Asian Journal of Surgery (2019) 42, 443–449

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-asianjournalsurgery.com

ORIGINAL ARTICLE

Is liquid-based hyaluronic acid equivalent to sodium hyaluronate-based bioresorbable membrane to reduce small bowel obstruction in patients undergoing colorectal surgery☆

Woon Kee Lee [a], Yeon Ho Park [a], Sangtae Choi, Won-Suk Lee*

Department of Surgery, Gil Medical Center, Gachon University, Incheon, South Korea

Received 21 May 2018; received in revised form 16 July 2018; accepted 20 September 2018
Available online 24 October 2018

KEYWORDS
Small bowel obstruction;
Antiadhesive;
Surgery

Summary *Objective:* We performed a prospective randomized study to assess whether the use of sodium hyaluronate-based bioresorbable membrane (Seprafilm®) and liquid-based hyaluronic acid and carboxymethyl cellulose solution (Guardix) to reduce postoperative small bowel small bowel obstruction in patients undergoing colorectal surgery. This study aimed to compare the incidence of postoperative bowel obstruction.
Methods: One hundred seven patients were assigned to the Seprafilm® group and 155 were assigned to the Guardix® group during the study period. The control group of 166 patients received no anti-adhesive. Patients were randomly assigned.
Results: The overall small bowel obstruction rate was 7.6% (N = 37/488 patients). Small bowel obstruction developed in 9 patients (5.8%) in the Guardix® group and 9 patients (7.1%) in the Seprafilm® group and 19 patients (11.4%) in the control group. Seprafilm® group had significantly lower obstruction rate as compared to control group (P = 0.036). Guardix® solution and Seprafilm® did not alter the liver and renal function, as assessed by the blood chemistry.
Conclusions: The use of Seprafilm significantly reduces the incidence of postoperative small bowel obstruction in patients undergoing colorectal surgery. We observed no difference in the incidence of postoperative small bowel obstruction after the application of Seprafilm® and Guardix® in patients undergoing colorectal surgery.

☆ This work was supported by funding from the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education NRF-2017R1D1A1B03035453 to W.-S. Lee.

* Corresponding author. Department of Surgery, Gil Medical Center, Gachon University, School of Medicine, 1198 Guwol-dong, Namdong-gu, Incheon 405-760, South Korea. Fax: +82 2 460 3009.
E-mail address: lws@gilhospital.com (W.-S. Lee).
[a] Woon Kee Lee and Yeon Ho Park equally contributed as first authors.

https://doi.org/10.1016/j.asjsur.2018.09.009

1. Introduction

Postoperative intra-abdominal adhesions are the most frequent complication of laparotomy surgery; although these adhesions are often not recognized, they are observed in nearly 95% of patients at the time of subsequent surgery.[1] Adhesions are internal post-traumatic "scars" that form through a complex process that involves the injured tissues and the peritoneum. Although intra-abdominal adhesions are asymptomatic in most patients, in some patients these adhesions can cause intestinal obstruction, infertility, chronic abdominal pain, and an increased rate of complications during subsequent operations.[2]

Several clinical studies have announced that the use of a sodium hyaluronate-based bioresorbable membrane (Seprafilm®; Genzyme Corp., Cambridge, MA, USA) significantly reduces the incidence and severity of adhesions after abdominopelvic surgery, with no adverse or toxic effects.[3,4] Additionally, a liquid-based hyaluronic acid (HA) and carboxymethyl cellulose (CMC) mixture are available as an adhesion reduction agent (Guardix®; Hanmi Medicare, Seoul, Korea).

HA is a key component of the extracellular matrix and is involved in several steps of the wound healing process. This hydrophilic and non-immunogenic macromolecule easily coats and lubricates mucus membranes, thereby reducing friction and/or preventing trauma after surgery.[5,6] HA is expected to be effective at surgical sites where a film-type anti-adhesive agent is difficult to apply. CMC is a nontoxic polysaccharide made from monochloroacetate and cellulose and is used in the cosmetic, food, and drug industries.[7] Guardix® is a sterile, transparent, colorless adhesion barrier, formulated as a viscous gel consisting of two anionic polysaccharides, sodium hyaluronic acid (HA) and sodium carboxymethyl cellulose (CMC). Guardix can apply to lubricate in the surgical area for effective anti-adhesion (product information, Hanmi Medicare).

