Surgery Today (2019) 49:1003–1012
https://doi.org/10.1007/s00595-019-01841-6

ORIGINAL ARTICLE

End-to-end intestinal anastomosis using a novel biodegradable stent for laparoscopic colonic surgery: a multicenter study

Mingyu Chen[1,2] · Jiasheng Cao[1] · Diyu Huang[1] · Bin Zhang[1] · Long Pan[1] · Zhongtao Zhang[3] · Zhenjun Wang[4] · Yingjiang Ye[5] · Dianrong Xiu[6] · Dechuan Li[7] · Xiujun Cai[1,2]

Received: 16 March 2019 / Accepted: 2 June 2019 / Published online: 29 June 2019
© Springer Nature Singapore Pte Ltd. 2019

Abstract

Purpose Our animal studies have demonstrated the safety and feasibility of end-to-end intestinal anastomosis using a stent for laparoscopic colonic surgery. Therefore, we designed a non-inferiority trial to investigate the outcomes of stent anastomosis (SA) vs. those of conventional hand-sewn anastomosis (CA).

Methods A multicenter randomized controlled trial was conducted between December, 2016 and April, 2018. The primary outcome was the healing condition of the anastomoses, evaluated by endoscopy 6 months postoperatively. The secondary outcomes were the anastomotic completion time, anastomotic leak, intestinal obstruction, peritoneal effusion, and bleeding. Quality of life (QOL) was evaluated by questionnaires.

Results The subjects of this study were 60 patients, randomly divided into a SA group ($n=30$) and a CA group ($n=30$). There were no differences in anastomotic healing conditions ($P=1.00$). The stent procedure was associated with a significantly shorter anastomosis time than the hand-sewn anastomosis (13.517 ± 4.281 vs. 20.333 ± 2.998 min, respectively; $P<0.001$). There were no significant differences in anastomotic leakage, intestinal obstruction, peritoneal effusion, or bleeding between the groups. Questionnaires revealed almost no discrepancy between baseline QOL scores and those assessed 2, 4, 8, 12, and 24 weeks postoperatively in either group.

Conclusions Intestinal anastomosis with a stent is a non-inferior strategy for laparoscopic colonic surgery, which requires less time for the anastomosis.

Keywords Intestinal anastomosis · A novel stent · Laparoscopic colonic operation

Introduction

Intestinal anastomosis is a common surgical technique used to treat several disorders, including bowel tumors, inflammation, and diverticulosis [1]. The conventional hand-sewn procedure is the original and one of the most accepted methods of intestinal anastomosis and has been performed widely for over

Mingyu Chen and Jiasheng Cao contributed equally to this work.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00595-019-01841-6) contains supplementary material, which is available to authorized users.

✉ Xiujun Cai
srrsh_cxj@zju.edu.cn

[1] Department of General Surgery, Sir Run-Run Shaw Hospital, Zhejiang University, No.3 East Qingchun Road, Hangzhou 310016, China

[2] Key Laboratory of Endoscopic Technique Research of Zhejiang Province, Sir Run-Run Shaw Hospital, Zhejiang University, Hangzhou 310016, China

[3] Department of General Surgery, Beijing Friendship Hospital, Capital Medical University, Beijing 100032, China

[4] Department of Anorectal Surgery, Beijing Chao-yang Hospital, Capital Medical University, Beijing 100020, China

[5] Department of Gastrointestinal Surgery, Peking University People's Hospital, Beijing 100032, China

[6] Department of General Surgery, Peking University Third Hospital, Beijing 100089, China

[7] Department of Colorectal Surgery, Zhejiang Cancer Hospital, Hangzhou 310011, China

150 years. Although surgical skills have improved, the method for hand-sewn anastomosis is non-standardized because of suture distance, inter-suture distance to the anastomotic edge, and tension on the anastomosis [2].

Several alternative methods, including compression rings and buttons, stapling devices, laser tissue welding, and tissue glues, have been developed to simplify constructing the anastomosis and improve its healing [3–7]. In 1892, the first compression ring, named the "Murphy button" was invented; however, its use was discontinued because of the introduction of a foreign body and anastomotic necrosis caused by the mechanical compressive pressure. In 1908, Hültl Humer from Budapest [8] introduced a surgical stapling device, but its use was limited. Over the past 30 years, the use of stapling devices has grown with the development of disposable instruments [9]. However, the rate of anastomotic stenosis is much higher with staples than with the hand-sewn method, despite similar results of mortality and other adverse complications such as anastomotic leak and abscess [10–12]. After the biofragmentable anastomosis ring (BAR) [13–16] was developed in the 1980s, the rate of foreign body reaction decreased remarkably, but the compressive pressure was still high, which limited use of the improved version. Furthermore, Lim et al. [17] confirmed the foreign body reaction in stapled anastomosis, which could slow down the process of healing. Surprisingly, they found that the foreign materials inducing this reaction were the stapler cartridges. Moreover, tissue glues [18–20] and laser tissue welding [21, 22] were not utilized clinically due to the weakness of anastomotic adhesive force. None of these procedures are suitable for end-to-end intestinal anastomosis because of their respective adverse complications; thus, a novel surgical procedure that can achieve a relatively perfect goal is needed urgently.

In our previous studies [23–26], we introduced an intestinal stent which has a high degree of biosecurity. Using this stent reduced the operative time dramatically and the intestinal incision healed better than when anastomosis was performed without the stent in animal experiments. However, whether the results of this procedure for human colonic operation are as good as those for the animal experiments remains unclear.

The purpose of this randomized controlled trial (RCT) based on five hospitals was to investigate the efficacy, feasibility, and safety of this method, which uses a biodegradable stent for end-to-end intestinal anastomosis, compared with hand-sewn anastomosis.

Materials and methods

Study design

A prospective, multicenter, randomized, non-inferiority trial was conducted at the following five hospitals in China between December, 2016 and April, 2018: Sir Run Run Shaw Hospital, Zhejiang Cancer Hospital, Beijing Friendship Hospital, Peking University Third Hospital and Peking University People's Hospital. The aim was to compare the short-term outcomes of stent anastomosis (SA) using a novel stent vs. conventional anastomosis (CA) for human colonic operations. This study was officially registered at clinicalTrails.gov (ID: NCT02752360).

