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Prospective Cohort Study

Assessment of a circular powered stapler for creation of anastomosis in left-sided colorectal surgery: A prospective cohort study

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ABSTRACT

Background: Circular staplers perform a critical function for creation of anastomoses in colorectal surgeries. Powered stapling systems allow for reduced force required by surgeons to fire the device and may provide advantages for creating a secure anastomosis. The objective of this study was to evaluate the clinical performance of a novel circular powered stapler in a post-market setting, during left-sided colectomy procedures.

Materials and methods: Consecutive subjects underwent left-sided colorectal resections that included anastomosis performed with the ECHELON CIRCULAR™ Powered Stapler (ECP). The primary endpoint was the frequency in which a stapler performance issue was observed. Secondary endpoints included evaluation of ease of use of the device via a surgeon satisfaction questionnaire, and monitoring/recording of procedure-related adverse events (AEs).

Results: A total of 168 anastomoses were performed with the ECP. Surgical approaches included robotic-assisted (n = 74, 44.0%), laparoscopic (n = 71, 42.3%), open (n = 20, 11.9%), and hand-assisted minimally invasive (n = 3, 1.8%) procedures. There were 22 occurrences of device performance issues in 20 (11.9%) subjects during surgery. No positive intraoperative leak tests were observed, and only 1 issue was related to a procedure-related AE or surgical complication, which was an instance of incomplete surgical donut necessitating re-anastomosis. Postoperative anastomotic leaks were experienced in 4 (2.4%) subjects. Clavien-Dindo classification of all AEs indicated that 92.0% were Grades I or II. Participating surgeons rated the ECP as easier to use compared to previously used manual circular staplers in 85.7% of procedures.

Conclusion: The circular powered stapler exhibited few clinically relevant performance issues, an overall favorable safety profile, and ease of use for creation of left-sided colon anastomoses.

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Abbreviations

AE(s)	Adverse event(s)
AL(s)	Anastomotic leak(s)
ASA	American Society of Anesthesiologists
BMI	Body Mass Index
CD	Clavien-Dindo
ECP	ECHELON CIRCULAR™ Powered Stapler
Max	Maximum
Min	Minimum
MIS	Minimally invasive surgery
SAE(s)	Serious adverse effect(s)
SD	Standard deviation

1. Introduction

The integrity of the anastomosis in colorectal resections is dependent on many factors including intra-operative considerations such as preservation of adequate blood supply, minimal tension at the anastomotic line, healthy tissue, and surgical technique [1–3]. Among the most serious complications following colorectal procedures are anastomotic leaks (AL), which are associated with increased rates of reoperation, higher 30-day mortality, higher local disease recurrence in cancer patients, and reduced overall patient survival [4–9]. Postoperative leaks have been reported in 1–19% of colorectal anastomoses [10,11], with an overall AL rate of 5.6% observed for stapled anastomosis in a large systematic review [11]. In a meta-analysis that included only laparoscopic anterior resection, the AL rate was 6.3% [12]. Higher rates of AL may occur in low anterior resections, in part due to the narrow pelvic compartment resulting in difficulty with positioning the linear stapler and potential need for multiple stapler firings for transection of the bowel [12–15]. Though many factors related to anastomotic complications are non-modifiable, there is still a need for innovative surgical strategies and technologies that may help to standardize the anastomotic step of an operation and lower the risk of AL.

Circular staplers and the double stapling technique were first introduced into clinical practice more than 30 years ago to facilitate creation of left-sided low anastomoses in colorectal resection [6,16,17]. With this approach, bowel transections are carried out using a linear stapler, followed by circular stapling to create the anastomosis. Although this technique has been widely adopted, difficulties with firing and technical errors have remained issues with manually fired mechanical circular staplers [18,19]. The use of powered stapling systems provides firing of the stapler with the push of a button, which minimizes the physical force required by the surgeon to fire the device. This potentially reduces unwanted movement at the distal tip and allows for better control of stapler placement and formation of the staple line. The circular powered stapler tested in this study was developed for easier, more stable firing, and provides a 3D staple design, to help create a more secure anastomosis. Preclinical analysis of this device demonstrated reduced force to fire, less movement during device application, and less leaking at the staple line compared to manual circular stapling [20]. An initial clinical review of 17 left-sided anastomoses performed with the circular powered stapler noted favorable safety results and anastomotic integrity in all cases immediately following surgery [21]. The primary objective of the current study was to assess intraoperative performance of the circular powered stapler during left-sided colectomy procedures performed in the setting of a post-market multicenter trial. Secondary objectives included evaluating surgeon ease of use and safety surveillance of the study device.

