Intraluminal flexible sheath for the protection of low anastomosis after anterior resection: results from a First-In-Human trial on 15 patients

Antonio D'urso, Niels Komen, Jérémie H. Lefevre

► To cite this version:

Antonio D'urso, Niels Komen, Jérémie H. Lefevre. Intraluminal flexible sheath for the protection of low anastomosis after anterior resection: results from a First-In-Human trial on 15 patients. *Surgical Endoscopy*, 2019, 10.1007/s00464-019-07279-8 . hal-02414262

HAL Id: hal-02414262

<https://hal.sorbonne-universite.fr/hal-02414262>

Submitted on 16 Dec 2019

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

[Click here to view linked References](#)

Intraluminal flexible sheath for the protection of low anastomosis after anterior resection:

Results from a First-In-Human trial on 15 patients

Antonio D'Urso, (MD, PhD)¹, Niels Komen (MD, PhD)², Jérémie H. Lefevre (MD, PhD)³

1. University Hospital of Strasbourg, Department of General, Digestive, and Endocrine Surgery, Strasbourg, France

2. Department of Abdominal Surgery, University Hospital Antwerp, University of Antwerp, Edegem, Belgium

3. Sorbonne Université, Department of Digestive Surgery, AP-HP, Hôpital Saint Antoine, F-75012, Paris, France.

Corresponding author:

Jérémie H. Lefevre

Sorbonne Université, Department of Digestive Surgery, AP-HP, Hôpital Saint Antoine, 284 rue du Faubourg Saint-Antoine, 75012 Paris, France.

Phone : +33149282563

Fax : +33149282567

Mail: jeremie.lefevre@aphp.fr

Funding information:

This study has been funded by SafeHeal.

SafeHeal is the manufacturer of the Colovac device.

This study was presented as an oral communication at the 2019 SAGES Meeting in Baltimore, MD, USA.

1 ABSTRACT

2 Background

3 Defunctioning ostomy is commonly used to protect patients from anastomotic leakage
4 complications after low anterior resection but is fraught with its own deleterious effects. This
5 first-in-human study examines the safety and preliminary efficacy of Colovac, an anastomosis
6 protection device. The Colovac consists of a flexible bypass sheath, placed in the lumen of the
7 colon and anchored above the anastomosis using a vacuum-stent.
8

9 Methods

10 15 patients underwent anterior resection (AR) with anastomosis protection by a Colovac, at 3
11 European-centers. After 14 days, the anastomosis integrity was examined by CT-scan and
12 endoscopy. The device was then endoscopically removed. Data regarding demographics,
13 surgical details, 30 day post-operative complications, and patient satisfaction were collected
14 prospectively.
15

16 Results

17 15 patients (10 male) underwent laparoscopic AR with Colovac placement. Preoperative
18 neoadjuvant therapy was administered to 54% of patients. Device placement was uneventful in
19 all patients with a median duration of 7 min and placement was judged as easy or very easy in
20 93% of the cases. Patients did not report major discomfort during the 14 days. Endoscopic
21 removal (10 min) was judged as easy or very easy in 87% of the cases. Absence of feces below
22 the Colovac anchoring site was observed in 100% of the cases. 4 anastomotic leakages were
23 observed (including 3 device migrations). Overall 5 patients (33%) required a planned stoma
24 creation. At 3 months, 1 had already been closed.
25

26 Conclusion

27 Colovac provides a minimally-invasive protection of the anastomosis during the healing
28 process by avoiding the need for a diverting ostomy for two thirds of patients who will not
29 experience anastomotic complications and allowing safe conversion to standard of care for
30 patients requiring extended anastomotic protection. A larger study is ongoing to confirm these
31 results.
32

33 **Keywords:** rectal cancer; stoma; bypass sheath; stent; anastomotic leakage.

1 INTRODUCTION

2 Colorectal cancer represents the third most common cancer and the second most common cause
3 for cancer mortality worldwide, with 1.8 million diagnoses and 881,000 expected deaths in
4 2018. [1] Despite improvement in the peri-operative management of anterior resection for rectal
5 cancer, the rate of anastomotic leakages is still around 17% in recent randomized studies. [2, 3]

6 Anastomotic leakage is associated with increased morbidity and mortality, rate of definitive
7 stoma [4, 5] and recurrence [6]. The only protective measure is the use of a diverting stoma. [7]
8 Although the anastomosis typically heals in 10-15 days, the ostomy remains for 2-6 months.
9 This timeframe is necessary for ostomy maturation (2 months) or the accomplishment of
10 adjuvant therapy (3-6 months). During this period, patients are exposed to complications (up to
11 77%) such as dehydration, peristomal skin breakdown, skin burn, stoma prolapses or retraction
12 in addition to the psychological impact of carrying a stoma.

13 Additionally, stoma closure carries a risk of postoperative complications around 8%, including
14 anastomotic leakage of the ileo-ileal anastomosis (1%). [8] Following stoma closure, the
15 morbidity is still high with a 10% risk of surgery for incisional hernia at the stoma site. [9]
16 Moreover, around 20% of ostomies are not reversed. [10] This has a significant impact on the
17 quality of life of the patients, and implies life-long maintenance and associated costs.

