on general clinical data such as gender, Body Mass Index (BMI), ASA grade, and intestinal composition. Additionally, pathology data including cancer stage, distal resection margins, and lateral resection margins were examined. The cancer stage was determined using the TNM stage based on the AJCC version 8<sup>th</sup> in 2017 [15].

The patient's ability to defecate was assessed by outpatient care following surgery or up to the second year after the restoration of the intestinal fistula. The Wexner Incontinence Score (WIS) was employed to assess the extent of fecal incontinence in every patient [16]. The evaluation of postoperative bowel function was selected as a relevant factor for this investigation, based on the utilization of the "low anterior resection syndrome score card" from a prior study [17]. Anorectal manometry was conducted to objectively evaluate anal function, utilizing a Dynacompact apparatus manufactured by Menfis Biomedica Corp. in Bologna, Italy.

All statistical analyses were performed using version 25 of IBM SPSS Statistics (SPSS Inc, Chicago, IL, USA). Numerical variables are represented by their median values and ranges, whereas category variables are represented as percentages. The Mann-Whitney U test or the student t-test is used for numerical

variables, and the Pearson's chi-square test or Fisher's accuracy test is used for category data. A p-value below 0.05 was considered statistically significant. This retrospective cohort study was approved by the ethics committee and the Institutional Review Board (IRB No. 05-2023-208) of Pusan National University Yangsan Hospital and written informed consent was waived because of its retrospective nature.

## RESULTS

The study included a total of 112 patients, 67 males (59.8%) and the average age was 63.0 (range, 59-67) years. There were no instances of observable conversion during laparoscopic surgery in either of the two groups. There were no significant statistical differences seen between the two groups in terms of age, sex ratio, and body obesity index, body grade classification according to the American Society of Anesthesiology, cancer stage, cancer lesion, and temporary loop ileostomy composition ratio (Table 1). There were no statistical differences between the two groups in the operation time, distal resection margin, and the distance from the anal verge to the anastomosis analyzed as surgical and pathological factors (Table 2). Postoperative complications occurred in 34 cases (30.4%), and there were no cases of death within 30 days in both groups. Postoperative complications of the study group and the control group occurred in 14 cases (25.9%) and 20 cases (34.5%), respectively, and there was no statistical difference in the incidence of complications between the two groups (Table 2). Among mild complications, ileus occurred the most (12 cases, 10.7%), and anastomotic leakage occurred in 2 cases (1.8%) as a severe complication requiring additional procedures and surgical treatment.

**Tab. 1.** Clinicopathological characteristics of the patients

Variables		Study Group (n=54)	Control Group (n=58)	p-Value
Age (years)		60.8 ± 1.1	65.1 ± 2.7	NS*
Gender	Male	36 (66.7%)	31 (53.4%)	NS†
	Female	18 (33.3%)	27 (46.6%)	
Body mass index (kg/m <sup>2</sup> )		24.6 ± 3.0	23.6 ± 3.1	NS*
ASA class	I-II	49 (90.7%)	53 (91.4%)	NS†
	III	5 (9.3%)	5 (8.6%)	
Stage	I-II	28 (51.9%)	33 (56.9%)	NS†
	III	26 (48.1%)	25 (43.1%)	
Stoma Formation		39 (72.2%)	45 (77.6%)	NS†
Tumor size (cm)		3.7 ± 0.2	3.5 ± 0.4	NS*

Values are expressed as mean ± standard deviation or n (%).

ASA = American Society of Anesthesiologists; CEA = Carcinoembryonic Antigen; NS = Not Significant;

\*Student t-test †Pearson chi-square

The patient's bowel function was regularly evaluated for a period of two years after the restoration of normal bowel movements, in case there was a reversal of a bowel fistula formation. The assessment is summarized in table 3. There was no statistically significant difference in fecal incontinence scores between the two groups within the initial 3-month period. Nevertheless, the study group exhibited a statistically significant increase in stool frequency (p=0.041), stool urgency (p=0.036), and seepage (p=0.039). In contrast, the study group had a statistically significant reduction in symptoms associated with tenesmus (p=0.042). No statistically significant difference was seen between the two groups in terms of stool frequency, stool urgency, seepage, or fecal inconti-

nence score during the 6 months after the surgery. Nevertheless, the control group still exhibited a significant degree of tenesmus (p=0.038). Over the course of one year, the study group had a statistically significant decrease in stool frequency compared to the control group (p=0.039). In addition, the study group showed significantly less symptoms of tenesmus (p=0.024). Following a duration of around 2 years, the study group demonstrated a statistically significant decrease in fecal incontinence score (p=0.025), stool frequency (p=0.032), and tenesmus (p=0.012) in comparison to the control group. Additionally, they exhibited a statistically significant improvement in defecation function compared to the control group.