2. Methods

2.1. Study design

A prospective, open label, multicenter, single-arm clinical study of left-sided colon anastomoses was completed at 12 sites (6 in the USA and 6 in Europe) with the first subject consenting on November 28, 2017 and the last subject's final follow-up visit on January 15, 2020. The initial design of the study was to include a comparative cohort of manual circular staplers, which was then removed for increased time-efficiency of data collection. All procedures included in the analysis utilized the ECHELON CIRCULAR™ Powered Stapler (ECP, Ethicon Endo-Surgery, Inc., Cincinnati, OH, USA) for creation of stapled anastomoses. For operation of the ECP stapler, the user presses a firing trigger which executes the powered firing sequence. A green light is illuminated to signal that firing is complete and the stapler can be removed. Evaluated ECP models were the 29 mm (CDH29P) and 31 mm (CDH31P) versions. Procedures were carried out with a minimally invasive approach or via open surgery, based on the surgeons' preference. Robotic assistance, use of a hand port, conversion from laparoscopic to open, and proximal fecal diversion (loop ileostomy) were all permissible for inclusion in the study. Each site used consecutive screening and enrollment in order to minimize selection bias and to generate a representative patient sample. Visits consisted of screening for subject eligibility, performance of the operation and postoperative recovery through discharge, and follow-up at 28 $\pm$ 14 days after the surgery. The protocol and consent form were approved by each investigator's Institutional Review Board or Independent Ethics Committee, and informed consent was obtained for all subjects. The study was conducted in accordance with Good Clinical Practice and the Declaration of Helsinki, as well as any other applicable local, state, and federal requirements, and is registered with ClinicalTrials.gov (registry number NCT03326895). This work has been reported in line with the STROCSS criteria [22].

2.2. Selection of subjects

Consecutive patients who were scheduled to undergo elective colectomy procedures that involved a left-sided anastomosis performed with a circular stapler were considered for inclusion. Additional inclusion criteria were a willingness to give consent and comply with all study-related evaluations, and a minimum age of 18 years. Subjects were considered enrolled once an anastomosis had been attempted with the ECP study device. Criteria for exclusion were concurrent enrollment in a different clinical study, any condition (physical or psychological) that would impair study participation or impact endpoints, emergency surgery, American Society of Anesthesiologists (ASA) status $\geq$ 4, unwillingness to provide follow-up information post-procedure, multiple synchronous colon resections, colon anastomosis creation that was not distal to the splenic flexure, or no anastomosis attempted with the ECP, or any intraoperative finding that would preclude anastomosis performed with a circular stapler.

2.3. Surgical procedures

Procedures with left-sided circular stapled anastomosis were performed via robotic-assisted, laparotomy, laparoscopic, or hand-assisted minimally invasive approaches as determined by the surgeon's preference. In all operations, the ECP was utilized to create the anastomosis according to the device's instructions for use. Intra-operative details of anastomotic reconstruction were recorded including configuration, distance from anal verge, results of leak testing, endoscopic assessment of the staple-line, and any technical issues or complications related to the device or procedure. Leak tests with air insufflation into the rectum were completed to evaluate anastomotic integrity in every procedure. The decision to perform a diverting ileostomy was left to the discretion of the surgeon. Subjects were followed for signs of AL or other

complications according to the institution's usual care. Surgeon characteristics including age, height, weight, gender, hand length and grip strength (using dynamometry) were recorded.

2.4. Device performance and safety endpoints

The primary performance endpoint was the number of subjects in whom a stapler performance issue was noted. A stapler issue was defined as a failure of the ECP to perform per its instructions for use. This included: difficulty placing or removing the stapler, misfire/failure of the device to fully fire, staple line defects, incomplete or thin anastomotic donuts (as determined by the surgeon based on overall morphology/size and completeness of the donut), tissue damage, positive intraoperative leak testing, detached components, unformed staples, or any other device failure. Any actions necessary to resolve an issue were recorded as well as the result of the action. Secondary endpoints included completion of a surgeon satisfaction questionnaire after each procedure to evaluate subjective ease of use of the ECP device and recording of all intraoperative or postoperative adverse events (AEs). For this study, an AE was defined as any undesirable clinical event, such as anastomotic leak, that may be attributable to the procedure or specifically to the ECP device. The investigator and clinical staff followed all subjects for signs of anastomotic leak. Clinical suspicion of AL was confirmed visually (intra-operative) or by diagnostic imaging according to the clinician's standard of care (postoperative). The severity of ALs was classified by the International Study Group of Rectal Cancer grading scale (Grade A managed with no intervention, Grade B requiring therapeutic intervention but manageable without re-laparotomy, and Grade C requiring surgical intervention/re-laparotomy) [23]. The ALs were followed to resolution, stable state, or end of study (whichever occurred first).

2.5. Statistical methods

Analysis of performance and safety endpoints was completed with the Full Analysis Set, consisting of all subjects who were enrolled in the study who had an anastomosis attempted with the ECP. Categorical variables were summarized descriptively by frequencies and associated percentages. Continuous variables were summarized by number of subjects, mean, standard deviation, median, minimum, and maximum. Confidence intervals were also estimated for procedure-related variables. All analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC). For comparisons of questionnaire and grip strength data, p-values were determined based on Fisher's exact test. P values ≤ 0.05 were considered significant.

One hundred sixty-five (165) subjects were planned to be enrolled in the study. This sample size was sufficient for a descriptive summary of circular stapler performance issues though confidence interval estimation and evaluation of safety. Available literature suggested that stapler performance issues were observed in 15%–20% of subjects in whom a circular stapler was used, and 165 subjects would provide a margin of error for a one-sided confidence interval that does not exceed 5.1% for estimation of the true rate of stapler performance issues.