18 Therefore, there is a critical need to develop a device which would protect the anastomosis
19 temporarily to reduce complications associated with ostomies and takedown interventions, and
20 would maintain digestive tract functionality for better recovery outcomes. Attempts to develop
21 medical devices based on a flexible lining to protect the anastomosis proved the applicability
22 of the concept [11], but anchoring these devices by an easily reversible mechanism proved
23 challenging. [12, 13]

24 The Colovac Colorectal Anastomosis Protection Device (Colovac, SafeHeal, France) is a single
25 use, temporary intraluminal bypass device consisting of a flexible bypass sheath, which is
26 endoscopically placed into the lumen of the colon and anchored above the anastomosis using a
27 vacuum stent. The Colovac thus creates a functional colorectal anastomosis protection reducing
28 contact of fecal content with the anastomotic site. Until now, no clinical data were available to
29 evaluate this device.

30 The aim of this first-in-human pilot study was to evaluate the preliminary safety and efficacy
31 of the Colovac.

MATERIALS AND METHODS

Study Design

This clinical study was a pilot, prospective, open-label, multi-center (Europe), single arm study, which enrolled 15 subjects undergoing low anterior resection with total mesorectal excision (TME) for rectal cancer. Procedures were performed by experienced colorectal surgeons at three European tertiary centers (Hospital Saint-Antoine, Paris; IHU, Strasbourg; UZA, Antwerp). The study protocol, its amendments, and study associated documents were reviewed and approved by the appropriate Ethics Committee (EC) and Competent Authorities (CA). This study was registered online on the ClinicalTrials.gov website under the following identifier: NCT03352570.

It was conducted in accordance with the standard ISO 14155:2011 and the recommendations guiding physicians in biomedical research involving human subjects adopted by the 18th World Medical Assembly, Helsinki, Finland, 1964 and later revisions.

Objective & endpoints

The primary study objective was to demonstrate safety using the device. It was assessed by recording all Serious Adverse Events (SAEs) in terms of type, frequency, severity and relationship with the use of the Colovac during 3 months follow-up. Any readmission, unscheduled admission greater than 24 hours or initial hospitalization extending beyond a 14-day average length of stay due to an adverse event were considered as a serious adverse event.

The secondary objectives were to assess the clinical efficacy of bypass anastomosis protection, the overall procedural feasibility, the procedural success with placing and retrieving the device, the average procedure time, and the patient acceptance of the device.

Patients

Patients who underwent an anterior resection (AR) with TME with low anastomosis less than 20 cm from the anal verge were considered for inclusion.

1 Inclusion criteria were as follow: age ≥ 18 and ≤ 65 years old with an indication for colorectal
2 resection, eligible to bear a loop ileostomy, willing to comply with protocol-specified follow-
3 up evaluations and having signed a written informed consent.

4 Exclusion criteria were the following: patient with inflammatory bowel disease, pregnant or
5 nursing female subject (a pregnancy test should be conducted the day prior to the procedure for
6 all women of childbearing age), known allergy to nickel or other components of the Colovac,
7 any significant medical condition which, in the investigator's opinion, may interfere with the
8 subject's optimal participation in the study, subject already enrolled in another investigational
9 drug or device study that has not completed the primary endpoint or that clinically interferes
10 with the endpoints of this study, or patient unable to give consent.

11 After inclusion, subjects were studied pre and post procedure, with scheduled follow- up at 1,
12 2, 4 weeks and 3 months, as well as a phone call at 6 weeks.

14 *Data collection*

15 Safety and efficacy of the Colovac were analyzed during the implantation period (0-14 days)
16 and after 90 days follow-up. Data regarding demographics, surgical details, 90-day morbidity
17 and patient satisfaction were collected prospectively. All stapled anastomoses were considered
18 as colorectal anastomoses and all handsewn anastomoses were considered as coloanal
19 anastomoses.

20 Feasibility was defined by the ability to introduce, deploy and retrieve the Colovac to/from the
21 desired location in the colon. Procedural success was defined by acute efficacy placing the
22 device at the desired location. Procedure time was defined as time from insertion of the
23 introducer to the vacuum system being ready to be connected and begin vacuum application.
24 Migration rate was defined by the number of devices migrated over the anastomosis divided by
25 the number of devices placed. The sheath internalization is defined as the retraction of the
26 Colovac sheath within the colon lumen, and no more external protrusion through the anus.
27 Patient acceptance and tolerability was analyzed using the NIH's PROMIS health measurement
28 questionnaires to assess parameters like pain, bowel incontinence, constipation, diarrhea, or
29 anxiety and social isolation. [14]

30 An independent Data Safety Monitoring Board (DSMB) has been appointed by the sponsor to
31 assess, at monthly intervals, the progress of the clinical investigation, the safety data and the

critical performance endpoints, and to recommend to the sponsor whether to continue, suspend, modify, or stop the clinical investigation. All members of the DSMB had no relationship with the sponsor or the investigators.