The study was approved by the Ethics Committee of the above five hospitals (2016-P1-械-006-02). We provided detailed disclosure of risk to voluntary patients and obtained written informed consent from all of them. The patients were assigned randomly, using a computerized module, to undergo laparoscopic colonic surgery with either SA or CA in a one-to-one ratio.

Participants

All eligible patients were over 18 years old and scheduled to undergo a colonic operation with intestinal anastomosis for malignant or benign lesions located in the ascending, transverse, or descending colon, as diagnosed by colonoscopy and biopsy. Exclusion criteria were as follows: age > 80 years; surgical emergencies; severe preoperative comorbidities and inability to undergo surgery; diagnosed poor nutritional status, diabetes mellitus (DM) or other diseases which delay healing; two or more locations needing anastomosis; lesions needing ileocolonic anastomosis; combined with complete intestinal obstruction; distant metastasis (M1); history of intestinal surgery; and pregnancy. All patients underwent a standardized preoperative examination. Enhanced abdominal CT-scan was performed to evaluate the size, extramural invasion, and resectability of lesions. All patients were restricted from drinking alcohol and smoking for more than 2 weeks before surgery.

The biodegradable stent

The stent utilized in the procedure was produced by the Institute of Polymer Science of Zhejiang University (Fig. 1). The biocompatible qualities of the stent were approved by the State Food and Drug Administration of China (no. G20090993). The shape of the stent was described in previous articles [24–26]. It is synthesized from PGA and decomposes to carbon dioxide (CO2) and water by 14–21 days after surgery, which means that it has a high level of biosecurity. The relationship between the degradation time and molecular mass in vitro was described in our previous article [25]. Liu et al. [26] concluded that the stent degrades completely after 15–30 days in the porcine colon. Furthermore, the stent contains barium sulfate ($BaSO_4$) so that the disintegration can be tracked under radiography. Abdominal X-ray was performed weekly after surgery until the stents could not be

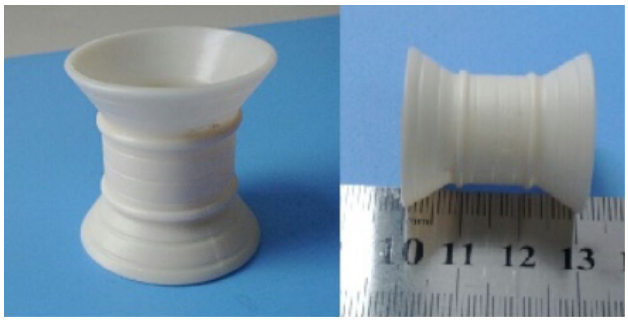

Fig. 1 Shape of the biodegradable stent

seen. The stents had disappeared by 3 weeks postoperatively in all patents. Figure 2 shows the most typical images in one patient.

Preoperative preparation and surgical procedures

All patients drank fluids only the day before surgery and received mechanical bowel preparation (poly-ethylene-glycol) the night before. They were also given prophylactic antibiotics (cefuroxime 1.5 g and metronidazole 500 mg) at the time of induction of anesthesia. To avoid potential bias caused by the learning curve of the laparoscopic colonic operation under general anesthesia, participants were operated on by five expert surgical teams, each consisting of two surgeons with at least 10 years' experience of laparoscopic colectomy and one camera assistant.

Stent anastomosis group

In the stent anastomosis group, laparoscopic colonic surgery was carried out according to the standardized procedure, using standard laparoscopic instruments. Multiple small ports were inserted for intracorporeal colon mobilization, abdominal exploration, and ligation of the vascular pedicle. Through a small incision, the section of bowel containing the lesion was removed and an anastomosis was performed outside [27]. With its marginal vessels ligated, the relative bowel segment was resected and end-to-end intestinal anastomosis was performed with a stent (Fig. 3 and Online Resource 1).

First, we removed the intestinal contents, cleaned the lumen, and then disinfected the incisional margins. Second, we utilized only one absorbable traction suture (VCP311, Ethicon, Inc.) to approximate the mesenteric borders of the incisional margins for accurate tissue apposition, after which two absorbable binding sutures (VCP311, Ethicon, Inc.) crossed the mesentery and surrounded the intestinal wall, 10 mm from the incisional margins of both sides. Third, both ends of the biodegradable stent were placed in the relative intestinal cavities with the anastomosis in the middle, and binding sutures were tightened, knotted, and fixed. If necessary, another 1–3 sutures were added to approximate both cut edges more accurately to prevent anastomotic leakage and intestinal volvulus. Finally, the peritoneum was closed with continuous sutures and the abdomen was closed with two layers of interrupted sutures.

Conventional hand-sewn anastomosis group

Laparoscopic colectomy was performed in the CA group as in the SA group, with hand-sewn end-to-end intestinal anastomosis done in the same way, excluding the placement of a stent. However, we inserted 8–12 inverting interrupted sutures (VCP311, Ethicon, Inc.) for a single-layer intestinal