3. Results

3.1. Subject selection and demographic data

Signed informed consent was obtained and screening was completed for 232 total subjects (Fig. 1). Sixty-four were excluded from the study, including 42 screen failures and 22 cases in which a manual circular stapler had been used. The Full Analysis Set included 168 subjects, who underwent a left-sided colectomy procedure using the ECP device for creation of an anastomosis. All 168 subjects completed the study through the final postoperative follow-up visit. Demographic data and preoperative characteristics for the Full Analysis Set are shown in Table 1. The majority of subjects were White (88.7%) with a median age of 61.5 years (range 22.0–89.0). Similar percentages of male and female subjects participated in the study. A relatively high proportion (97.1%)

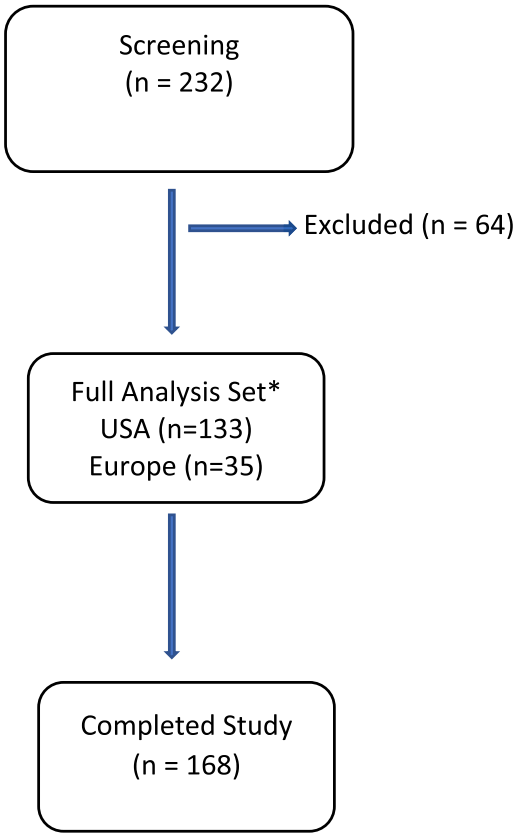

Fig. 1. Subject Flow Diagram. *All subjects who underwent surgery and had an anastomosis attempted with the ECP stapler were included in performance and safety analyses.

Table 1
Subject Demographics and Preoperative characteristics.

Characteristic	Full Analysis Set N = 168
Gender	
Male	89 (53.0%)
Female	79 (47.0%)
Age at Consent (yrs)	
Mean (SD)	59.9 (13.0)
Median (Min, Max)	61.5 (22.0, 89.0)
Race	
White	149 (88.7%)
Black or African American	5 (3.0%)
Asian	3 (1.8%)
Not reported or Unknown	11 (6.5%)
Body mass index (kg/m^2)	
Mean (SD)	28.5 (5.9)
Median (Min, Max)	28.4 (6.0, 50.9)
Body mass index $\geq$ 30	59 (35.1%)
Hypertension	70 (41.7%)
Diabetes mellitus	15 (8.9%)
Smoking*	93 (55.4%j)
Neoadjuvant Chemo and/or GI radiation	19 (11.3%)
ASA Scores	
I	5 (2.9%)
II	90 (53.6%)
III	73 (43.5%)

(SD) standard deviation; (Min, Max) range minimum and maximum; (ASA) American Society of Anesthesiologists physical status: I = healthy patient, II = presence of mild systemic disease, III = presence of severe systemic disease.
* Current or former smoker.

had ASA physical status scores of II or III, indicating the presence of mild or severe systemic disease in most subjects. Obesity (BMI ≥ 30) and diabetes were present in 35.1% and 8.9% of subjects, respectively. Neoadjuvant chemotherapy and/or radiotherapy had been performed in 11.3% of subjects.

3.2. Surgical indications and procedural information

Operations were performed by a total of 38 surgeons/investigators across the 12 sites. Operative data are summarized in Table 2. The most common indications for surgery were colorectal cancer or diverticulitis in 75 (44.6%) and 53 (31.5%) subjects, respectively. The predominant surgical approaches were robotic-assisted in 74 (44.0%) and laparoscopic in 71 (42.3%) subjects. An open approach was used in 20 (11.9%) procedures. Among the total 148 minimally invasive operations, 8 cases were converted to open surgery. None of the conversions were related to use of the ECP device. Anastomoses with the ECP were completed in all 168 procedures. Thirty-five (20.8%) subjects underwent creation of proximal diverting ostomies at the time of surgery, for which the primary listed reasons were low pelvic anastomoses and/or neoadjuvant chemoradiotherapy in 32 cases, and malnutrition, chronic inflammation, or surgeon preference in 3 other patients.

3.3. Device performance and safety results

Summarization of the primary endpoint for this study (frequency of ECP device performance issues) is shown in Table 3. A total of 22 stapler performance issues were recorded in 20 (11.9%) subjects. Sixteen of the issues occurred in 15 robotic-assisted procedures, with the remaining 6 occurring in 5 laparoscopic subjects. The majority of issues (14 of 22) consisted of incomplete or thin anastomotic donuts. Intraoperative anastomotic air-leak tests performed for all 168 procedures were negative. Importantly, only 1 of the 22 total issues was related to an AE. This was recorded as an instance of incomplete/thin donut that necessitated creation of a new anastomosis, and an unplanned diverting ileostomy. In this case, only the proximal donut was actually retrieved when the initial anastomosis was created, (i.e. the distal donut was missing). The remaining device issue types consisted mainly of difficulties with operating or removing the stapler (Table 3), with no relationship to an AE, or surgical complication.