Investigational device

The Colovac is intended to reduce contact of faecal content with the colorectal anastomotic site, following colorectal surgery (open or laparoscopic). It is indicated to be used in adult patients scheduled to receive a diverting loop ileostomy following colorectal surgery, who have been assessed by a multi-disciplinary team as per standard of care. The Colovac is a short-term minimally-invasive device delivered and positioned through the anus. It is a sterile, single use disposable device consisting of one introducer pre-loaded with the Colovac.

The Colovac is made of two elements: an anchor made of a covered stent delimiting a vacuum chamber connected to a vacuum tube; a flexible polymer cylindrical sheath attached to the anchor, covering the anastomosis with appropriate length so that it protrudes about five centimeters outside the patient's anus (Figure 1) in order to avoid any feces backflow in the colon at the open extremity of the sheath and to allow surveillance of the stent placement.

Procedure

Patients received fibre-free dietary regimen 2-3 days before surgery and mechanical bowel preparation (PEG based) the day before surgery (3-4 L). After the creation of the anastomosis, Colovac was inserted endoluminally through the anus under direct laparoscopic or laparotomic vision, using a dedicated flexible introducer (external diameter 17 mm) preloaded with Colovac. Once positioned at the correct location, approximatively 20 cm above the anastomosis, the stent was delivered and expanded. Upon removal of the introducer, the sheath and the vacuum tube were self-deployed distally past the anastomosis and the anus. After a vacuum efficacy test, the vacuum tube was then connected to a vacuum system (Redon vial of 600 ml), fixating the mucosa against the stent during the implantation period. Redon vacuum sets are meant for postoperative wound drainage. It consists of a high vacuum drainage system. The set is connected to the Colovac device via the aspiration tube, using a specific connector. The device was left in situ up to fourteen days post-implantation. Use of a pelvic drain was left at the discretion of the investigator.

1 The surgeon was asked to grade the ease of introducer introduction and removal using a 5 points
2 Lickert scale ranked from very easy to impossible.

3 A low fiber diet was given while the stent was in place. For the purpose of the study, all patients
4 remained hospitalized for the entire duration of the Colovac implantation. **Follow-up included**
5 **daily clinical examination of the abdomen and the sheath length, CRP levels at post-operative**
6 **day 1, 3 and 5. [15, 16]** After 12 to 13 days, the anastomosis integrity was examined by a CT
7 scan with IV contrast agent and/or trans anal injected contrast CT-scan before taking the patient
8 to the OR for the retrieval. The Colovac was retrieved at day 14 in the OR. An endoscopy was
9 performed between the sheath and the colonic mucosa to verify the anchoring site and the
10 absence of stool between the sheath and the colonic wall. Then the device was removed
11 endoscopically through the anus by pulling on the retrieval loops located at the distal and
12 proximal ends of the stent.

14 **RESULTS**

15 *Subjects demographics and surgical procedures*

16 Fifteen patients were enrolled between November 2017 and June 2018 at three sites in Europe
17 (Hôpital Saint Antoine, Paris, France n=8 - CHU Strasbourg, n=3 - UZA, Antwerp, Belgium,
18 n=4). One patient was screened but not included in this study as he declined participation in a
19 clinical trial. Patient characteristics and surgical procedures details are summarized in Table 1.

20 There were 10 men (67%) with a median age of 60 (46-70) years. All patients were diagnosed
21 with a rectal cancer. Majority of patients were staged cT3 (53%). 67% of patients received
22 neoadjuvant radiotherapy and/or chemotherapy.

23 All anterior resections were performed through a laparoscopic approach, 26.7% of patients
24 underwent a coloanal anastomosis and 60% of cases received a side-to-end anastomosis.

25 Two patients (14%) had associated procedures (right hepatectomy and two wedge resections
26 for synchronous metastatic lesions). Details of surgical procedures are given in Table 1.

27 *Colovac procedure*

- 28 • Colovac placement and anchoring

1 The Colovac placement was scored as very easy or easy by the surgeon in 93% of cases. The
2 median duration of placement was 7 (3-10) min. In 1 out of the 15 cases (7%), the Colovac was
3 accidentally pulled down during introducer removal. The device was then removed and replaced
4 by a second one, without additional difficulties. Details about Colovac placement are
5 summarized in Table 2.

6 One (7%) patient experienced a Colovac sheath internalization (retraction from anus) at Day 1.
7 As the patient was asymptomatic, he was closely monitored but nothing was done to reverse
8 the sheath internalization. The device was removed according to the protocol on Day 14.