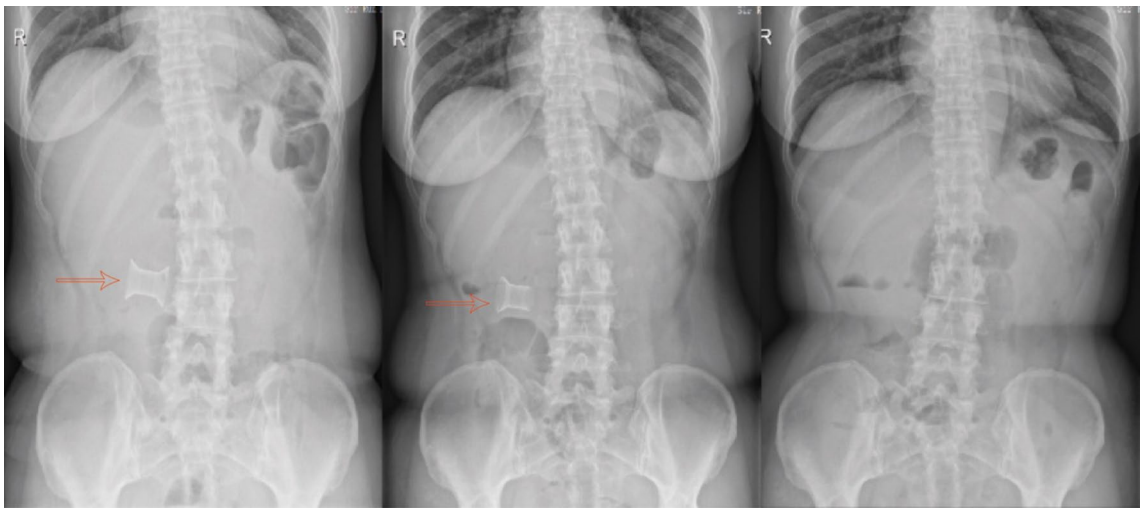

Fig. 2 Radiographic tracking images (arrow) 1 week (**a**) 2 weeks (**b**) and 3 weeks (**c**) postoperatively

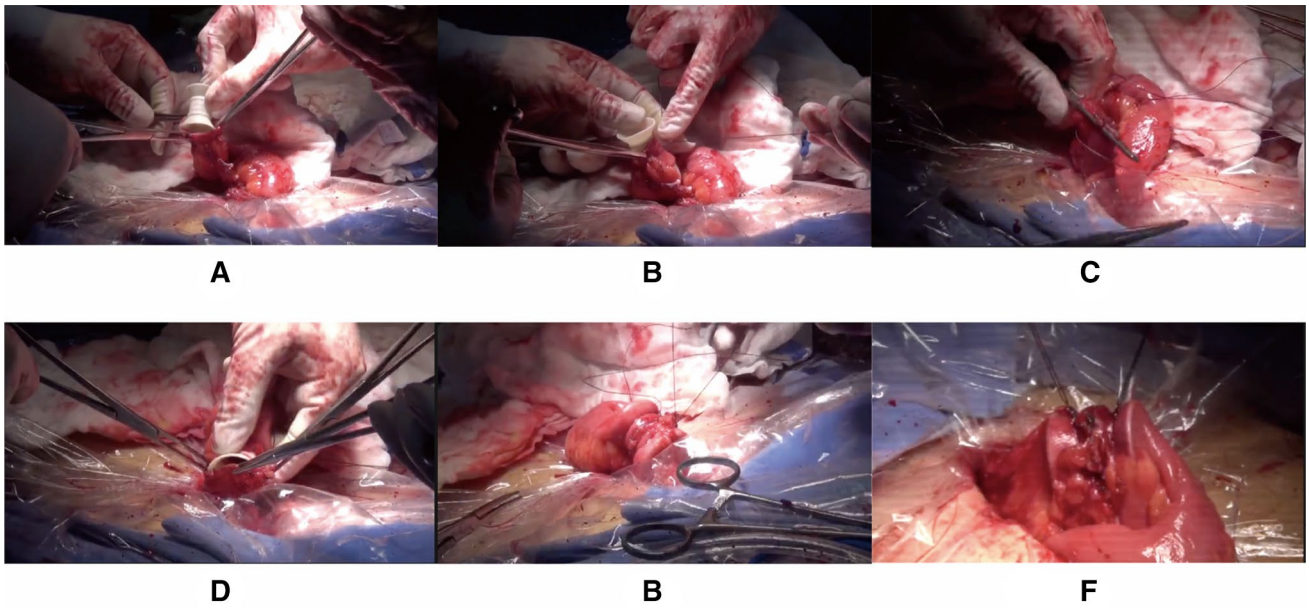

Fig. 3 Operative images of the stent anastomosis. **a** One end of the stent was placed in the intestinal. cavity; **b** a binding suture was tightened, knotted, and fixed; **c** the intestinal cavity approached; **d** the other end of the stent was placed in the intestinal cavity; **e** another binding suture was tightened, knotted, and fixed; **f** the procedure was completed with the anastomosis in the middle

anastomosis. Closure of the abdomen was done as in the SA group.

Endpoints

The primary endpoint was the healing condition of the anastomotic sites, defined as "good" or "poor". Colonoscopy was performed 6 months after surgery to assess the condition of the anastomosis. Good healing was defined by a single, large, mucosal venous vessel running perpendicular to and across the anastomotic line, whereas poor healing was defined by a lack of neovascularity in the anastomosis, reflecting a state of relative ischemia and predisposing toward stricture formation [28]. The secondary endpoints were as follows: duration of the anastomosis, defined as the time from insertion of the first suture at the cut edges to the last suture at the anastomotic site; anastomotic leak; intestinal obstruction; and postoperative bleeding. According to the International Study Group of Rectal Cancer in 2010 [29], we defined anastomotic leak as a defect of the anastomosis site. In this study, anastomotic leak was diagnosed by symptoms and signs of clinical peritonitis, including abdominal pain, leukocytosis, and fecal discharge through the intra-abdominal drainage catheter. Abdominopelvic-CT scan was performed whenever anastomotic leak was suspected [30].

Other operative complications were observed and recorded, including intraoperative intestinal injury, fat necrosis, wound infection, deep venous thrombosis (DVT), respiratory complications, and urinary tract infection. Bowel function recovery, defined by the time to first flatus and first bowel movement was a meaningful indicator of intestinal function. We also recorded and compared the in-hospital mortality of both groups to establish the safety of this method using a novel stent.

Data collection and follow-up

A standardized data form about preoperative, intraoperative, and postoperative outcomes was designed and collected by a single observer in each study center, blind to the randomization group. All participants were followed up systematically in the outpatient department and with questionnaires about gastrointestinal quality of life index (GIQLI) [31], with scores in total and for each item completed preoperatively the evening before the operation and in postoperative weeks 2, 4, 8, 12, and 24. The questionnaire included four domains: symptoms, physical function, emotional function, and social function with the response to each question scoring from 0 (the worst) to 4 (the best).