Although both the film-type (Seprafilm®) and liquid-type (Guardix®) commercially available preparations of HA and CMC have been used to prevent adhesions after surgery, no currently available published data have directly compared Seprafilm® and Guardix® in terms of their abilities to reduce the rate of small bowel obstruction after colorectal surgery. In the present study, we performed a prospective randomized study to assess whether Seprafilm® or Guardix® could reduce the rate of small bowel obstruction including small bowel atony in patients who underwent colorectal surgery.

2. Methods

The study proposal was finalized and approved by our institutional review board prior to study initiation. Written informed consent was required from all participants. This investigator-initiated randomized controlled trial (RCT) was performed at Gachon University Gil Hospital between September 2013 and December 2014 (clinical trial number: NCT02168426, www.clinicaltrials.gov). All patients at our institution who required Colorectal surgery during the study period were randomized using to receive Seprafilm® or Guardix®. A simple randomization table was used to randomize the patients.

2.1. Exclusion criteria

For the 663 patients were screened (Seprafilm® and Guardix® group and no additive group) using the following study exclusion criteria: 1) patient refusal; 2) APCT o or sonographic findings indicating an intra-abdominal abscess; 3) history of cirrhosis and/or coagulation disorders and/or hemodynamic instability; 4) other contraindications to general anesthesia (severe cardiac and/or pulmonary disease); 5) inability to provide informed consent because of mental disability; 6) pregnancy; 7) use of any other investigational product; 8) history of peritoneal irrigation or radiation; 9) incomplete medical records during screening and after the randomization; 10) signs of peritonitis due to anastomosis leakage or presence of small bowel obstruction before surgery and 11) stage IV patients and/or patients needing ileostomy or colostomy. Of the remaining curatively resected stage I to III patients, 167 were assigned to the Seprafilm® group, 155 were assigned to the Guardix® group and 166 received no antiadhesive (Fig. 1).

2.2. Products used in the study

Seprafilm® is a membrane developed for the temporary separation of tissues damaged mechanically during surgery. It is available in 12.7 cm × 15.2 cm sheets and comprises chemically modified sodium hyaluronate, a glycosaminoglycan, and CMC. No adverse or toxic effects have been described with the use of these substances.[3,7]

Guardix is a liquid-based anti-adhesive agent with the following characteristics: nonpyrogenic, nontoxic sodium hyaluronic acid and carboxymethyl cellulose, colorless, transparent, viscous solution; and pH of 6.0—8.0. All of the patients received 5 g of Guardix® which contains 5 mL of antiadhesive solution.

2.3. Operative procedure

Two colorectal surgeons participated in this study. These surgeons followed the standard procedures for colectomy and proctectomy with lymph node dissection and anastomoses. All enrolled patients received Guardix® or Seprafilm® to the surface of the small intestine under the