Tab. 2. Surgical outcomes		Variables	Study Group (n=54)	Control Group (n=58)	p-Value
		Operation time (min)	270.0 (175.0 - 545.0)	262.5 (155.0 - 660.0)	NS*
		Distal surgical margin (cm)	2.8 ± 0.3	2.7 ± 0.4	NS <sup>†</sup>
		Anastomotic level from anal verge (cm)	4.5 ± 0.6	4.7 ± 0.3	NS <sup>†</sup>
Complication		None	40 (74.1%)	38 (65.5%)	NS <sup>‡</sup>
		Ileus	5 (9.3%)	7 (12.1%)	-
		Urinary	4 (7.4%)	5 (8.6%)	-
		Pulmonary	2 (3.8%)	3 (5.3%)	-
		Wound infection	1 (1.8%)	2 (3.4%)	-
		Anastomotic leak	1 (1.8%)	1 (1.7%)	-
		Others	1 (1.8%)	2 (3.4%)	-

Values are expressed as median (range), mean ± standard deviation, or n (%).

NS = Not Significant;

\*Mann-Whitney U-test †Student t-test ‡Pearson chi-square

Tab. 3. Functional results at different times after stoma closure (3, 6, 12, 24 months)	Variables	3 months			6 months			12 months			24 months		
		Study Group (n=54)	Control Group (n=58)	p- Value	Study Group (n=54)	Control Group (n=58)	p-Value	Study Group (n=54)	Control Group (n=58)	p- Value	Study Group (n=54)	Control Group (n=58)	p- Value
	Wexner incontinence score <sup>a)</sup>	6.6 ± 3.1	6.1 ± 4.4	NS*	5.2 ± 4.2	3.9±4.3	NS*	3.9 ± 4.8	3.7 ± 4.4	NS*	2.2 ± 3.4	4.0 ± 4.7	0.025*
	Stool frequency (per day)	14.2 ± 4.6	6.4 ± 2.5	0.041*	4.5 ± 1.6	4.3±1.5	NS*	1.6 ± 0.9	3.4 ± 1.3	0.039*	1.5 ± 1.2	2.3 ± 1.9	0.032*
	Stool urgency <sup>b)</sup>	53 (98.1%)	45 (77.6%)	0.036 <sup>†</sup>	37 (68.5%)	27 (46.6%)	NS <sup>†</sup>	22 (40.7%)	24 (41.4%)	NS <sup>†</sup>	19 (35.2%)	22 (37.9%)	NS <sup>†</sup>
	Seepage <sup>c)</sup>	35 (64.8%)	26 (44.8%)	0.039 <sup>†</sup>	18 (33.3%)	20 (34.5%)	NS <sup>†</sup>	13 (24.1%)	17 (29.3%)	NS <sup>†</sup>	12 (22.2%)	13 (22.4%)	NS <sup>†</sup>
	Tenesmus <sup>d)</sup>	18 (33.3%)	29 (50.0%)	0.042 <sup>†</sup>	14 (25.9%)	22 (37.9%)	0.038 <sup>†</sup>	9 (16.7%)	22 (37.9%)	0.024 <sup>†</sup>	4 (7.41%)	27 (46.6%)	0.012 <sup>†</sup>

Values are expressed as mean ± standard deviation, or n (%).

<sup>a)</sup> Wexner incontinence score: 0 = perfect continence; 20=major incontinence

<sup>b)</sup> Stool urgency: degree of urgency measured by the ability to defer defecation for 30 min

<sup>c)</sup> Seepage: any accidental leakage of the liquid stool

<sup>d)</sup> Tenesmus: sensation of incomplete evacuation

\*Student t-test †Pearson chi-square

An anorectal manometry was conducted to assess the physiological and anatomical alterations in from 40.9 mmHg to 45.9 mmHg in the control group. The study group showed a considerable in- the anorectum with the use of anti-adhesive agents in the pelvic cavity (Table 4). The Resting Anal crease in Maximum anal Squeezing Pressure (MASP) from 146.3 mmHg to 178.9 mmHg, whereas Squeezing Pressure (RASP) increased from 34.5 mmHg to 41.1 mmHg in the study group and the control group showed an increase from 149.6 mmHg to 176.0 mmHg. However, there was no

statistically significant difference between the two groups ( $p=0.838$ ). There were no significant statistical differences found between the two groups in terms of additional anorectal pressure-related parameters, such as resting pressure, duration of sustained sphincter contraction, length of the anal sphincter, and the high-pressure zone.