Statistical analysis

Quantitative data reported as means ± standard deviation were analyzed with the Student *t* test or Mann–Whitney test, depending on data distribution. Qualitative data were reported as the number of patients (%) and compared with either the Pearson χ^2 test or the Fisher exact test, depending on sample size. Quality of life (QOL) questionnaires

were analyzed using the analysis of covariance (ANCOVA) method with repeated measures. Significance was defined as $P < 0.05$ and statistical analyses were performed using the SPSS 20.0 software program (SPSS Inc., Chicago, IL, USA).

Results

Study population

During the study period, 60 participants were randomized into the SA group ($n = 30$) and the CA group ($n = 30$). Table 1 summarizes the demographic characteristics and partial clinical data of the two groups. There was no discrepancy in baseline characteristics (age, sex, BMI, smoking and drinking) or tumor location between the two groups. Although the operative time was shorter in the SA group than the CA group, the difference was not significant (176.73 ± 59.9 vs. 183.21 ± 53.8 min, respectively; $P = 0.899$), meaning that SA was non-inferior to CA in relation to the duration of the procedure. Intraoperative blood loss was minimal and similar in the SA group and the CA group (67.6 ± 44.3 vs. 64.6 ± 50.6 ml, respectively; $P = 0.770$). No blood transfusion was needed in either group.

Table 1 Characteristics and clinical data of the patients in the two groups

Characteristics	SA group $n = 30$	CA group $n = 30$	P
Age (years)	56.7 ± 11.9	60.6 ± 13.2	0.482
Sex			0.187
Male	20 (33.3%)	15 (50%)	
Female	10 (66.7%)	15 (50%)	
Smoking			0.310
Yes	17	12	
No	13	18	
Drinking			0.299
Yes	11	16	
No	19	14	
BMI	25.2 ± 2.0	25.2 ± 2.2	0.282
Location of lesion			0.173
Ascending colon	18	11	
Transverse colon	2	2	
Descending colon	10	17	
Operation time (min)	176.73 ± 59.9	183.21 ± 53.8	0.899
Blood transfusion			1.00
Yes	0	0	
No	30	30	
Blood lose (ml)	67.6 ± 44.3	64.6 ± 50.6	0.770

SA stent anastomosis, *CA* conventional anastomosis, *BMI* body mass index

Outcomes

The primary endpoint of the study; namely, healing of the anastomosis, was good in all the SA group patients and in all except one of the CA group patients, without a significant difference between the groups ($P = 1.00$; Table 2; Fig. 4). Similar findings were obtained when comparing the secondary outcomes, except for the duration of anastomosis. To be specific, less time was spent on intestinal anastomosis in the SA group than in the CA group (13.517 ± 4.281 vs. 20.333 ± 2.998 min, respectively; $P < 0.001$). None of the patients in the SA group suffered anastomotic leakage, intestinal obstruction, or bleeding, although one was found to have peritoneal effusion because of bowel damage during surgery. Notably, one patient from the CA group suffered anastomotic leak, which was a severe complication. There were other analogical postoperative complications in both groups ($P = 1.00$) but no differences were found between the groups in relation to any of these complications ($P = 0.671$). Thus, the SA group was non-inferior to the CA group in short-term postoperative complications. Postoperative recovery outcomes, including the time to first flatus and first bowel movement did not differ between the groups (5.800 ± 2.565 vs. 4.967 ± 1.973 days, $P = 0.164$; 3.233 ± 2.095 vs. 3.167 ± 0.791 days, respectively; $P = 0.871$), although it took longer for patients in the SA group to pass first flatus and bowel movement. There were no hospital deaths in either group.

Quality of life assessment

The GIQLI revealed no significant differences in baseline QOL scores preoperatively between the groups. Moreover, there were no significant differences between the SA and CA group in QOL scores 2, 4, 8, 12, and 24 weeks postoperatively, although emotional function was slightly higher in the SA group than in the CA group 2, 4, 8, 24 weeks postoperatively (14.83 ± 3.31 vs. 13.87 ± 3.15, $P = 0.25$; 16.00 ± 2.61 vs. 15.73 ± 2.07, $P = 0.66$; 16.63 ± 1.71 vs. 16.43 ± 1.92, $P = 0.67$; 16.70 ± 1.90 vs. 16.00 ± 1.76, respectively; $P = 0.14$). On postoperative week 8, the SA group patients reported a lower extent of pain as a gastrointestine-specific item, than the CA group patients (3.87 ± 0.35 vs. 3.40 ± 0.62, respectively; $P = 0.001$; Table 3).

Discussion

We developed a novel biodegradable intestinal stent to use in end-to-end intestinal anastomosis for laparoscopic colonic surgery and conducted this RCT to compare the effectiveness of SA vs. CA. After the randomization of 60 patients into two groups of 30, most results showed a high degree

Table 2 Perioperative outcomes of the two groups

Variables	SA group $n=30$	CA group $n=30$	P
Primary endpoint			
Healing of the anastomosis (good/poor)	30/0	29/1	1.00
Secondary endpoints			
Time of anastomosis (min)	13.517 ± 4.281	20.333 ± 2.998	< 0.001*
Anastomotic leak	0	1`	1.00
Intestinal obstruction	0	1	1.00
Peritoneal effusion	1	1	1.00
Bleeding	0	1	1.00
Other complications			
Intraoperative intestinal injury	1	0	1.00
Fat necrosis	0	1	1.00
Wound infection	0	1	1.00
Deep venous thrombosis	0	2	0.492
Respiratory complications	1	0	1.00
Urinary tract infection	1	1	1.00
Patients with other complications	2	3	1.00
Patients with any complications	2	4	0.671
Recovery outcomes			
Time to first flatus (day)	5.800 ± 2.565	4.967 ± 1.973	0.164
Time to first bowel movement (day)	3.233 ± 2.095	3.167 ± 0.791	0.871
In-hospital mortality	0	0	–