There were 37 (22.0%) subjects who experienced one or more procedure-related postoperative AEs during the study (Table 4). Many of the observed events were consistent with those expected in colon resection procedures such as postoperative ileus in 3 (1.8%) subjects, colonic obstruction, rectal obstruction, small bowel obstruction, anastomotic stenosis, and rectal hemorrhage occurring in 1 (0.6%) subject each. In addition, the most commonly occurring AEs were abdominal pain in 12 (7.1%) subjects, nausea/vomiting in 8 (4.8%), and procedural pain in 5 (3.0%) subjects. All of the AEs were scored according to the Clavien-Dindo (CD) classification of surgical complications (Table 4) [24]. Of the 137 total recorded AEs, 126 (92.0%) were CD Grades I or II, and the remaining 11 (8.0%) were Grade IIIa or IIIb. Nine AEs (6.6%) were classified as related to use of the ECP device and occurred in 6 subjects. The 9 device-related events included 4 Grade I, 3 Grade IIIa, and 2 Grade IIIb complications. Among the device-related AEs there

Table 2
Operative data.

Variable	Full Analysis Set N = 168
Surgery Indications	
Colorectal carcinoma	75 (44.6%)
Diverticulitis	53 (31.5%)
Other[1]	15 (8.9%)
Rectal prolapse	6 (3.6%)
Ulcerative colitis	6 (3.6%)
Colostomy takedown/reversal	5 (3.0%)
Colorectal polyps or polyp syndrome	3 (1.8%)
Colovesical fistula	3 (1.8%)
Crohn's disease	2 (1.2%)
Estimated Anastomosis Level	
Sigmoid colon	64 (38.1%)
Upper rectum	55 (32.7%)
Mid rectum	27 (16.1%)
Lower rectum	22 (13.1%)
ECP Stapler Used	
CDH29P (diameter 29 mm)	126 (75.0%)
CDH31P (diameter 31 mm)	42 (25.0%)
Surgical Approach	
Robotic-Assistance	74 (44.0%)
Laparoscopic	71 (42.3%)
Open Laparotomy	20 (11.9%)
Hand-assisted MIS	3 (1.8%)
Procedure Duration (hrs)	
Mean (SD)	4.1 (1.6)
Median (Min, Max)	4.0 (1.25, 10.43)
Length of Hospital Stay (days)	
Mean (SD)	6.0 (7.36)
Median (Min, Max)	4.0 (2.0, 82.0)
Type of Anastomosis	
End to End	135 (80.4%)
Side to End	33 (19.6%)
Distance from Anal Verge[2] (cm)	
Mean (SD)	11.5 (5.51)
Median (Min, Max)	12.0 (0, 45)
Diverting Ostomy Created	35 (20.8%)

(MIS) minimally invasive surgery; (SD) standard deviation; (Min, Max) range minimum and maximum.

[1] Other various indications with n = 1 for each indication.

[2] Estimated distance of anastomoses from the anal verge.

Table 3
Summary of technical/performance issues related to ECP stapler use.

Variable	Full Analysis Set N = 168
Subjects With At Least One Issue n (%)[1]	20 (11.9%)
95% Exact Confidence Interval	(7.4%, 17.8%)
Number of Issues Observed	22
Issue Types n (%)[1]	
Incomplete or thin donuts	14 (8.3%)
Difficulty removing the stapler	2 (1.2%)
Difficulty coupling anvil to stapler	1 (0.6%)
Tissue damage	1 (0.6%)
Green light appears yellow in cycle	1 (0.6%)
Loose spike/knob during coupling	1 (0.6%)
Problem advancing spike	1 (0.6%)
Rotation knob not tightening properly	1 (0.6%)

[1] Percentage of Full Analysis Set.

Table 4
Clavien-Dindo (CD) Classification of adverse events (AEs).

Category	# of AEs n (%)[1]	# of Subjects n (%)[2]
Procedure-Related		
AEs (total)	137 (100.0%)	37 (22.0%)
SAEs	19 (13.9%)	13 (7.7%)
CD Scoring[3]		
Grade I	98 (71.5%)	29 (17.3%)
Grade II	28 (20.4%)	15 (8.9%)
Grade IIIa	4 (2.9%)	3 (1.8%)
Grade IIIb	7 (5.1%)	6 (3.6%)
Device-Related		
AEs	9 (6.6%)	6 (3.6%)
SAEs	6 (4.4%)	3 (1.8%)
CD Scoring		
Grade I	4 (2.9%)	3 (1.8%)
Grade II	0 (0.0%)	0 (0.0%)
Grade IIIa	3 (2.2%)	2 (1.2%)
Grade IIIb	2 (1.5%)	2 (1.2%)

[1] Percentage of total number of AEs.

[2] Percentage of Full Analysis Set (N = 168).

[3] Some subjects had 2 or more AEs with different CD scores therefore the total of subjects in CD scoring is greater than 37; (SAEs) serious adverse effects.

were 6 serious adverse effects (SAEs) that occurred in 3 subjects. These consisted of: 1 subject who had post-procedure hemorrhage, incision site pain, anastomotic stenosis and bowel obstruction; 1 subject with post-operative AL; and 1 who experienced a pelvic abscess. The device-related SAEs were resolved with surgical intervention (n = 4), or observation (n = 2). Among all 168 subjects, no blood transfusions were required.