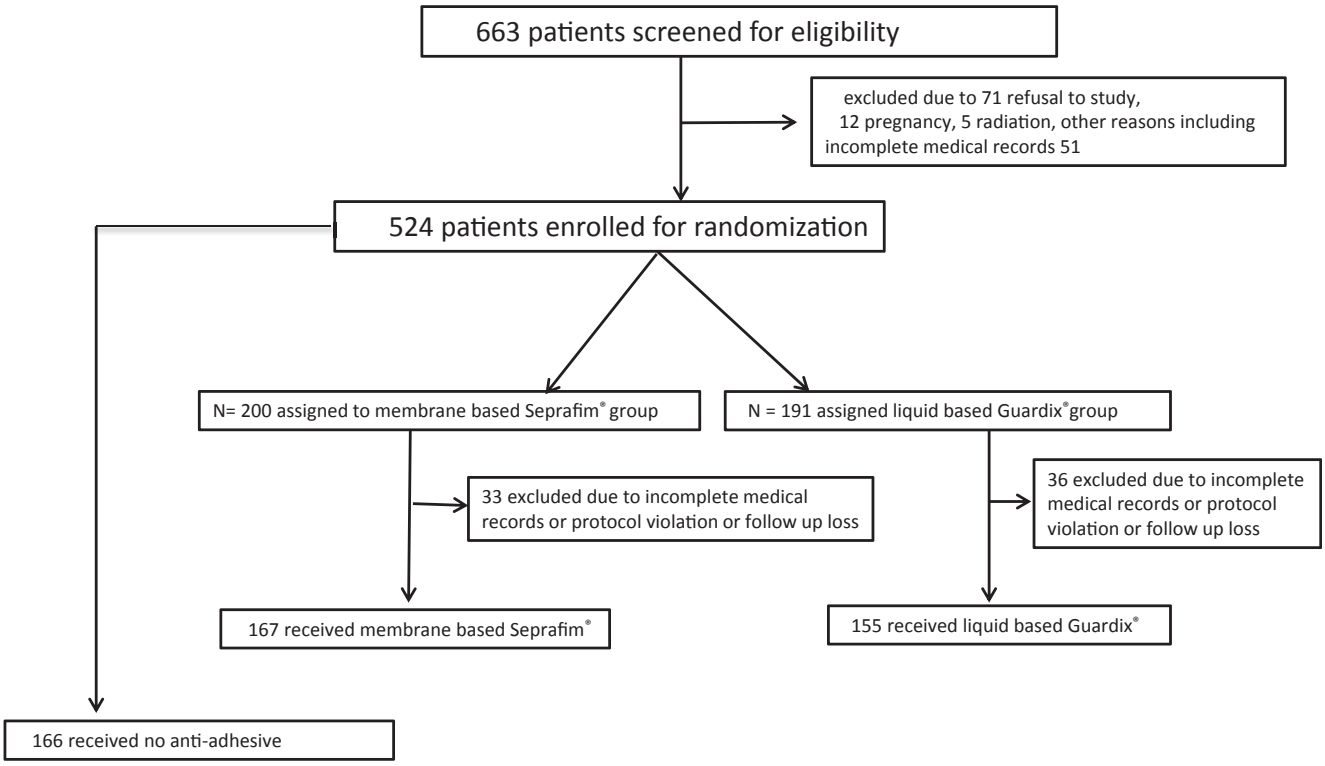

Figure 1 Patient allocation.

main abdominal wound. Contact with the anastomoses was avoided. A routine 24 h fentanyl based intravenous patient controlled analgesia was used. No prokinetic drugs were given.

2.4. Data collection

Data were collected according to a previously published protocol.[7] Age, gender, body weight, height, medical history, use of preoperative chemotherapy, and history of abdominal surgery were recorded at the time of admission to the hospital. The following postoperative parameters were documented: type of operation, use of postoperative radiation therapy, perioperative complications such as intra-abdominal abscess, anastomotic site leakage, peritonitis, and early postoperative intestinal obstruction, and perioperative mortality. In addition, laboratory tests (complete blood cell count and aspartate aminotransferase, alanine aminotransferase, blood urea nitrogen, and serum creatinine levels) were performed on postoperative day 3. All of the patients took a routine simple abdomen to access immediate postoperative obstruction.

After their initial discharge, all patients were followed up at an outpatient department 2—3 week after surgery. All patients were instructed to revisit the clinic if they developed any symptoms such as abdominal pain/distension or a failure to pass gas. Any adverse events and concomitant medications were assessed as previously described by Lee et al.[7]

The primary endpoint of this study was the incidence of postoperative bowel obstruction. The diagnostic criteria were similar to those previously described by Hayashi et al.[6] Small bowel obstruction was confirmed on the basis of clinical symptoms (e.g., nausea, vomiting, abdominal pain, abdominal distension, and the absence of defecation or gas passage in the previous 24 h), physical examination findings (e.g., abdominal tenderness, accentuated bowel sounds, and tympanic sounds on percussion), simple abdominal radiographs showing an air-fluid level in a patient while in an erect position, and a dilated small bowel on enhanced computed tomography (CT) scans. Diagnosis of small bowel obstruction was made according to findings on the simple abdominal radiographs or enhanced abdominopelvic CT scans and the presence of at least 3 of the aforementioned clinical symptoms and physical examination findings. Postoperative morbidity and mortality were also evaluated within 60 days from the initial surgery.[7] This study included patients with bowel atony or impairment of bowel movement after immediate operation since this influence of atony on the results cannot be omitted during the study.

2.5. Therapy for bowel obstruction

All patients received intravenous basic fluid therapy and broad-spectrum antibiotics as indicated. If evidence of small intestinal dilatation was seen on plain abdominal radiographs or enhanced abdominopelvic CT scans, a 16- or 18-French Levin nasogastric tube was placed.