SA stent anastomosis, *CA* conventional anastomosis

* Means $P < 0.01$

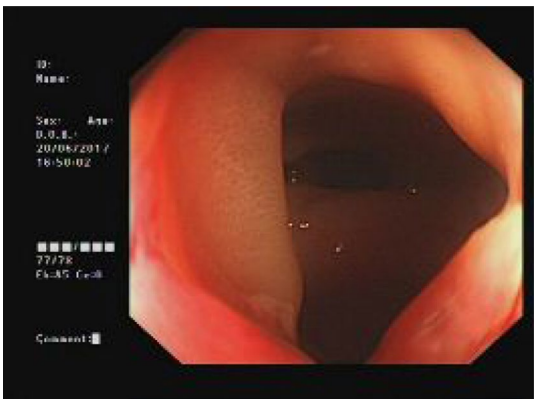

Fig. 4 A typical colonoscopy image

of consistency between the groups, which indicated that performing laparoscopic colonic surgery with stent anastomosis is non-inferior to that with traditional hand-sewn anastomosis.

Several animal experiments have been designed to assess laparoscopic colonic surgery using an anastomotic stent, which is synthesized with other different materials. Kuo et al. [1] performed end-to-end intestinal anastomosis using intraluminal agarose stents on New Zealand white rabbits and concluded that it took less time and the anastomotic sites healed better and faster when stents were used than with the hand-sewn procedure. Likewise, Wang et al. [25] carried out colonic anastomosis with a degradable stent synthesized with 1,3-propanediol, 1,2-propanediol and sebacic acid in a porcine model, and proved that the method was safe and feasible with less operative time and better healing conditions. Ma et al. [23] performed colonic stent anastomosis successfully by laparoscopy in a porcine model, using the same stent as that described by Wang et al. [25]. They concluded that laparoscopic colonic stent anastomosis had the potential to be a substitute for conventional hand-sewn anastomosis. However, clinical trials and multicenter RCTs were needed to compare the outcomes of SA and CA for laparoscopic colonic surgery.

The present RCT was designed carefully to establish whether there was non-inferiority in the SA group to avoid the pitfalls of previously published reports. We evaluated the efficacy, feasibility, and safety of intestinal anastomosis utilizing a novel stent. First, as a primary outcome, follow-up colonoscopy confirmed good healing of the anastomotic sites in all of the patients in the SA group but poor healing was seen in one of the CA group patients who suffered severe anastomotic leakage: one of the most dreaded complications of intestinal surgery [32]. Consequently, postoperative complications such as intestinal obstruction, peritoneal effusion, and anastomotic bleeding occurred simultaneously

Table 3 Items in the questionnaire on gastrointestinal quality-of-life index and scores in total and for each item

Items	Pre-operation			2 weeks			4 weeks			8 weeks			12 weeks			24 weeks		
	SA $n=30$	CA $n=30$	P	SA $n=30$	CA $n=30$	P	SA $n=30$	CA $n=30$	P	SA $n=30$	CA $n=30$	P	SA $n=30$	CA $n=30$	P	SA $n=30$	CA $n=30$	P
GIQLI																		
Overall	110.13 ± 5.84	109.40 ± 5.20	0.61	100.53 ± 6.46	102.00 ± 6.88	0.40	112.03 ± 6.00	112.57 ± 5.53	0.72	120.03 ± 4.12	119.73 ± 4.39	0.79	122.77 ± 4.02	123.93 ± 3.98	0.26	125.03 ± 3.70	123.37 ± 4.58	0.13
Symptoms	69.33 ± 4.63	68.10 ± 4.89	0.32	59.63 ± 5.17	61.33 ± 5.29	0.21	65.43 ± 3.98	66.43 ± 4.44	0.36	69.33 ± 4.04	69.30 ± 3.45	0.97	68.53 ± 3.33	69.17 ± 3.31	0.46	69.70 ± 3.48	69.37 ± 3.40	0.71
Physical	16.33 ± 1.71	15.87 ± 1.46	0.26	13.27 ± 2.18	13.73 ± 2.21	0.41	16.37 ± 1.92	16.17 ± 1.90	0.69	17.63 ± 1.38	17.37 ± 1.92	0.54	20.67 ± 1.92	21.40 ± 2.08	0.16	21.37 ± 1.65	21.07 ± 1.66	0.49
Emotional	11.73 ± 2.57	12.77 ± 2.31	0.11	14.83 ± 3.31	13.87 ± 3.15	0.25	16.00 ± 2.61	15.73 ± 2.07	0.66	16.63 ± 1.71	16.43 ± 1.92	0.67	16.47 ± 1.59	16.57 ± 1.85	0.82	16.70 ± 1.90	16.00 ± 1.76	0.14
Social	12.73 ± 1.05	12.67 ± 1.03	0.80	12.80 ± 1.16	13.07 ± 1.20	0.39	14.23 ± 1.61	14.23 ± 1.45	1.00	16.43 ± 1.36	16.63 ± 1.45	0.58	17.10 ± 0.80	16.80 ± 0.71	0.13	17.27 ± 0.78	16.93 ± 0.78	0.11
Gastrointestine-specific items																		
Pain	3.70 ± 0.46	3.67 ± 0.48	0.79	2.80 ± 0.41	2.80 ± 0.48	1.00	2.90 ± 0.31	3.00 ± 0.64	0.45	3.87 ± 0.35	3.40 ± 0.62	0.001*	3.90 ± 0.31	3.73 ± 0.52	0.14	3.97 ± 0.18	3.83 ± 0.38	0.09
Fullness	3.63 ± 0.49	3.60 ± 0.50	0.80	1.60 ± 0.56	1.53 ± 0.68	0.68	2.80 ± 0.48	2.80 ± 0.48	1.00	3.77 ± 0.50	3.77 ± 0.57	1.00	3.90 ± 0.30	3.93 ± 0.25	0.65	3.93 ± 0.25	3.97 ± 0.18	0.56
Diarrhea	4.00	4.00	–	3.87 ± 0.35	3.90 ± 0.31	0.69	3.97 ± 0.18	3.97 ± 0.18	1.00	4.00	3.93 ± 0.25	0.15	4.00	3.97 ± 0.18	0.32	4.00	4.00	–
Constipation	3.93 ± 0.25	3.96 ± 0.18	0.56	3.73 ± 0.45	3.70 ± 0.65	0.82	3.73 ± 0.45	3.80 ± 0.48	0.58	3.87 ± 0.34	3.90 ± 0.31	0.69	3.83 ± 0.38	3.87 ± 0.35	0.72	3.93 ± 0.25	3.93 ± 0.25	1.00
Nausea	3.90 ± 0.31	3.87 ± 0.35	0.70	3.07 ± 0.37	3.00 ± 0.26	0.42	3.67 ± 0.55	3.77 ± 0.43	0.43	3.83 ± 0.38	3.90 ± 0.31	0.46	3.93 ± 0.25	3.97 ± 0.18	0.56	4.00	3.97 ± 0.18	0.32
Blood in stool	3.96 ± 0.17	3.93 ± 0.24	0.31	2.90 ± 0.31	2.93 ± 0.25	0.65	3.96 ± 0.17	3.93 ± 0.24	0.31	3.93 ± 0.25	3.96 ± 0.18	0.56	4.00	4.00	–	4.00	4.00	–
Obstruction	3.67 ± 0.61	3.63 ± 0.62	0.83	2.97 ± 0.18	2.93 ± 0.37	0.66	4.00	4.00	–	4.00	4.00	–	4.00	4.00	–	4.00	4.00	–