9 Of the 15 devices implanted, 3 (20%) migrated before the end of the implantation period (2
10 device malfunctions related to a vacuum defect and 1 device misplacement (stent component
11 of the Colovac device placed in immediate proximity (i.e. 4 cm) of the distal end of the J-
12 pouch)). These three patients experienced moderate fever at post-operative D3 to D5 and a
13 control CT-scan was performed showing device migration. Devices were endoscopically
14 removed in the operating room and conversion to loop ileostomies were performed without any
15 complication in order to extend the anastomosis protection. For 2 patients, conversion to loop
16 ileostomy was performed during the course of the implantation period, while for the third
17 patient, loop ileostomy conversion was considered at the time of scheduled removal, owing to
18 the presence of a millimetric fistula communicating with the vaginal wall, resulting from a
19 vaginal wall laceration during the initial surgery.

- Colovac retrieval

21 All devices were removed endoscopically (14/15) or manually (1/15), without the need for
22 surgery at postoperative Day 4 to 17 days. All Colovac retrievals were scored as very easy or
23 easy by the endoscopist except the two (13%) first cases of the study, judged as difficult given
24 the time required for removal (15 minutes). The median duration of the retrieval procedure was
25 10 (5-20) minutes. Following successful Colovac retrieval at postoperative day 14, all patients
26 without anastomotic leakage (n=10) were discharged the day after the endoscopic retrieval
27 procedure.

28 The absence of feces below the Colovac anchoring site was confirmed by endoscopy performed
29 between the colonic wall and the sheath in all the patients with the Colovac in place. The
30 mucosal appearance was endoscopically evaluated and rated as normal or inflammatory in 80%
31 of cases above the anchoring site and at the anastomotic level. The remaining 20% didn't
32 require any further surveillance even if rated as ulcerated or bleeding. At the device anchoring

1 site, in 27% of patients, small bleeding lesions were experienced, not requiring any surveillance.
2 Details about Colovac retrieval procedures are summarized in Table 2.

3 *Post-operative course (Figure 2)*

4 • Post operative morbidity

5 The overall postoperative morbidity was 47% (n=9). (Table 3). Major morbidity (Dindo III-IV)
6 was 33%.

7 Major postoperative complications during the Colovac implantation period were device
8 migrations with anastomotic leakages (20%), and incomplete anastomosis healing diagnosed at
9 the end of the Colovac implantation (13%). They were all managed by an ostomy placement
10 for longer protection of the anastomosis. **One (7%) patient with a colonic J pouch anastomosis**
11 **who experienced a Colovac migration in the first week after the implantation was operated for**
12 **the removal of the device, colonic lavage and a loop ileostomy creation. Unfortunately he**
13 **presented few hours later a peritonitis requiring a second re-intervention for abdominal lavage.**
14 **The recovery after the second operation was uneventful.**

15 **The other two patients who presented with Colovac migration during the implantation period**
16 **were re-operated. The Colovac was removed and the loop ileostomy created without any**
17 **complications. No other patients experienced during the implantation period any morbidity**
18 **related to the anastomosis. As reported in the table 3 one patient with previous right**
19 **hepatectomy developed an ascites medically treated.** Post-operative complications during the
20 post-Colovac retrieval period (14 days to 3 months) were dominated by pelvic collection (n=3)
21 in patients who did not experience leaks during the immediate post-operative period. All pelvic
22 collections were managed conservatively by antibiotics.

23 • Patient acceptance and success rate

24 Colovac was well tolerated by patients with a full or very good acceptance of vacuum system
25 presence for 80% of them and a NIH's PROMIS median score of 15 (8-20) at 3 months (Table
26 3). The Colovac device provided effective protection of the anastomosis in 12/15 (80%)
27 subjects during the 14 day implantation period and allowed avoidance of ostomy creation in
28 10/15 (67%). Among the 5 patients converted to ostomy, 1 (7%) had his stoma reversed at 3
29 months, 2 were still under chemotherapy treatment and the remaining two are planned to have
30 a stoma closure at 6 months following surgery.

DISCUSSION

The current standard of care to minimize the sequelae of anastomotic leakage is the creation of a temporary diverting ostomy in order to protect the anastomosis [7]. A recent meta-analysis by Phan et al. of 8 randomized studies with 892 anterior resections confirms that a stool diversion following rectal surgery can effectively reduce anastomotic complications. [17] The Colovac presents an alternative to ostomy by creating a functional intraluminal bypass which is endoscopically placed into the lumen of the colon and anchored above the anastomosis using a vacuum stent.

This first preliminary study showed that the Colovac procedure is feasible with promising initial results in terms of protection of the anastomosis: 80% of subjects protected during the 14 days implantation period and avoidance of ostomy creation in 10/15 (67%). Given the known incidence of clinical complications due to ostomy creation and ostomy reversal, avoidance of ostomy could potentially reduce morbidity in these patients. Typically, ostomy patients are exposed to a 43% postoperative complication rate (including risk of readmission, dehydration, and acute renal failure). [8] Most patients with a temporary ileostomy will keep their ostomy at least 3 months, and it is not unusual that the ostomy is left in place much longer, and for 20% of patients it becomes permanent. [8] Closure of the temporary ileostomy is associated with a low mortality, but the morbidity may be more than 20%. [8]

Of the 15 Colovac devices placed, 3 migrated before the end of the implantation period (2 device malfunctions related to a vacuum defect, 1 device misplacement related to the placement of the stent component of the device in the immediate proximity of the distal end of the J-pouch). For those 3 cases, initial device placement and introducer removal were uneventful.