Postoperative AL at the colorectal anastomosis staple line of low anterior colon resection was identified in 3 (1.8%) patients and these were considered potentially device related. A fourth patient who underwent surgery for colostomy closure, experienced an anastomotic leak at an unrelated small bowel staple line not associated with the colorectal anastomosis or ECP device. Of the 3 potentially device-related leaks, one was a Grade C that required diagnostic laparoscopy, diverting loop ileostomy and liberal drainage. The other two device-related leaks were minor (Grade A, managed with observation alone) and well contained (Grade B, treated with drainage and IV antibiotics only). Primary surgical indications included colorectal cancer in 2 cases and diverticulitis in the third subject.

3.4. Device questionnaires and surgeon grip strength

Additional performance data were collected by asking the surgeons/investigators to complete a satisfaction questionnaire after each procedure (see appendix for full questionnaire and associated data). Investigators considered the ECP as easier to use in 144 of 168 (85.7%) procedures compared to the manual circular staplers that they commonly use. Likewise, the device was thought to have less movement during firing and reduced force required to fire compared to previously used manual staplers in 89.9% and 94.6% of procedures, respectively. Questionnaires were also analyzed according to surgeons' gender (10 females and 28 males). The ECP was found easier to use in 88.0% of operations performed by males and in 79.1% of procedures by females, ($p = 0.2044$). With regard to device movement, 91.2% and 86.0% of procedures performed by males and females, respectively, noted reduced movement by ECP, ($p = 0.3808$). Less force to fire was found by male surgeons in 96.8%, and by female surgeons in 88.4% of surgeries, ($p = 0.0488$). Grip strength was determined after each procedure, with mean values of 42.4 kg (range 10.0–80.0) for all 38 surgeons, 30.7 kg for females, and 44.6 kg for males, ($p < 0.0001$ comparing genders).

4. Discussion

The primary aim of this study was to assess the frequency of performance issues observed with use of a novel powered circular stapler during creation of colorectal anastomoses. This objective was important due to the continued presence of issues associated with manual circular staplers, which are widely utilized in colon resections. The current study showed no instances of positive air-leak tests, and ECP performance issues were noted in 20 (11.9%) of 168 procedures. In a single-institution review of 349 left-sided colon and rectal resections, technical errors were found with the manual EEA circular stapler in 67 (19%) procedures [19]. Positive leak tests were observed in 19 (5.4%) operations with the EEA stapler and were the most common type of technical error [19]. Based on the findings of our study, the performance issue rate for the ECP device is lower than errors associated with manual circular stapling, although the data are limited. Only 1 (0.6%) issue in this study (a missing donut that necessitated subsequent surgical repair of the anastomosis) was considered related to a surgical complication or AE. Similarly, in a recent retrospective clinical study of 17 patients who underwent left-sided colorectal anastomosis with the ECP device, just 1 technical issue was noted [21]. This was an instance of difficulty docking with the anvil, which was remedied by re-opening and re-tightening the stapler followed by uneventful firing.

Risks for AL include many non-modifiable factors such as the presence of malignant disease, size of tumors, various comorbidities, ASA scores >2, and proximity of the anastomosis to the anal verge [6,10,12,25]. In the current study, postoperative AL was experienced in four patients even though all intraoperative air-leak tests were negative. The reliability of an air-leak test for prediction of clinical AL is not universal [10,26], as postoperative leaks may develop independently as a result of compromised gastrointestinal healing or other factors [27]. The incidence of postoperative AL in this study was lower than published rates in several large reviews of colorectal procedures [10–12]. For all types of AEs observed in our analysis, including the SAEs, none were scored higher than CD Grade IIIb, and 92.0% were mild Grade I or II events.

Surgeon questionnaires indicated that the ECP device exhibited reduced movement and easier firing relative to manual circular stapling. The surgeons' responses, when analyzed by gender for ease of use and less movement, did not show a statistical difference between male and female surgeons, except for a marginally significantly higher majority of males that viewed the ECP as requiring less force to fire. It is logical to suspect that the increased force necessary to fire a mechanical circular stapler plays a role in device movement, technical issues, and circular stapling malfunction rates. Evidence in the surgical literature has suggested that some surgeons do in fact have difficulty with adequate grip-strength required for stable firing of circular staplers [18,28]. In this study, the mean grip-strength was significantly greater for male surgeons, though ease of use for the ECP was judged nearly equally high by each gender, indicating that grip-strength is not a factor for effective use of the device. The ECP is, to our knowledge, the only currently marketed powered circular stapler. It was designed specifically for stability during firing and generation of consistent compression, which may contribute toward fewer staple-line leaks.

The primary limitation of this report is the lack of a randomized comparison between the ECP stapler and a control circular stapler. However, the objective was to obtain an accurate estimate of technical issues and complications/AEs associated with use of the novel ECP device. The single-arm approach was advantageous for time-efficient collection of data toward this objective. An additional limitation is the follow-up of only 4–6 weeks post-operation. Subjects who received proximal diversion should ideally be followed for a longer time to evaluate any anastomotic complications after reversal of the stoma. Strengths of the study included the representative, consecutively screened subject population and performance of procedures at multiple global centers providing real-world evidence.

5. Conclusion

In summary, the ECP exhibited effective performance during creation of anastomoses in left-sided colon resections. These findings were consistent with two smaller reports [21,28], that demonstrated uneventful postoperative outcomes of colorectal operations performed using the ECP stapler. Finally, the safety results for ECP with respect to postoperative anastomotic leaks compared favorably with published data [10–12].

Ethical approval

The protocol and consent form were approved by each investigator's Institutional Review Board or Independent Ethics Committee, and informed consent was obtained for all subjects.