SA stent anastomosis, *CA* conventional anastomosis, *GIQLI* gastrointestinal quality of life index

* Means $P<0.01$

in this patient. Surprisingly, in the CA group, although there was no leak from the anastomotic sites, one patient suffered peritoneal effusion. Colonoscopy showed reparative change response to inflammation 1 cm distal from the anastomosis and this incidental complication in the SA group was attributed to intraoperative injury rather than to the stent. Despite the exception, no differences were seen in anastomotic recovery between the groups. Moreover, because we sutured much less using the stent, less time was spent on anastomotic completion than in CA (13.517 ± 4.281 vs. 20.333 ± 2.998, respectively; $P < 0.001$), which meant that there was less exposure time of the intestinal incision. In other words, the faster the surgery, the less the damage. Besides, measured as time to first flatus and bowel movement, postoperative bowel function recovery showed no discrepancy in either group. Finally, no patients died during hospitalization in the SA group, which could be strongly indicative of the safety of the SA method for colonic surgery.

Laparoscopic colectomy compromised the QOL of patients in the short term [33]. As there were no significant differences in the QOL of the two groups before surgery, we could ensure the highest methodological quality of the questionnaire. No differences were found in GIQLI between the groups on postoperative weeks 2, 4, 12, 24. Interestingly, 8 weeks after the operation, the patients in the SA group reported less pain than those in the CA group. We speculate that the stent had been expelled by this time and that the discomfort caused by the stents had disappeared in the SA group. Because we informed patients of what type of surgery would be performed, those in the SA group would have possibly felt more satisfied than those in the CA group.

BAR was introduced by Hardy et al. as a similar valtrac device [34] Although BAR has been proven to be safe in both emergency and elective operations [35, 36], it has not gained widespread popularity [37]. On comparing BAR with our stent, their shape and composition are similar; however, our stent requires only one absorbable traction suture (VCP311, Ethicon, Inc.) to approximate the mesenteric borders of the incisal margins for accurate tissue apposition, whereas the BAR requires two scalloped rings of the device to be closed with a 1.5–2.5-mm gap between them. The different closure used for our stent helps prevent anastomotic tissue ischemia to some extent. Most importantly, a meta-analysis by Slesser et al. [38] showed that the BAR was not superior to the conventional hand-sewn method, but rather, it increased the risk of bowel obstruction. Conversely, our study showed that stent anastomosis is non-inferior to hand-sewn anastomosis in complications, including bowel obstruction, and it requires less time to perform the anastomosis.

A comparison of our stent with the stapled method also seems to be important. Wood et al. [15] found that the BAR method required equivalent or less time than the stapled techniques, and the cost of BAR was equivalent to one intestinal stapler. To be specific, the costs for BAR and the Premium Plus CEEA intestinal stapler were $600 and $910, respectively [39]. In our study, the anastomosis time for the SA group was 13.517 ± 4.281 min, which was similar to the mean 15.2 min for the BAR method [40]. The cost of our stent would also be less than BAR; therefore, compared with stapled anastomosis, our stent anastomosis method would have more advantages with less anastomosis time and costs. These conclusions are our speculations and considering the differences in these methods; namely, end-to-end anastomosis in the SA group and end-to-side anastomosis in the stapled method, we doubt that there is comparability between them.

Our multicenter RCT should help with the introduction of the sutureless procedure with a tension-free anastomosis for laparoscopic colonic surgery. Most importantly, it is time-saving for surgeons to perform the procedure by laparoscopy, and the short-term outcomes are non-inferior to those of conventional anastomosis. Besides, the high-biosecurity stent decomposes to CO_2 and water in 2–3 weeks without leaving residual stent material or any foreign body. With $BaSO_4$ in the stent, surgeons can track its position and degradation accurately to enhance the safety of this novel procedure. This novel stent could also be suitable for other disorders that require end-to-end anastomosis after the resection of intestine, such as colorectal lesions, small bowel tumors, inflammation, diverticulosis, and recovery operations after jejunostomy, based on the efficacy, feasibility, and safety of the procedure with SA. Thus, it may be generalized to include gastrojejunostomy and cholangioenterostomy.

The major limitation of this RCT is the small sample size, with complication rates of $n = 1$ or $n = 2$ for most variables, making accurate statements about the risk of severe complications, especially anastomotic leak, difficult. Although we speculated that a relatively normal anatomy with physical functions and the barrier provided by the stent may benefit anastomotic recovery, larger studies should be performed to ascertain if there is a significant difference in the postoperative complication rate and healing conditions of anastomosis between the groups. Patients with diseases causing delayed healing and those undergoing emergency procedures should be included in future RCTs to expand the indications for stent anastomosis. To further confirm the efficacy of SA for colonic surgery, long-term comparison results should be analyzed, especially regarding abdominal adhesion following surgery, overall survival, and disease-free survival, as well as histological examination, which is the gold standard for evaluating the condition of anastomotic healing.