The endoscopic use of stents in the gastrointestinal tract has been instrumental in the treatment of unresectable esophageal cancer, esophageal leak, and as a bridge to surgery in case of colonic obstruction. The historical use of colorectal stents for the protection of anastomotic leak has been limited due to technical issues, leading to migration of the stent in up to 58% of patients. [18-20]

Regarding the Colovac migration whose associated conversion to ostomy caused a peritonitis: this case has been considered as probably related to a misplacement of the device and the lavage during the first re-operation. It was the first case of Colovac placement above a colic J-pouch.

1 The device was placed at 13 cm above the anastomosis (3-4cm above the distal part of the J-
2 pouch, in front of the sacral promontory). So the distal part of the Colovac was too close to the
3 proximal dilated part of the pouch leading maybe to an ease and early migration of the device.

4 Instructions for use have been revised to recommend device anchoring above the promontory,
5 at 20 cm above the anastomosis in order to avoid further similar complications. In recent
6 studies, the rate of post-operative peritonitis requiring reintervention ranges between

7 The Colovac-related migration rate (13%) - related to vacuum defect - reported in the current
8 study is much lower than the migration rate for standard colonic stents reported in the literature
9 and confirms the efficacy of the vacuum system for anchoring the device. Additional
10 surveillance measures have been implemented in order to identify early signs of migration
11 (daily control of the external sheath length) and/or vacuum malfunction, enabling swift action
12 if required (conversion to ostomy for example) and thus reducing the potential complications
13 associated with this migration.

14 Regardless of the migrations, the incidence of anastomotic leakages in the SAFE-1 study
15 population, during the Colovac implantation period (0-14 days), was 13%. This rate was within
16 the same range as AL rate reported for similar patient populations receiving a diverting ostomy
17 (12% to 17%). [2, 3, 21]

18 It is widely accepted that following rectal surgery, some patients will experience anastomotic
19 complications such as anastomotic leakage. The process of anastomotic healing will therefore
20 be longer for these patients.

21 Regardless of the efficacy of the Colovac at protecting the anastomosis during the first 14
22 postoperative days, it is anticipated that a proportion of patients will still demonstrate
23 incomplete anastomotic healing as it is the case with systematic stoma diversion. [2, 3] In such
24 cases, the Colovac should be removed and a fecal diversion required to provide long-term
25 anastomotic protection. Results obtained in this first 15-patient cohort are aligned with these
26 observations. It is likely that the rate of conversion to diverting ostomy is inherent to the
27 anastomotic healing problem.

28 Additionally, a trend toward delayed anastomotic healing and/or fistulisation was observed for
29 patients with evidence of extensive local disease and/or patients for whom colorectal resection
30 was combined with additional surgical procedures such as hepatectomy. The two patients from
31 this cohort who underwent a hepatectomy required stoma conversion. This suggests that a 14

1 day protection period is likely to be insufficient for this subset of population. Mitigation
2 measures, consisting of improved patient selection criteria have been implemented to reduce
3 the occurrence in the future. The improved patient selection criteria exclude patients for whom
4 rectal surgery is associated with a secondary procedure such as liver resection, due to a higher
5 risk of anastomotic complications requiring prolonged protection and will make the population
6 more homogenous.

7 In addition to this, we would like to highlight that patients converted to ostomy to ensure a
8 longer protection of their anastomosis have not experienced any major complication related to
9 this conversion surgery except for the peritonitis following the per-operative lavage that
10 required a new intervention. All stoma creations were planned, and not performed in an
11 emergent situation due to the clinical symptoms of the patients.

12 Clinical complications during the follow-up period were dominated by late pelvic collections
13 (20%). The occurrence of a collection more than 8 days after the Colovac retrieval is advocating
14 for a late fistulation, as reported in the literature. The nature of the collected liquid converges
15 along those lines. The study from Alves and al. [22] reports a leakage rate between 1 and 4 %
16 after early ostomy closure (between 7 and 14 days), and the study by Yin and al. supports the
17 same rate. [23] Nelson and al. reported intra-abdominal collection rate at 14% after early
18 ostomy closure (between 14 and 28 days). [24] These late pelvic complications were managed
19 conservatively, by antibiotic treatments.

20 Regarding procedural feasibility, this study showed that delivery of the Colovac during
21 colorectal surgery and endoscopic device retrieval are feasible and safe. Indeed, no anastomotic
22 trauma was reported by the investigators.

23 In addition, delivery of the Colovac is likely to require less time than ostomy creation with no
24 major differences in terms of hospital stay. The consistent delivery time signifies the simplicity
25 of the procedure, especially when considering that three different physicians placed the devices
26 at differing times.