Source of funding

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Research Registration Unique Identifying Number (UIN)

1. Name of the registry: ClinicalTrials.gov

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anastomotic site. Atraumatic Gripping Surface Technology reduces the compressive forces on tissues, and along with 3D Stapling Technology allows a better compression distribution throughout the anastomosis and a better hemostasis [6].

The objective of the present study was to assess whether these technical improvements of the ECPS have an impact on left-sided colorectal AL rate compared to current manual circular staplers (MCS).

Materials and methods

A cohort study was carried out in patients consecutively included between January 2017 and February 2020, in whom a left-sided circular stapled colorectal anastomosis above 5 cm from the anal verge was performed. A retrospective analysis of a prospectively maintained database was conducted. Patients were divided into two groups depending on which circular stapler was used to perform the anastomosis (ECPS vs MCS), and the AL rate was analysed. The inclusion criteria were patients aged over 18 years who had a colorectal anastomosis after left colectomy, sigmoidectomy or anterior rectal resection, for benign or malignant pathology. Hartmann reversal cases were also included. Exclusion criteria were anastomosis < 5 cm from the anal verge, diverting stoma, preoperative radiotherapy, American Society of Anesthesiologists (ASA) score > IV and transanal total mesorectal excision.

No changes were made during the study period in perioperative care or surgical principles. The splenic flexure was mobilized in all cases. The same group of dedicated colorectal surgeons performed all surgeries. ECPS was introduced in our hospital in June 2019 and used preferentially unless otherwise unavailable. The 30-day AL rate was recorded and cases were diagnosed according to the International Study Group of Rectal Cancer AL definition, as a defect of the intestinal wall at the anastomotic site leading to a communication between the intra- and extraluminal compartments, or as an abscess adjacent to the anastomosis [7]. Computed tomography (CT) scan with rectal contrast was performed in patients with suspected AL in the absence of unquestionable clinical signs of peritonitis, which would indicate urgent surgery. On postoperative day 4, C-reactive protein (CRP) levels were determined in all cases. Those patients with a CRP > 200 mg/L, went on to have a CT scan. The CT findings suggestive of anastomotic failure were: contrast leakage from inside the bowel to the pelvis and/or abdominal cavity, abscess and/or perianastomotic collection associated or not with localized pneumoperitoneum.

The study variables were age, sex, Charlson index, preoperative hemoglobin (Hb), ASA score, body mass index (BMI), type of pathology, surgical technique, open or laparoscopic approach, location of anastomosis, operative time and circular stapler device (ECPS vs MCS). The outcome variables were AL and degree of morbidity according to the Clavien-Dindo classification. The ECPS cases were matched to MCS cases by propensity score matching to obtain comparable groups of patients.

Statistical analysis

Descriptive statistics were provided for all variables. Absolute values and frequencies for qualitative variables were calculated. Quantitative variables normality was assessed with the Shapiro–Wilk test, expressing data as median and range. Subsequently, the possible relationship between the quantitative variables and the objective variables was investigated using parametric or non-parametric tests depending on the variable distribution. The relationship between the qualitative variables was established using the χ^2 test. MCS and ECPS AL risk were presented as odd ratios (OR) with 95% confidence intervals (95% CI).

Propensity score matching was used with the aim of obtaining homogeneous and comparable groups; 1:2 pairing was performed according to the device (ECPS vs MCS). Confounding variables used to compute the propensity score were age, sex, BMI, ASA, Charlson index, preoperative Hb, type of pathology and surgical approach. Logistic regression without substitution as an estimation and nearest-neighbour pairing algorithm was performed. Caliber of 0.2 was used. Relative multivariate imbalance was calculated: 0.197 before matching and 0.167 after matching. Significance was set at $p < 0.05$. The statistical software used was SPSS® v25 (SPSS Inc. Chicago, IL, USA, 2017) and R Core Team (3.2.0) for statistical analyses (R Foundation for Statistical Computing, Vienna, Austria, 2013). Propensity score matching was carried out using the *PsMatching* script of R integrated into SPSS.

Results

Two hundred seventy-nine patients met the inclusion criteria. Baseline clinical and demographic characteristics are outlined in Table 1. A MCS anastomosis was performed in 218 patients and an ECPS anastomosis in 61 (21.9%). Overall, AL was observed in 25 (9%) cases, 18 patients (6.4%) were reoperated on. The remaining seven AL were diagnosed as minor leaks (abscess or perianastomotic collection) and treated conservatively. Factors significantly associated with AL were ASA score ($p = 0.025$) and the type of circular stapler device used ($p = 0.021$). The following variables were not related to AL: age ($p = 0.882$), sex ($p = 0.513$), BMI ($p = 0.757$), preoperative Hb ($p = 0.061$), preoperative albumin ($p = 0.315$), Charlson's index ($p = 0.486$), operating