In conclusion, compared with conventional hand-sewn anastomosis, laparoscopic intestinal anastomosis with a novel stent is a non-inferior strategy for colonic surgery, which requires less time to perform the anastomosis. We

recommend this technique as a potential alternative that could become a standard surgical treatment.

Acknowledgements Mingyu Chen, Diyu Huang, Zhongtao Zhang, Zhenjun Wang, Yingjiang Ye, Dianrong Xiu, and Dechuan Li performed the research, Jiasheng Cao and Long Pan collected and analyzed the data, Mingyu Chen, Jiasheng Cao, and Bin Zhang designed the research study and wrote the paper, and Xiujun Cai contributed to the design of the study.

Funding This work was funded by Key Social Development Projects of Major Science and Technology Projects of Zhejiang Province, Grant numbers 2017C01018 and 2014C03043-1. The authors have no potential conflicts of interest to declare.

References

1. Kuo WY, Huang HC, Huang SW, Yu KH, Cheng FP, Wang JH, Wu JT. Benefits of intraluminal agarose stents during end-to-end intestinal anastomosis in New Zealand white rabbits. Comp Med. 2017;67(6):504–7 **(Pmc5713165)**.
2. Slieker JC, Daams F, Mulder IM, Jeekel J, Lange JF. Systematic review of the technique of colorectal anastomosis. JAMA Surg. 2013;148(2):190–201. https://doi.org/10.1001/2013.jamasurg.33].
3. Kennedy GD, Heise C, Rajamanickam V, Harms B, Foley EF. Laparoscopy decreases postoperative complication rates after abdominal colectomy: results from the national surgical quality improvement program. Ann Surg. 2009;249(4):596–601. https://doi.org/10.1097/SLA.0b013e31819ec903].
4. Corman ML, Prager ED, Hardy TG Jr, Bubrick MP. Comparison of the Valtrac biofragmentable anastomosis ring with conventional suture and stapled anastomosis in colon surgery. Results of a prospective, randomized clinical trial. Dis Colon Rectum. 1989;32(3):183–7.
5. Vignali A, Gianotti L, Braga M, Radaelli G, Malvezzi L, Di Carlo V. Altered microperfusion at the rectal stump is predictive for rectal anastomotic leak. Dis Colon Rectum. 2000;43(1):76–82.
6. Giuratrabocchetta S, Rinaldi M, Cuccia F, Lemma M, Piscitelli D, Polidoro P, Altomare DF. Protection of intestinal anastomosis with biological glues: an experimental randomized controlled trial. Tech Coloproctol. 2011;15(2):153–8. https://doi.org/10.1007/s10151-010-0674-0].
7. Choi HJ, Kim HH, Jung GJ, Kim SS. Intestinal anastomosis by use of the biofragmentable anastomotic ring: is it safe and efficacious in emergency operations as well? Dis Colon Rectum. 1998;41(10):1281–6.
8. Robicsek F, Konstantinov I. Humer Hultl: the father of the surgical stapler. J Med Biogr. 2001;9(1):16–9. https://doi.org/10.1177/096777200100900106].
9. Dowson HM, Gage H, Jackson D, Qiao Y, Williams P, Rockall TA. Laparoscopic and open colorectal surgery: a prospective cost analysis. Colorectal Dis. 2012;14(11):1424–30. https://doi.org/10.1111/j.1463-1318.2012.02988.x].
10. Cohen SM, Clem MF, Wexner SD, Jagelman DG. An initial comparative study of two techniques of laparoscopic colonic anastomosis and mesenteric defect closure. Surg Endosc. 1994;8(2):130–4.
11. Fok M, Ah-Chong AK, Cheng SW, Wong J. Comparison of a single layer continuous hand-sewn method and circular stapling in 580 oesophageal anastomoses. Br J Surg. 1991;78(3):342–5.
12. Lustosa SA, Matos D, Atallah AN, Castro AA. Stapled versus handsewn methods for colorectal anastomosis surgery. Cochrane Database Syst Rev. 2001;3:CD003144. https://doi.org/10.1002/14651858.CD003144.
13. Schneider IH, Schneider C, Thaler K, Reck T, Kockerling F. Intraperitoneal colon anastomosis with laparoscopic purse string suture clamp and Valtrac ring. Langenbecks Arch Chir. 1994;379(3):188–92.
14. Forde KA, Goodell KH, DellaBadia M. A 10-year single-institutional study of the biofragmentable anastomosis ring. Am J Surg. 2006;191(4):483–7. https://doi.org/10.1016/j.amsurg.2006.01.005].
15. Wood JS, Frost DB. Results using the biofragmentable anastomotic ring for colon anastomosis. Am Surg. 1993;59(10):642–4.
16. Bubrick MP, Corman ML, Cahill CJ, Hardy TG Jr, Nance FC, Shatney CH. Prospective, randomized trial of the biofragmentable anastomosis ring. The BAR Investigational Group. Am J Surg. 1991;161(1):136–42 **(discussion 42–43)**.
17. Lim CB, Goldin RD, Darzi A, Hanna GB. Characterization of materials eliciting foreign body reaction in stapled human gastrointestinal anastomoses. Br J Surg. 2008;95(8):1044–50. https://doi.org/10.1002/bjs.6071].
18. Capitan Morales LC, Rodriguez Nunez E, Morales Conde S, Sanchez Ganfornina F, Del Rio Lafuente FD, Cabot Ostos E, Ortega Bevia JM, Loscertales Abril J, Cantillana Martinez J. Experimental study of sutureless colorectal anastomosis. Hepatogastroenterology. 2000;47(35):1284–90.
19. van der Ham AC, Kort WJ, Weijma IM, van den Ingh HF, Jeekel J. Effect of fibrin sealant on the healing colonic anastomosis in the rat. Br J Surg. 1991;78(1):49–53.
20. Haukipuro KA, Hulkko OA, Alavaikko MJ, Laitinen ST. Sutureless colon anastomosis with fibrin glue in the rat. Dis Colon Rectum. 1988;31(8):601–4.
21. Kuramoto S, Ryan PJ, Kawahara M, Masaki Y. Experimental laser anastomosis of the colon—long-term results and histologic-findings after laser closure of colotomies. Dis Colon Rectum. 1994;37(12):1198–204. https://doi.org/10.1007/Bf02257782].
22. Rochkind S, Rabau MY, Goldman G, Bar-Nea L, Wiznitzer T. Low-energy CO_2 laser intestinal anastomosis: an experimental study. Lasers Surg Med. 1988;8(6):579–83.
23. Ma L, Cai XJ, Wang HH, Yu YL, Huang DY, Ge GJ, Hu HY, Yu SC. Laparoscopic colonic anastomosis using a degradable stent in a porcine model. World J Gastroenterol. 2016;22(19):4707–15. https://doi.org/10.3748/wjg.v22.i19.4707.
24. Wang Y, Cai X, Jin R, Liang Y, Huang D, Peng S. Experimental study of primary repair of colonic leakage with a degradable stent in a porcine model. J Gastrointest Surg. 2011;15(11):1995–2000. https://doi.org/10.1007/s11605-011-1593-8].
25. Wang YF, Cai XJ, Cai HJ, Liang YL, Huang DY, Liang X. Experimental study of colonic anastomosis with a degradable stent in a porcine model. Am J Surg. 2010;199(6):833–9. https://doi.org/10.1016/j.amjsurg.2009.05.044.
26. Liu K, Yu H, Zhang M, Yu Y, Wang Y, Cai X. Sutureless primary repair of colonic perforation with a degradable stent in a porcine model of fecal peritonitis. Int J Colorectal Dis. 2012;27(12):1607–17. https://doi.org/10.1007/s00384-012-1511-x].
27. Tedesco MM, Curet MJ. Laparoscopic-assisted colectomy for colon cancer. Expert Rev Med Devices. 2006;3(4):415–9. https://doi.org/10.1586/17434440.3.4.415].
28. Harris MT, Laudito A, Waye JD. Colonoscopic features of colonic anastomoses. Gastrointest Endosc. 1994;40(5):554–7.
29. Jang JH, Kim HC, Huh JW, Park YA, Cho YB, Yun SH, Lee WY, Yu JI, Park HC, Park YS, Park JO. Anastomotic leak does not impact oncologic outcomes after preoperative chemoradiotherapy and resection for rectal cancer. Ann Surg. 2017. https://doi.org/10.1097/sla.0000000000002582.
30. Rahbari NN, Weitz J, Hohenberger W, Heald RJ, Moran B, Ulrich A, Holm T, Wong WD, Tiret E, Moriya Y, Laurberg S, den Dulk