27 Device retrievals were performed endoscopically or manually. The mean retrieval duration was
28 10 min, except for one case, which took longer due to the learning experience. The longer time
29 (15 min) associated with the first case is attributed to the learning curve effect, since colonic
30 stent retrieval is not routinely performed in the standard GI practice. As for the device

1 placement, the consistent retrieval time after the first cases signifies the simplicity of the
2 procedure.

3 This initial study also provided the first evidence that this novel concept was well-tolerated by
4 patients. Limited discomfort related to the presence of a drain and a sheath through the anus
5 was reported during the 14 day period, which can be counterbalanced by the discomfort
6 associated with the ostomy for a much longer period of time. For the purpose of the study,
7 patients were not discharged before the end of the implantation period (ie. 14 days) but earlier
8 patient discharge could be envisioned in the future.

9 There are some limitations to this study. The number of included patients is low and the study
10 population is a convenience cohort of rectal cancer patients treated at expert centers. Results
11 may not be generalizable to all rectal cancer patients and other centers. Second, the use of
12 Colovac should be limited to patients undergoing rectal resections without concomitant surgery
13 given the associated increased risk of complications.

14 Other attempts to replace ileostomy by intraluminal approaches confirm the clinical need for
15 minimally invasive protection of colorectal anastomosis. Recently, Reshef, et al reported the
16 use of an intraluminal device (CG-100), confirming the beneficial impact of this approach. [25]
17 However, the patient population addressed in this study was different from our cohort. The
18 mean anastomosis height was 10 cm, demonstrated to be less prone to anastomotic
19 complications than low to very low colorectal anastomosis, as included in our study. [26]

20 Colovac provides a local, temporary, minimally invasive protection of the anastomosis during
21 the healing process, avoiding the need for a diverting ostomy for patients who will not
22 experience anastomotic complications and allowing safe conversion to standard of care
23 diverting ostomy for patients requiring prolonged anastomotic protection. By optimizing
24 conditions of use and patient selection, Colovac could become an effective patient management
25 alternative for patients undergoing low anterior resection. This should be confirmed in a larger
26 and randomized study.

27 28 **REFERENCES**

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A (2018) Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 68:394-424
2. Denost Q, Rouanet P, Faucheron JL, Panis Y, Meunier B, Cotte E, Meurette G, Kirzin S, Sabbagh C, Loriau J, Benoist S, Mariette C, Sielezneff I, Lelong B, Mauvais F, Romain B, Barussaud ML, Germain C, Picat MQ, Rullier E, Laurent C, French Research Group of Rectal Cancer S (2017) To Drain or Not to Drain Infraperitoneal Anastomosis After Rectal Excision for Cancer: The GRECCAR 5 Randomized Trial. *Ann Surg* 265:474-480
3. Lefevre JH, Mineur L, Kotti S, Rullier E, Rouanet P, de Chaisemartin C, Meunier B, Mehrdad J, Cotte E, Desrame J, Karoui M, Benoist S, Kirzin S, Berger A, Panis Y, Piessen G, Saudemont A, Prudhomme M, Peschaud F, Dubois A, Loriau J, Tuech JJ, Meurette G, Lupinacci R, Goasgen N, Parc Y, Simon T, Tiret E (2016) Effect of Interval (7 or 11 weeks) Between Neoadjuvant Radiochemotherapy and Surgery on Complete Pathologic Response in Rectal Cancer: A Multicenter, Randomized, Controlled Trial (GRECCAR-6). *J Clin Oncol* 34:3773-3780
4. Celerier B, Denost Q, Van Geluwe B, Pontallier A, Rullier E (2015) The risk of definitive stoma formation at ten years after low and ultra-low anterior resection for rectal cancer. *Colorectal Dis*
5. Maggiori L, Bretagnol F, Lefevre JH, Ferron M, Vicaut E, Panis Y (2011) Conservative management is associated with a decreased risk of definitive stoma after anastomotic leakage complicating sphincter-saving resection for rectal cancer. *Colorectal Dis* 13:632-637
6. Mirnezami A, Mirnezami R, Chandrakumaran K, Sasapu K, Sagar P, Finan P (2011) Increased local recurrence and reduced survival from colorectal cancer following anastomotic leak: systematic review and meta-analysis. *Ann Surg* 253:890-899
7. Matthiessen P, Hallbook O, Rutegard J, Simert G, Sjodahl R (2007) Defunctioning stoma reduces symptomatic anastomotic leakage after low anterior resection of the rectum for cancer: a randomized multicenter trial. *Ann Surg* 246:207-214
8. Danielsen AK, Park J, Jansen JE, Bock D, Skullman S, Wedin A, Marinez AC, Haglind E, Angenete E, Rosenberg J (2017) Early Closure of a Temporary Ileostomy in Patients With Rectal Cancer: A Multicenter Randomized Controlled Trial. *Ann Surg* 265:284-290