2.6. Statistical analysis

A sample size was calculated using a 2-proportions power analysis. Previous studies reported that the incidence of

small bowel obstruction after colorectal surgery ranged from 10% to 38.5%.[8] Assuming that a 20% incidence of small bowel obstruction after Colorectal surgery in the conventional arm would decrease to 10% in the study arm with a α-error of 0.05 and β-power of 80%, the total target sample size was 150 patients. Differences in continuous variables were analyzed using Student's t-test. For categorical variables, differences were analyzed with the χ^2 test. For multiple comparisons between groups, Bonferroni corrected P value less than 0.017 were considered statistically significant. The cumulative incidence of small bowel obstruction was calculated according to the Kaplan–Meier method, and the resulting curves were compared using the log-rank test. The reported probability values are 2-sided; P-values <0.05 were considered to indicate statistical significance.

3. Results

Of the 322 eligible patients in the antiadhesive group, 167 received Seprafilm® and 155 received Guardix® (Fig. 1). All of the patients had complete medical data set for analysis. The mean follow-up duration was 16.2 months (range: 5–30 months). There were no significant differences in baseline characteristics between the groups (Table 1). Regarding operative data, there were no significant differences between the groups in terms of the level of anastomosis (rectum vs. colon, P = 0.415; Table 2). Combined resection including small bowel segmental resection and total hysterectomy was done in 5.0% of all patients. There was no difference between the groups regarding combined resection (P = 0.793). There was no difference among the groups regarding types of surgery (Table 2). The serum laboratory values did not significantly differ between the groups on postoperative day 3 (Table 3), and the mean values were within normal ranges. Additionally, there were no differences in the incidence rates of wound infection and anastomotic leakage between the groups (Table 4). All cases of anastomosis leakage occurred in patients who underwent low anterior resections, and all patients were diagnosed within 12 h of leakage.

The overall small bowel obstruction rate was 7.6% (N = 37/488 patients). Small bowel obstruction developed in 9 patients (5.8%) in the Guardix® group and 9 patients (7.1%) in the Seprafilm® group and 19 patients (11.4%) in the control group. Seprafilm® group had significantly lower obstruction rate as compared to control group (P = 0.036). Guardix® group had a tendency toward lower obstruction rate but was not found to be statistically significant (P = 0.055) as compared to the control group (Table 4). All 37 patients were treated conservatively and recovered. The mean time to small bowel obstruction was similar between the groups (5.0 days vs. 5.8 days vs. 4.1 days respectively, P = 0.741; Table 4). The mean number of days required for obstruction treatment did not differ significantly between the groups (6.7 days vs. 6.2 days, and 5.5 days, respectively, P = 0.879; Table 3).

The overall complication rates did not differ significantly between the Guardix® and Seprafilm® groups (12.9% vs. 15.5% vs. 18.7%; P = 0.533; Table 4). No in-hospital deaths occurred in either group. The median blood loss volumes were 137 mL (range: 10–340 mL) in the Guardix® group and 141 mL (range: 10–290 mL) in the Seprafilm® group (P = 0.143; Table 4).

Laparoscopic surgery group had a lower incidence of small bowel obstruction (25/345 vs 12/143). However, did not reach statistical significance in this study (P = 0.081). We did find that Seprafilm® reached statistical significance in reducing small bowel obstruction as compared to control group (P = 0.031) in laparoscopic surgery. Guardix® group had a tendency toward lower obstruction rate but did not reach statistical significance (P = 0.073) as compared to the control group (Table 4).

4. Discussion

In this randomized study, no significant difference in the incidence of small bowel obstruction after colorectal surgery was detected between the Seprafilm® and Guardix® groups, despite the slightly lower overall incidence in the Seprafilm® group than in the Guardix® group (5.8% vs. 7.1%; P = 0.377). The 7.6% overall incidence of small intestinal obstruction was acceptable when compared with previous reports (range: 11.7–38.5%).[10] Furthermore, the blood loss volume and operation time did not differ significantly between the groups. The groups were also similar with respect patient characteristics, including body mass index and disease stage, as well as operative data, including experience level of the surgeon and types of colorectal surgery performed. Additionally, we analyzed the serum laboratory variables on the third postoperative day and found no significant differences between the groups. All

Table 1 Patient demographics (N = 488).