Variables	3 months		6 months		12 months		24 months		p- Value	
	Study group (n=54)	Control group (n=58)	Study group (n=54)	Control group (n=58)	Study group (n=54)	Control group (n=58)	Study group (n=54)	Control group (n=58)	Within group	Between group
<b>RASP (mmHg)</b>	34.5 ± 21.8	40.9 ± 12.4	33.6 ± 18.2	36.0 ± 20.5	39.1 ± 10.7	42.0 ± 29.3	41.1 ± 12.6	45.9 ± 30.4	0.094	0.899
<b>MASP (mmHg)</b>	161.8 ± 46.6	159.6 ± 47.2	175.1 ± 44.8	161.6 ± 44.9	181.5 ± 44.9	175.5 ± 58.3	178.9 ± 38.4	176.0 ± 78.7	0.002	0.838
<b>Sustained duration (sec)</b>	2.7 ± 0.8	4.8 ± 2.9	4.9 ± 2.3	4.1 ± 1.6	5.0 ± 2.5	3.3 ± 0.8	3.5 ± 1.0	2.3 ± 0.7	0.139	0.585
<b>Sphincter length (cm)</b>	4.1 ± 0.7	4.3 ± 0.5	4.0 ± 0.8	4.0 ± 1.2	3.6 ± 0.7	4.1 ± 0.9	3.7 ± 0.7	3.6 ± 0.9	0.246	0.717
<b>High pressure zone (cm)</b>	2.5 ± 0.7	2.6 ± 0.5	2.4 ± 0.4	2.5 ± 0.4	2.4 ± 0.6	2.6 ± 1.1	2.1 ± 0.2	2.6 ± 1.1	0.97	0.803

Values are expressed as mean ± standard deviation.

RASP = resting anal squeezing pressure; MASP = maximum anal squeezing pressure;

Student t-test

## DISCUSSION

This study aimed to assess the potential improvement in postoperative bowel function and quality of life by analyzing variables related to bowel ability in rectal cancer patients after applying anti-adhesion agents in the pelvic cavity during rectal resection. The potential causes for bowel dysfunction resulting from a low anterior resection include reduced rectal compliance and volume, impairment of the autonomic nervous system, damage to the anal sphincter caused by the insertion of an automatic anastomosis device, and a decrease in the sampling reflex that helps differentiate bowel properties [6, 7]. The authors proposed the hypothesis that resecting the rectum through total mesorectal excision leads to the formation of adhesions in the pelvic cavity. These adhesions restrict the movement of the left colon and cause damage to the neurovascular complex (neurovascular bundle) surrounding the rectum, resulting in bowel dysfunction. Furthermore, it is anticipated that by using an anti-adhesion agent in the pelvic cavity during surgery to limit the local inflammatory response, fibrosis can be diminished [10, 11]. This, in consequence, can expedite the restoration of nerve activity and bowel efficacy, ultimately leading to a long-term reduction in complaints related to bowel dysfunction [12].

Previous studies have been conducted to reduce the symptoms of LARS and improve bowel function. Nakada et al. performed an abdominal stabilized side-to-end anastomosis using the abdominal approach to avoid damaging the sphincter and anal canal that can occur when inserting the automatic anastomosis device into the anal canal during the conventional straight end-to-end anasto-

mosis procedure [18]. Consequently, 61 patients (88.4%) reported that their bowel movement per day decreased to less than 4 times 2 months following the surgery. In addition, colonic J-pouch surgery, which increases the volume of the neorectum, was introduced with the aim of reducing bowel dysfunction that occurs when a straight end-to-end anastomosis is performed [19, 20]. It has been reported that surgery to make the colonic j-pouch restores the volume of the neorectum, improves the compliance and sensory of rectum, and consequently maintains the anal pressure better [21, 22]. However, further research has shown that the length of the remaining rectum and the height of the anastomosis affect the bowel function rather than the colonic pouch itself [15, 16, 19]. There has also been controversy over whether it is necessary to make such a pouch since the anal rectal function is significantly restored within 1 years-2 years after surgery [23-25]. In addition, as an alternative in patients who have a very narrow pelvis making it difficult to use a bulky J-pouch, a transverse coloplasty pouch is also being attempted to increase the volume of the neorectum and decrease the colon propulsion movement by performing a longitudinal incision in the proximal colon and then suture horizontally [26]. However, the bowel function after surgery is comparable to that of the J-pouch, but several studies have shown potential risks, such as anastomotic leaks, associated with this procedure [27-29].