- 1 9. Maggiori L, Moszkowicz D, Zappa M, Mongin C, Panis Y (2015) Bioprosthetic mesh
2 reinforcement during temporary stoma closure decreases the rate of incisional
3 hernia: A blinded, case-matched study in 94 patients with rectal cancer. *Surgery*
4
5 4
6 5 10. den Dulk M, Smit M, Peeters KC, Kranenbarg EM, Rutten HJ, Wiggers T, Putter H, van
7 6 de Velde CJ, Dutch Colorectal Cancer G (2007) A multivariate analysis of limiting
8 7 factors for stoma reversal in patients with rectal cancer entered into the total
9 8 mesorectal excision (TME) trial: a retrospective study. *Lancet Oncol* 8:297-303
10
11 9
12 10 11. Morks AN, Havenga K, Ploeg RJ (2011) Can intraluminal devices prevent or reduce
13 11 colorectal anastomotic leakage: a review. *World J Gastroenterol* 17:4461-4469
14
15 12
16 13 12. Egozi L, Sorrento JJ, Golub R, Schultz EH (1993) Complication of the intracolonic
17 14 bypass. Report of a case. *Dis Colon Rectum* 36:191-193
18
19 15
20 16 13. Bakker IS, Morks AN, Hoedemaker HO, Burgerhof JG, Leuvenink HG, Ploeg RJ,
21 17 Havenga K (2012) The C-seal trial: colorectal anastomosis protected by a
22 18 biodegradable drain fixed to the anastomosis by a circular stapler, a multi-center
23 19 randomized controlled trial. *BMC Surg* 12:23
24
25 20
26 21 14. Hays RD, Bjorner JB, Revicki DA, Spritzer KL, Cella D (2009) Development of physical
27 22 and mental health summary scores from the patient-reported outcomes
28 23 measurement information system (PROMIS) global items. *Qual Life Res* 18:873-880
29
30 24
31 25 15. Benoit O, Faron M, Margot N, Creavin B, Debove C, Tired E, Parc Y, Lefevre JH (2019)
32 26 C-Reactive Protein Values After Colorectal Resection: Can We Discharge a Patient
33 27 With a C-Reactive Protein Value >100? A Retrospective Cohort Study. *Dis Colon*
34 28 *Rectum* 62:88-96
35
36 29
37 30 16. Waterland P, Ng J, Jones A, Broadley G, Nicol D, Patel H, Pandey S (2016) Using CRP
38 31 to predict anastomotic leakage after open and laparoscopic colorectal surgery: is
39 32 there a difference? *Int J Colorectal Dis* 31:861-868
40
41 33
42 34 17. Phan K, Oh L, Ctercteko G, Pathma-Nathan N, El Khoury T, Azam H, Wright D, Toh
43 35 JWT (2019) Does a stoma reduce the risk of anastomotic leak and need for re-
44 36 operation following low anterior resection for rectal cancer: systematic review and
45 37 meta-analysis of randomized controlled trials. *J Gastrointest Oncol* 10:179-187
46
47 38
48 39 18. Fernandez Lobato R, Pinto I, Maillo C, Paul L, Fradejas JM, Moreno Azcoita M (1999)
49 40 Rectovesical fistula treated by covered self-expanding prosthesis: report of a case.
50 41 *Dis Colon Rectum* 42:812-815
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65

19. Jeyarajah AR, Shepherd JH, Fairclough PD, Patchett SE (1997) Effective palliation of a colovaginal fistula using a self-expanding metal stent. *Gastrointest Endosc* 46:367-369
20. Paul L, Pinto I, Gomez H, Fernandez-Lobato R, Moyano E (2002) Metallic stents in the treatment of benign diseases of the colon: preliminary experience in 10 cases. *Radiology* 223:715-722
21. Matthiessen P, Hallbook O, Andersson M, Rutegard J, Sjodahl R (2004) Risk factors for anastomotic leakage after anterior resection of the rectum. *Colorectal Dis* 6:462-469
22. Alves A, Panis Y, Lelong B, Dousset B, Benoist S, Vicaut E (2008) Randomized clinical trial of early versus delayed temporary stoma closure after proctectomy. *Br J Surg* 95:693-698
23. Yin TC, Tsai HL, Yang PF, Su WC, Ma CJ, Huang CW, Huang MY, Huang CM, Wang JY (2017) Early closure of defunctioning stoma increases complications related to stoma closure after concurrent chemoradiotherapy and low anterior resection in patients with rectal cancer. *World J Surg Oncol* 15:80
24. Nelson T, Pranavi AR, Sureshkumar S, Sreenath GS, Kate V (2018) Early versus conventional stoma closure following bowel surgery: A randomized controlled trial. *Saudi J Gastroenterol* 24:52-58
25. Reshef A, Ben-Arie G, Pinski I (2019) Protection of colorectal anastomosis with an intraluminal bypass device for patients undergoing an elective anterior resection: a pilot study. *Tech Coloproctol*
26. Law WL, Choi HK, Lee YM, Ho JW, Seto CL (2007) Anastomotic leakage is associated with poor long-term outcome in patients after curative colorectal resection for malignancy. *J Gastrointest Surg* 11:8-15

DISCLOSURES

Prof. J.H. Lefevre is a consultant for SafeHeal.

Prof. J.H. Lefevre has received funding from SafeHeal to support congress registration and travel fees.