	Guardix group	Seprafilm group	Control group	Guardix vs Seprafilm P value	Guardix vs Control P value	Seprafilm vs Control P value
Number	155	167	166			
Age	60.3	63.2	62.5	0.143	0.741	0.971
Gender M:F	87:68	103:64	87:78	0.477	0.432	0.553
Body mass index (range)	23.4	22.7	23.6	0.534	0.643	0.417
Height (cm)	164.7 ± 12.5	165.4 ± 13.1	164.2 ± 10.3	0.341	0.746	0.974
Colon	79	80	83	0.941	0.794	0.746
Rectum	81	82	83	0.913	0.884	0.941

Table 2 Operative type and clinical data.

	Guardix group (N = 155), %	Seprafilm group (N = 167), %	Control group (N = 166), %	Guardix vs Seprafilm P value	Guardix vs Control P value	Seprafilm vs Control P value
Location						
Colon:Rectum	81:74	81:86	83:83	0.872	0.746	0.531
Operation type				0.415	0.459	0.143
Anastomosis below peritoneal reflection	77 (49.7)	86 (51.5)	83 (50.0)			
Above peritoneal reflection	78 (50.3)	81 (48.5)	83 (50.0)			
Operation time (min)	101 ± 39.4	110 ± 27.7	107 ± 24.8	0.631	0.446	0.892
ASA class				0.402	0.134	0.746
I + II	137	151	146			
III + IV	17	16	20			
Mean blood loss (mL)	137 ± 43.1	141 ± 51.7	133 ± 49.7	0.143	0.416	0.613
Laparoscopic surgery	114 (73.5)	115 (68.9)	116 (69.9)	0.753	0.345	0.891
Open surgery	41 (26.5)	52 (31.1)	50 (30.1)			

Data are mean ± standard deviation.

Table 3 Laboratory data on postoperative 7 days.

	Guardix® group (N = 155)	Seprafilm® group (N = 167)	Control group (N = 166)	Guardix vs Seprafilm P value	Guardix vs Control P value	Seprafilm vs Control P value
Postoperative Day 1						
Aspartate aminotransferase (U/L)	26.0 ± 15.6	26.3 ± 20.4	22.6 ± 13.2	0.860	0.542	0.764
Alanine aminotransferase (U/L)	22.9 ± 17.7	22.0 ± 16.9	23.4 ± 18.1	0.652	0.731	0.554
Blood urea nitrogen (mg/dL)	14.0 ± 5.2	14.4 ± 5.0	13.0 ± 3.2	0.565	0.725	0.958
Serum creatinine (mg/dL)	0.7 ± 0.2	0.8 ± 0.4	0.5 ± 0.2	0.489	0.325	0.688
White blood cell count (/μL)	9743 ± 2475	9321 ± 3049	8995 ± 2475	0.721	0.538	0.574
Postoperative Day 5						
Aspartate aminotransferase (U/L)	37.9 ± 13.9	38.1 ± 14.6	29.7 ± 14.4	0.754	0.253	0.754
Alanine aminotransferase (U/L)	38.1 ± 15.3	37.5 ± 14.8	31.2 ± 16.8	0.403	0.621	0.845
Blood urea nitrogen (mg/dL)	14.4 ± 6.1	14.6 ± 5.7	16.5 ± 3.5	0.825	0.550	0.926
Serum creatinine (mg/dL)	0.5 ± 0.2	0.6 ± 0.3	0.4 ± 0.3	0.501	0.764	0.185
White blood cell count (/μL)	6905 ± 2393	6870 ± 2466	6205 ± 1994	0.907	0.457	0.625
Postoperative Day 7						
Aspartate aminotransferase (U/L)	29.3 ± 20.4	38.6 ± 93.8	25.3 ± 19.3	0.270	0.721	0.367
Alanine aminotransferase (U/L)	29.4 ± 29.0	38.8 ± 10.3	25.2 ± 14.2	0.308	0.136	0.852
Blood urea nitrogen (mg/dL)	11.6 ± 1.5	11.2 ± 1.5	13.6 ± 2.2	0.892	0.654	0.732
Serum creatinine (mg/dL)	0.5 ± 0.2	0.6 ± 0.5	0.5 ± 0.2	0.196	0.756	0.984
White blood cell count (/μL)	6976 ± 2352	6868 ± 2416	5976 ± 1842	0.976	0.345	0.356

Data are mean ± standard deviation.

such data were within the normal ranges. This lack of a significant difference between the groups suggests that Guardix® may be used as an alternative to Seprafilm®. However, a larger study with a longer follow-up period may be required to draw any concrete conclusions.