The recently published studies in obstetrics and gynecology, hepatic pancreatic surgery, and colorectal surgery have confirmed the safety and efficacy of anti-adhesion agents in addressing postoperative adhesions in patients undergoing abdominal and pelvic surgery [10, 11, 30-32]. During normal

tissue recovery, anti-adhesion agents physically separate traumatic and inflammatory adhesion-expressing tissues and organs. The HA-CMC mixture solution is considered safe because it undergoes complete absorption within 28 days of the acute phase of normal tissue recovery, and it begins to decompose on the seventh day. Anti-adhesion agents are utilized in both the preventive and therapeutic aspects as previously mentioned. Adanali et al. demonstrated a statistically significant increase in the number of viable axons and a decrease in perineal fibrosis three months following surgery in rabbits with sciatic nerve injury through the use of anti-adhesion agents [12]. According to the research evidence mentioned above, it was hypothesized that the application of an anti-adhesion agent in the pelvic cavity after rectal resection surgery would reduce adhesion in the pelvic cavity. This reduction in adhesion would lead to an increase in rectal compliance and volume, as well as minimize damage to the autonomic nervous system.

The results of this study corroborate the safety of the anti-adhesion agent, as there was no difference in complication morbidity and surgical results between the group that applied it and the group that did not. The analysis of factors related to bowel function 24 months after surgery demonstrates that the recovery of the nerve complex resulted in a statistically significant improvement in the symptoms of bowel dysfunction and smooth defecation in the group that applied the anti-adhesion agent. In the short-term results, there were numerous frequent stools, urgent stools, and defecation that were attributed to the relatively low resting sphincter pressure of the 2 groups. However, there was no statistically significant difference or change between the 2 groups. This was determined by comparing the 2 groups through the rectal anus physiology test. Furthermore, the long-term analysis results did not reveal any significant difference between the two groups in the following aspects: squeezing sphincter pressure, sphincter contraction duration, anal sphincter length, and high-pressure zone. Consequently, the direct effect of the application of anti-adhesion agent on the anatomical change of the rectal anus could not be confirmed. In contrast to the surgical method that was previously introduced, this technique offers numerous benefits. First, the current surgical procedure is unaltered and does not include any modifications or upgrades. This is a straightforward approach to administering the HA-CMC mixed solution to the pelvic cavity following intestinal anastomosis. In the second place, there is minimal additional time required. Only a few minutes are required to complete the pelvic cavity administration of the HA-CMC mixed solution. Lastly, there is no impact on postoperative complications and outcomes. It does not influence the occurrence of substantial complications, such as postoperative complications, particularly anastomotic leakage, as variables such as increased anastomosis and additional bowel resection do not occur as in existing methods. The utilization of physical topical compounds within and around the pelvic cavity to reduce fibrosis and isolate neurovascular complexes from adjacent surrounding inflammatory tissues is a novel approach.

This study is retrospective in nature and has several limitations. Initially, selection bias may be present as a result of the retrospective analysis and investigation of medical records. Nevertheless, the homogeneity of the 2 groups in terms of enrollment was comparatively maintained, as there was no significant difference between the 2 groups in general clinical characteristics and surgical results in the statistical analysis. Secondly, the reliability of the interpretation of the results of the statistical analysis may be compromised

due to the limited number of patients to be studied. Lastly, the correlation of the numerous factors that influence bowel dysfunction after rectal resection is not reflected. In order to overcome these limitations, it has been determined that a prospective large-scale multicenter investigation into bowel dysfunction following low anterior resection should be conducted in the future.

## CONCLUSION

The analysis of clinical outcomes between the group that applied the anti-adhesion agent and the group that did not confirmed that there was no significant difference between the two groups in terms of surgical results, complication, and morbidity. Additionally, the long-term evaluation revealed that the group that applied the anti-adhesion agent experienced an improvement in LARS.