Dr. A. D’Urso and Dr. N. Komen have no conflicts of interest to disclose.

FIGURES LEGENDS

Figure 1a. Colovac Device

Figure 1b. Colovac Device anchored in the colon with the high vacuum drainage system

Figure 2. Patients Overview

Table 1. Patients' characteristics and surgical procedures

	n (%)
Number of patients	15 (100)
Male Gender	10 (67)
Median Age (years (IQR))	60 (46-70)
Median BMI (kg/m² (IQR))	24 (22-28)
Active smoking	0 (0)
Diabetes	3 (20)
Arterial Hypertension	3 (20)
Clinical cancer staging	
T1	4 (27)
T2	2 (13)
T3	8 (53)
T4	1 (7)
Tumor Size	
<2.5 cm	6 (40)
>2.5 cm	9 (60)
Median Tumor height (distance from anal verge, cm (IQR))	5.14 (0-6)
Median time from diagnosis to surgery (months (IQR))	3.7 (1.5-4.6)
Neoadjuvant treatment	
Chemotherapy only	1 (7)
Radiotherapy only	1 (7)
Radio chemotherapy	8 (53)
No neoadjuvant treatment	5 (33)
Surgical approach	
Laparoscopy	15 (100)
Median duration of surgery (min (IQR))	260 (218 - 360)
Type of anastomosis	
Coloanal Handsewn	4 (26.7)
Colorectal Stapled	11 (73.3)
End to end	5 (33.3)
Side to end	9 (60)
J pouch	1 (6.7)
Median anastomosis height from anal margin (cm (IQR))	2 (1-4)
Use of pelvic drain	13 (87)
Concomitant surgery	
Right Hepatectomy	1 (7)
Hepatic wedge resection	1 (7)

Table 2. Colovac placement and removal.

Items	N (%)
Colovac placement	
Median duration	7 (3-10)
Technical ease of introducer introduction*	
Very easy	5 (33)
Easy	9 (60)
Moderate	1 (7)
Difficult	0 (0)
Impossible	0 (0)
Technical ease of introducer removal*	
Very easy	6 (40)
Easy	6 (40)
Moderate	3 (20)
Difficult	0 (0)
Impossible	0 (0)
Implantation site reached	
Yes	14 (93)
No	0 (0)
Accidental Colovac pullout during introducer removal – Replaced by another device	1 (7)
Colovac anchoring	
14 days of implantation	12 (80)
Device migration	3 (20)
Colovac retrieval	
Median duration	10 (5-20)
Technical ease of Colovac retrieval	
Very easy	6 (33)
Easy	7 (54)
Moderate	0 (0)
Difficult	2 (13)
Impossible	0 (0)
Absence of feces below the anchoring site	15 (100)
Mucosal appearance**	
At the anchoring site	
Normal	2 (13)
Inflammatory	6 (40)
Bleeding	4 (27)
Ulcer	2 (13)
Perforation	0 (0)
Above the anchoring site	
Normal	11 (73)
Inflammatory	1 (7)
Bleeding	2 (13)
Ulcer	0 (0)
Perforation	0 (0)
At the anastomotic level	
Normal	12 (80)
Inflammatory	0 (0)
Bleeding	2 (13)
Ulcer	0 (0)
Perforation	0 (0)

Times are given in min (IQR)

*Technical ease of introducer introduction and removal have been evaluated by investigators using a Lickert scale ranked from 1 (very easy) to 5 (impossible) depending on the deployment force.

**Missing data for one patient as Colovac was removed manually in the OR without access to endoscopic evaluation

Item	1 week N (%)	2 weeks N (%)	3 months N (%)
Overall morbidity	3 (20)	2 (13.3)	5 (33.3)
Medical complication			
Ascites		1 (7)	
Seizure			1 (7)
Surgical complication			
Incomplete anastomotic healing		2 (13.3)	
Device migration with leakage	3 (20)		
Pelvic collection			3 (20)
Bowel obstruction			1 (7)
Peritonitis	1(7)		
Patient tolerance to the presence of vacuum system			
1 (Full acceptance)	10 (66.7)	8 (53.3)	
2	5 (33.3)	4 (26.7)	
3	0 (0)	1 (7)	
4	0 (0)	0 (0)	
5 (No acceptance)	0 (0)	0 (0)	
Missing data*	0 (0)	2 (13.3)	
Patients tolerance to the presence of sheath protruding out of the anus			
1 (Full acceptance)	9 (60)	6 (40)	
2	5 (33.3)	4 (26.7)	
3	1 (6.7)	2 (13.3)	
4	0 (0)	1 (6.7)	
5 (No acceptance)	0 (0)	0 (0)	
Missing data*	0 (0)	1 (13.3)	
NIH's PROMIS health score (median IQR)	44 (38-51)	36 (15-46)	15 (8-20)
Stoma reversal			1 (20)

Some patients experienced more than one complication. *Questionnaires have not been fully filled by all patients.

Table 3. Patient acceptance and post operative morbidity