Adhesion develops in the vast majority of patients who have undergone abdominal surgery and may lead to complications. Intraperitoneal adhesions occur in as many as 60–90% of patients undergoing abdominal surgery.[9] As suggested in a previous study,[6] we used only 1 piece of Seprafilm® per patient in the Seprafilm® group and 1 vial of Guardix® per patient in the Guardix® group. Vrijland et al placed Seprafilm® at various locations in patients subjected to the Hartmann procedure and reported that this agent appeared to reduce the severity of postoperative adhesion.[10] Becker et al found that Seprafilm® significantly reduced the incidence, extent, and severity of postoperative abdominal adhesions in a randomized study in which patients in the Seprafilm® group received an average of 2 sheets each.[11] However, in that study, the incidence of obstruction was not significantly reduced. Fazio et al reported that the rate of adhesive small bowel obstruction requiring reoperation was significantly reduced by the application of 3–10 sheets of Seprafilm® to all organs and tissues sustaining direct trauma or considered at high risk for adhesion, although the overall rate of bowel

Table 4 Postoperative data and incidence of small bowel obstruction.

	Guardix® group (N = 155)	Seprafilm® group (N = 167)	Control group (N = 166)	P value	Guardix vs Seprafilm P value	Guardix vs Control P value	Seprafilm vs Control P value
Overall complication rate, %	20 (12.9)	26 (15.5)	31 (18.7)	0.533	0.495	0.336	0.271
Overall small bowel obstruction rate, %	9 (5.8)	9 (7.1)	19 (11.4)	0.287	0.377	0.055	0.036
Mean days of small bowel obstruction treated, days (range)	6.7 (5–18)	6.2 (5–19)	5.5 (3–15)				
Mean time to small bowel obstruction after operation, days ± SD	5.0 ± 1.7	5.8 ± 2.2	4.1 ± 2.1	0.741	0.425	0.341	0.751
Overall complication rate except obstruction, %	11 (7.0)	17 (10.0)	10 (6.0)	0.314	0.611	0.513	0.487
Pneumonia	4 (2.6)	4 (1.9)	5 (3.0)				
SSI[a]	5 (3.2)	9 (5.5)	5 (3.0)				
Anastomosis leakage	1 (0.6)	3 (1.9)	1 (0.6)				
Intra-abdominal abscess	1 (0.6)	1 (0.7)	1 (0.6)				
Hospital stay, days	9 (6–30)	8 (6–42)	8 (6–37)	0.327	0.952	0.672	0.415
Reoperation due to small bowel obstruction	0 (0%)	0 (0%)	0 (0%)				
Repeat obstruction	0 (0%)	0 (0%)	0 (0%)				
Laparoscopic	6/114	6/115	13/116	0.081	0.791	0.073	0.031
Open	3/41	3/52	6/50		0.613	0.066	0.069

SD: standard deviation.
[a] Surgical site infection.

obstruction was unchanged.[3] These findings raise the question of whether the use of additional sheets of Seprafilm® would further reduce the incidence of small bowel obstruction. Conversely, a larger randomized trial is needed to clarify whether the use of a larger amount of Guardix® would reduce the incidence of small bowel obstruction. Handling of these barrier agents must also be considered. Seprafilm® requires careful handling because it is brittle and cannot easily be moved after coming into contact with wet tissue. In contrast, Guardix® was straightforward and easily applied during surgery. However, the area covered by the liquid form is relatively small as compared to the film type.