## ABBREVIATIONS

ASA- American Society of Anesthesiology

BMI- Body Mass Index

CMC- Carboxymethyl cellulose

HA- Sodium Hyaluronate

LARS- Low Anterior Resection Syndrome

TME- Total Mesorectal Excision

WIS- Wexner Incontinence Score

## DECLARATIONS

Ethics approval and consent to participate

This study protocol was approved by the Institutional Review Board (IRB) of Pusan National University Yangsan Hospital. (IRB No. 05-2023-208). Written informed consent forms concerning colorectal resection were obtained for publication of the study.

## Consent for publication

We obtained written consent to publish all the personal details included in our dataset from all participants prior to surgery.

## Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

## Conflict of interests

The authors declare that they have no competing interest.

## Funding

The authors declare that no funding was received for the study.

## Authors' contributions

HSK designed the study, analyzed and interpreted the data, and made a draft and revised the manuscript. NO analyzed and interpreted data and wrote the manuscript. HY was responsible for the study's conception and design. All authors have read and approved the final manuscript.

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## REFERENCES

1. Billingham RP. Extended lymphadenectomy for rectal cancer: cure vs. quality of life. *Int Surg.* 1994;79:11-22.
2. Williams NS, Johnston D. Survival and recurrence after sphincter saving resection and abdominoperineal resection for carcinoma of the middle third of the rectum. *Br J Surg.* 1984;71:278-282.
3. Rasmussen OO, Petersen IK, Christiansen J. Anorectal function following low anterior resection. *Colorectal Dis.* 2003;5:258-261.
4. Lewis WG, Holdsworth PJ, Stephenson BM, Finan PJ, Johnston D. Role of the rectum in the physiological and clinical results of coloanal and colorectal anastomosis after anterior resection for rectal carcinoma. *Br J Surg.* 1992;79:1082-1086.
5. Williams NS, Price R, Johnston D. The long term effect of sphincter preserving operations for rectal carcinoma on function of the anal sphincter in man. *Br J Surg.* 1980;67:203-208.
6. Matsushita K, Yamada K, Sameshima T, Niwa K, Hase S, et al. Prediction of incontinence following low anterior resection for rectal carcinoma. *Dis Colon Rectum.* 1997;40:575-579.
7. Otto IC, Ito K, Ye C, Hibi K, Kasai Y, et al. Causes of rectal incontinence after sphincter-preserving operations for rectal cancer. *Dis Colon Rectum.* 1996;39:1423-1427.
8. Allgayer H, Dietrich CF, Rohde W, Koch GF, Tuschhoff T. Prospective comparison of short- and long-term effects of pelvic floor exercise/biofeedback training in patients with fecal incontinence after surgery plus irradiation versus surgery alone for colorectal cancer: clinical, functional and endoscopic/endosonographic findings. *Scand J Gastroenterol.* 2005;40:1168-1175.
9. Lundby L, Duelund-Jakobsen J. Management of fecal incontinence after treatment for rectal cancer. *Curr Opin Support Palliat Care.* 2011;5:60-64.
10. Takeuchi H, Kitade M, Kikuchi I, Shimanuki H, Kinoshita K. A novel instrument and technique for using Seprafilm hyaluronic acid/carboxymethylcellulose membrane during laparoscopic myomectomy. *J Laparoendosc Adv Surg Tech A.* 2006;16:497-502.
11. Vrijland WW, Tseng LN, Eijkman HJ, Hop WC, Jakimowicz JJ, et al. Fewer intraperitoneal adhesions with use of hyaluronic acid-carboxymethylcellulose membrane: a randomized clinical trial. *Ann Surg.* 2002;235:193-199.
12. Adanali G, Verdi M, Tuncel A, Erdogan B, Kargi E. Effects of hyaluronic acid-carboxymethylcellulose membrane on extraneural adhesion formation and peripheral nerve regeneration. *J Reconstr Microsurg.* 2003;19:29-36.
13. Adas G, Karatepe O, Arýkan S, Battal M, Kemik O, et al. The effect of hyaluronic acid carboxymethyl cellulose on the healing of colonic anastomosis in rats. *Bratisl Lek Listy.* 2009;110:210-214.