M, van de Velde C, Buchler MW. Definition and grading of anastomotic leakage following anterior resection of the rectum: a proposal by the International Study Group of Rectal Cancer. Surgery. 2010;147(3):339–51. https://doi.org/10.1016/j.surg.2009.10.012].
31. Eypasch E, Williams JI, Wood-Dauphinee S, Ure BM, Schmulling C, Neugebauer E, Troidl H. Gastrointestinal Quality of Life Index: development, validation and application of a new instrument. Br J Surg. 1995;82(2):216–22.
32. Hyman N, Manchester TL, Osler T, Burns B, Cataldo PA. Anastomotic leaks after intestinal anastomosis: it's later than you think. Ann Surg. 2007;245(2):254–8. https://doi.org/10.1097/01.sla.0000225083.27182.85.
33. Stucky CC, Pockaj BA, Novotny PJ, Sloan JA, Sargent DJ, O'Connell MJ, Beart RW, Skibber JM, Nelson H, Weeks JC. Long-term follow-up and individual item analysis of quality of life assessments related to laparoscopic-assisted colectomy in the COST trial 93-46-53 (INT 0146). Ann Surg Oncol. 2011;18(9):2422–31. https://doi.org/10.1245/s10434-011-1650-2.
34. Hardy TG Jr, Pace WG, Maney JW, Katz AR, Kaganov AL. A biofragmentable ring for sutureless bowel anastomosis. An experimental study. Dis Colon Rectum. 1985;28(7):484–90.
35. Forde KA, McLarty AJ, Tsai J, Ghalili K, Delany HM. Murphy's Button revisited. Clinical experience with the biofragmentable anastomotic ring. Ann Surg. 1993;217(1):78–81. https://doi.org/10.1097/00000658-199301000-00013.
36. Buchberg BS, Masoomi H, Bergman H, Mills SD, Stamos MJ. The use of a compression device as an alternative to hand-sewn and stapled colorectal anastomoses: is three a crowd? J Gastrointest Surg. 2011;15(2):304–10. https://doi.org/10.1007/s11605-010-1376-7.
37. Aggarwal R, Darzi A. Compression anastomoses revisited. J Am Coll Surg. 2005;201(6):965–71. https://doi.org/10.1016/j.jamcollsurg.2005.06.255].
38. Slesser AA, Pellino G, Shariq O, Cocker D, Kontovounisios C, Rasheed S, Tekkis PP. Compression versus hand-sewn and stapled anastomosis in colorectal surgery: a systematic review and meta-analysis of randomized controlled trials. Tech Coloproctol. 2016;20(10):667–76. https://doi.org/10.1007/s10151-016-1521-8.
39. Galizia G, Lieto E, Castellano P, Pelosio L, Imperatore V, Canfora F, Pignatelli C. Comparison between the biofragmentable anastomosis ring and stapled anastomoses in the extraperitoneal rectum: a prospective, randomized study. Int J Colorectal Dis. 1999;14(6):286–90.
40. Konishi F, Saito Y, Ugajin H, Okada M, Kashiwagi H, Sato T, Kanazawa K. Sutureless anastomosis using a biofragmentable anastomosis ring. Surg Today. 1995;25(9):783–9.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.