The early postoperative complication was also evaluated in this study. In previous clinical studies, Seprafilm® has not been associated with significant differences in complication rates.[6,12,13] Similarly, no significant difference in morbidity after Colorectal surgery was observed between the 2 groups in our study. Anastomotic dehiscence patient occurred in 3 rectal cancer patients in the Seprafilm® group and 1 patient in the Guardix® group. It is difficult to ascertain whether both products were associated more strongly with anastomotic dehiscence because we avoided wrapping or spraying around anastomoses. Beck et al reported that wrapping the anastomosis with Seprafilm® should be avoided because of an increased risk of anastomotic leakage.[8] We observed no increases in postoperative morbidity, including intra-abdominal abscess, surgical site infection, or intestinal fistula, associated with either product in patients undergoing Colorectal surgery. These findings are consistent with the results of previously released studies.[8,12] The major weakness in this study was that we were unable to design a double blind comparison. Due to the nature of the product being liquid and a film. Another weakness is that both laparoscopic and open approach is included. This may be a confounding variable and the results should be interpreted accordingly.

In summary, we observed no difference in the incidence of postoperative obstruction after the application of Seprafilm® and Guardix® in patients undergoing Colorectal surgery. Seprafilm significantly lowered postoperative obstruction while Guardix had a tendency toward a lower rate of small bowel obstruction. Guardix® and Seprafilm are equivalent in the development of subsequent small bowel obstruction and may be used safely.

Conflict of interest

All of the listed authors claim no conflict of interest.

References

1. Menzies D, Parker M, Hoare R, Knight A. Small bowel obstruction due to postoperative adhesions: treatment patterns and associated costs in 110 hospital admissions. *Ann R Coll Surg Engl*. 2001;83(1):40–46.
2. Kusunoki M, Ikeuchi H, Yanagi H, et al. Bioresorbable hyaluronate-carboxymethylcellulose membrane (Seprafilm) in surgery for rectal carcinoma: a prospective randomized clinical trial. *Surg Today*. 2005;35(11):940–945.

3. Fazio VW, Cohen Z, Fleshman JW, et al. Reduction in adhesive small-bowel obstruction by Seprafilm adhesion barrier after intestinal resection. *Dis Colon Rectum*. 2006;49(1):1—11.
4. Gall Y. [Hyaluronic acid: structure, metabolism and implication in cicatrisation]. *Ann Dermatol Venereol*. 2010;137(Suppl 1): S30—S39.
5. Hadaegh A, Burns J, Burgess L, et al. Effects of hyaluronic acid/-carboxymethylcellulose gel on bowel anastomoses in the New Zealand white rabbit. *J Gastrointest Surg*. 1997;1(6):569—575.
6. Hayashi S, Takayama T, Masuda H, et al. Bioresorbable membrane to reduce postoperative small bowel obstruction in patients with gastric cancer: a randomized clinical trial. *Ann Surg*. 2008;247(5):766—770.
7. Lee WS, Baek JH, Lee WK. Direct comparison of Seprafilm (R) versus Adept (R) versus no additive for reducing the risk of small-bowel obstruction in colorectal cancer surgery. *Surg Today*. 2013;43(9):995—1002.
8. Beck DE, Cohen Z, Fleshman JW, Kaufman HS, van Goor H, Wolff BG. A prospective, randomized, multicenter, controlled study of the safety of Seprafilm adhesion barrier in abdominopelvic surgery of the intestine. *Dis Colon Rectum*. 2003; 46(10):1310—1319.
9. Lower AM, Hawthorn RJ, Ellis H, O'Brien F, Buchan S, Crowe AM. The impact of adhesions on hospital readmissions over ten years after 8849 open gynaecological operations: an assessment from the Surgical and Clinical Adhesions Research Study. *BJOG*. 2000;107(7):855—862.
10. Vrijland WW, Tseng LN, Eijkman HJ, et al. Fewer intraperitoneal adhesions with use of hyaluronic acid-carboxymethylcellulose membrane: a randomized clinical trial. *Ann Surg*. 2002;235(2): 193—199.
11. Becker JMDM, Fazio VW, Beck DE, 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(4):10.
12. Mohri Y, Uchida K, Araki T, et al. Hyaluronic acid-carboxycellulose membrane (Seprafilm) reduces early postoperative small bowel obstruction in gastrointestinal surgery. *Am Surg*. 2005;71(10):861—863.
13. Salum MR, Lam DT, Wexner SD, et al. Does limited placement of bioresorbable membrane of modified sodium hyaluronate and carboxymethylcellulose (Seprafilm) have possible short-term beneficial impact? *Dis Colon Rectum*. 2001;44(5): 706—712.