Table 1 Baseline demographic and outcome characteristics of the overall series

Age (years)[a]	66.5 (60)
Sex: male	178 (64)
BMI[a]	26.62 (29.6)
Preoperative Hg[a]	13.8 (14)
Charlson index[a]	4 (13)
ASA score	
I	9 (3.2)
II	152 (54.7)
III	114 (41)
IV	3 (1.1)
Malignant disease	190 (68.3)
Diagnosis	
Hartmann procedure	53 (19.1)
Rectal prolapse	3 (1.1)
Diverticular disease	27 (9.71)
Sigmoid cancer	81 (29.14)
Left colon cancer	22 (8)
Rectal cancer	92 (33.09)
Laparoscopic approach	179 (64.4)
Conversion to open surgery	12 (6.7)
Surgical technique	
Hartmann's reversal	53 (19.1)
Left colectomy	22 (8)
Sigmoidectomy	111 (39.9)
Anterior rectal resection	92 (33.09)
ECPS	61 (21.9)
Anastomosis level	
Middle rectum (5–10 cm)	143 (51.4)
Upper rectum (10–15 cm)	136 (49.6)
Operative time[a]	160 (371)
Morbidity (Clavien-Dindo)	
None	182 (65.5)
I	20 (7.2)
II	38 (13.7)
IIIa	4 (1.4)
IIIb	17 (6.1)
IVa	7 (2.5)
IVb	7 (2.5)
V	3 (1.1)
Anastomotic leakage	25 (9)
Minor	7 (2.5)
Major	18 (6.4)

Values in parentheses are percentages

BMI body mass index, *Hb* haemoglobin, *ASA* American Society of Anesthesiologists, *ECPS* Echelon circular powered stapler

[a]Median (range)

time ($p=0.136$), laparoscopic approach ($p=0.828$), diagnosis ($p=0.310$) or surgical technique ($p=0.224$). AL was observed in 24 (11.1%) patients in the MCS group and in 1 (1.6%) patient in the ECPS group ($p=0.021$). The anastomosis was performed in the mid rectum (between 5–10 cm from the anal verge) in 144 patients Table 2.

Outcomes after propensity score matching

After adjusting the cases with propensity score matching, two new groups of patients were generated: 119 MCS cases versus 60 ECPS cases (Fig. 1). Both groups were totally comparable after case matching (Table 2). AL was observed in 14 (11.8%) patients in the MCS group and in 1 (1.7%) patient in the ECPS group ($p=0.022$). ALs in the MCS group required reoperation in seven cases (5.8%) and the remaining seven patients with minor leaks were treated conservatively. The MCS group had higher AL risk (OR 1.258, 95% CI 1.132–1.398) than the ECPS group (OR 0.169, 95% CI 0.024–1.166). Postoperative morbidity according to the Clavien-Dindo classification was less frequent in the ECPS group ($p=0.054$).

Discussion

This cohort study showed that the left-sided colorectal AL rate significantly decreased from 11.8% (MSC) to 1.7% (ECPS) ($p=0.021$) when a different circular stapler was used. Cases were diagnosed according to the International Study Group of Rectal Cancer AL definition [7], including patients with abscess or perianastomotic collection that were managed conservatively. Surgery was required in 5.8% of cases of AL in the MCS group and 1.7% in the EPCS group. Circular stapling devices have the advantage of a shorter anastomosis time and greater reproducibility compared with hand-sewn anastomosis with similar safety and efficacy [8]. There is no scientific evidence to support either anastomotic technique [9, 10]. An end-to-end anastomosis was performed in all patients included in the present study.

The circular stapler has evolved over time, and a powered variant was introduced in 2019. The novel ECPS provides some design improvements in circular stapling technology: powered firing, 3D stapler configuration and Gripping Surface Technology. One of the potential problems with manual circular staplers is the force required to perform the anastomosis causing unwanted movements at the anastomotic site that could cause microvascular trauma and therefore compromise anastomotic healing [11]. The powered firing process improves stapling head stability and, along with the ergonomic design of the device, allows the firing to be carried out comfortably regardless of the size or the strength of the surgeon's hand. Gripping Surface Technology provides precise compression only where it is needed, to prepare tissue for staple formation facilitating smoother handling reduction in tissue compression forces.

Table 2 Demographic characteristics and outcomes of the MCS group compared to the EPCS group, pre- and post-Propensity Score Matching

	Pre-Propensity Score Matching			Post-Propensity Score Matching		
	MCS 217 (78.1)	ECPS 61 (21.9)	*p* value	MCS 119 (66.5)	ECPS 60 (33.5)	*p* value
Age (years)[a]	67 (60)	64 (52)	0.607	67 (60)	64 (52)	0.788
Sex:male	140 (64.5)	38 (62.3)	0.764	76 (63.9)	37 (61.7)	0.870
BMI[a]	26.61 (40.89)	26.37 (27.86)	0.792	26.7 (23.89)	26.39 (27.86)	0.849
Preoperative Hb[a]	13.85 (14)	13.4 (6.3)	0.721	13.6 (10.1)	13.62 (6.3)	0.975
Charlson index[a]	4 (13)	4 (10)	0.500	4 (9)	4 (10)	0.951
ASA			0.089			0.078
I	9 (4.1)	0		4 (3.4)	0	
II	116 (53.5)	36 (59)		61 (51.3)	35 (58.3)	
III	91 (41.9)	23 (37.7)		54 (45.4)	23 (38.3)	
IV	1 (0.5)	2 (3.3)		0	2 (3.3)	
Malignant disease	154 (71)	36 (59)	0.087	79 (66.4)	38 (60)	0.413
Laparoscopic approach	138 (63.6)	41 (67.2)	0.652	76 (63.9)	40 (66.7)	0.743
Conversion rate	9 (6.5)	3 (7.3)	1.000	5 (6.6)	3 (7.5)	1.000
Middle rectum anastomosis (5–10 cm)	113 (52.1)	30 (49.2)	0.772	66 (55.5)	30 (50)	0.528
Operative time[a] (min)	158 (360)	165 (222)	0.819	165 (435)	165 (222)	0.681
Morbidity (Clavien-Dindo)			0.091			0.054
None	134 (61.8)	48 (78.7)		73 (61.3)	47 (78.3)	
I	18 (8.3)	2 (3.3)		10 (8.4)	2 (3.3)	
II	31 (14.3)	7 (11.5)		17 (14.3)	7 (11.7)	
IIIa	4 (1.8)	0		4 (3.4)	0	
IIIb	16 (7.4)	1 (1.6)		5 (4.2)	1 (1.7)	
IVa	4 (1.8)	3 (4.9)		1 (0.8)	3 (5)	
IVb	7 (3.2)	0		6 (5)	0	
V	3 (1.4)	0		3 (2.5)	0	
Anastomotic leakage	24 (11.1)	1 (1.6)	0.021	14 (11.8)	1 (1.7)	0.022
Minor	7 (3.2)	0		7 (5.8)	0	
Major	17 (7.8)	1 (1.6)		7 (5.8)	1 (1.7)	