14. Buckenmaier CC 3rd, Summers MA, Hetz SP. Effect of the antiadhesive treatments, carboxymethylcellulose combined with recombinant tissue plasminogen activator and Seprafilm, on bowel anastomosis in the rat. *Am Surg.* 2000;66:1041-1045.
15. Amin MB, Edge SB, Greene FL, Byrd D, Brookland RK, et al. *AJCC cancer staging manual.* 8<sup>th</sup> ed. New York: Springer; 2017.
16. Oliveira L, Pfeifer J, Wexner SD. Physiological and clinical outcome of anterior sphincteroplasty. *Br J Surg.* 1996;83:502-505.
17. Juul T, Ahlberg M, Biondo S, Emmertsen KJ, Espin E, et al. International validation of the low anterior resection syndrome score. *Ann Surg.* 2014;259:728-734.
18. Nakada I, Kawasaki S, Sonoda Y, Watanabe Y, Tabuchi T. Abdominal stapled side-to-end anastomosis (Baker type) in low and high anterior resection: experiences and results in 69 consecutive patients at a regional general hospital in Japan. *Colorectal Dis.* 2004;6:165-170.
19. Hallböök O, Nyström PO, Sjödaahl R. Physiologic characteristics of straight and colonic J-pouch anastomoses after rectal excision for cancer. *Dis Colon Rectum.* 1997;40:332-338.
20. Seow-Choen F. Colonic pouches in the treatment of low rectal cancer. *Br J Surg.* 1996;83:881-882.
21. Hallböök O, Sjödaahl R. Comparison between the colonic J pouch-anal anastomosis and healthy rectum: clinical and physiological function. *Br J Surg.* 1997;84:1437-1441.
22. Ho YH, Tan M, Leong AF, Seow-Choen F. Ambulatory manometry in patients with colonic J-pouch and straight coloanal anastomoses: randomized, controlled trial. *Dis Colon Rectum.* 2000;43:793-799.
23. Hida J, Yasutomi M, Maruyama T, Fujimoto K, Nakajima A, et al. Indications for colonic J-pouch reconstruction after anterior resection for rectal cancer: determining the optimum level of anastomosis. *Dis Colon Rectum.* 1998;41:558-563.
24. Nicholls RJ, Lubowski DZ, Donaldson DR. Comparison of colonic reservoir and straight colo-anal reconstruction after rectal excision. *Br J Surg.* 1988;75:318-320.
25. Hida J, Yasutomi M, Fujimoto K, Okuno K, Ieda S, et al. Functional outcome after low anterior resection with low anastomosis for rectal cancer using the colonic J-pouch: prospective randomized study for determination of optimum pouch size. *Dis Colon Rectum.* 1996;39:986-991.
26. Fazio VW, Mantyh CR, Hull TL. Colonic "colooplasty": novel technique to enhance low colorectal or coloanal anastomosis. *Dis Colon Rectum.* 2000;43:1448-1450.
27. Remzi FH, Fazio VW, Gorgun E, Zutshi M, Church JM, et al. Quality of life, functional outcome, and complications of colooplasty pouch after low anterior resection. *Dis Colon Rectum.* 2005;48:735-743.
28. Ho YH, Brown S, Heah SM, Tsang C, Seow-Choen F, et al. Comparison of J-pouch and colooplasty pouch for low rectal cancers: a randomized, controlled trial investigating functional results and comparative anastomotic leak rates. *Ann Surg.* 2002;236:49-55.
29. Fazio VW, Zutshi M, Remzi FH, Parc Y, Ruppert R, et al. A randomized multicenter trial to compare long-term functional outcome, quality of life, and complications of surgical procedures for low rectal cancers. *Ann Surg.* 2007;246:481-488.
30. Beck DE, Cohen Z, Fleshman JW, Kaufman HS, van Goor H, et al. A prospective, randomized, multicenter, controlled study of the safety of Seprafilm adhesion barrier in abdominal/pelvic surgery of the intestine. *Dis Colon Rectum* 2003;46:1310-1319.
31. Becker JM, Dayton MT, Fazio VW, Beck DE, Stryker SJ, et al. Prevention of postoperative abdominal adhesions by a sodium hyaluronate-based bioresorbable membrane: A prospective, randomized, double-blind multicenter study. *J Am Coll Surg.* 1996;183:297-306.
32. Fazio VW, Cohen Z, Fleshman JW, van Goor H, Bauer JJ, et al. Reduction in adhesive small-bowel obstruction by Seprafilm adhesion barrier after intestinal resection. *Dis Colon Rectum* 2006;49:1-11.