Values in parentheses are percentages

BMI body mass index, *Hb* haemoglobin, *ASA* American Society of Anesthesiologists, *ECPS* Echelon circular powered stapler, *MCS* manual circular stapler

[a]Median (range)

Furthermore, the 3D stapling technology equally distributes the compression throughout the anastomosis. Both technological innovations contribute to promoting optimal conditions for anastomotic healing. In a study by Rojatkar et al., ex vivo testing of the powered stapler was compared to a manual circular stapler, concluding that ECPS required 97% lower force-to-fire, showed 33% lower compressive forces and reduced 37% anastomotic site movement during device firing. Anastomotic pressure testing by insufflating the bowel lumen, showed that ECPS had 61% less leaks at pressures of 30 mmHg or lower than the non-powered circular stapler [6].

Athalah et al. have recently published the first clinical validation series (17 patients) on the use of the ECPS. No device failures were reported, demonstrating its safety and efficacy in the clinical setting. Surgeon perception of anastomotic quality and device ease-of-use was rated to be above average [12]. To our knowledge, this is the first study comparing the clinical results of ECPS and MCS in a consecutive series of patients. Since the introduction of ECPS in our clinical practice, a significant decrease in AL rate was observed. Only one AL was observed in the ECPS group, a 75-year-old male patient, with BMI 35.9 kg/m2, diagnosed with metastatic sigmoid cancer that was managed with a "liver first" strategy. The patient required an urgent Hartmann´s procedure, is currently disease-free and pending restoration of intestinal continuity.

A wide variety of patient-related factors has been suggested to contribute to the development of AL: ASA score > 3, smoking, excessive alcohol consumption, diabetes mellitus, anemia, hypoproteinemia, obesity, age, sex, tumor stage, the use of steroids and neoadjuvant chemoradiotherapy, heart and lung failure, blood transfusion,

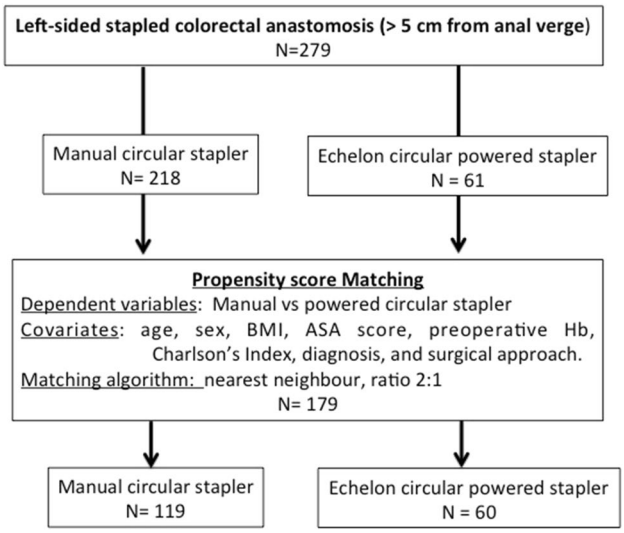

Fig. 1 Flow chart of population selection and matching by propensity score. *BMI* body mass index, *Hb* haemoglobin, *ASA* American Society of Anesthesiologists

the patient's microbiome and many others [2, 13, 14]. In our series, ASA score was the only factor predictive of AL amongst all the patient-related risk factors analysed. Some risk factors are modifiable aspects in the management of colorectal surgery that might reduce the anastomotic complications. Implementing a structural change in clinical practice can significantly reduce the AL rate after colorectal resections [15]. Multimodal prehabilitation programs enhancing nutritional status and functional capacity prior to surgery are being studied. The preoperative period might be the ideal moment for improvements that reduce the risk of postoperative complications [16].

Likewise perioperative care, surgical techniques and technologies have an important role in the incidence of AL. Several operative factors can influence left-sided anastomotic complications: surgical approach, anastomosis technique, anastomotic level, number of linear stapler firings during rectal transection, diverting stoma, intraoperative assessment of the anastomosis (air leak test, endoscopy, indocyanine green angiography (IGA)), intra-abdominal drainage and prophylactic transanal tube decompression [17]. The same perioperative management protocols were maintained during the entire study period. Similarly, the basic surgical principles were not modified and the same group of surgeons performed all the surgical procedures. IGA was not available to check colon and rectal perfusion in our hospital during the study period, so the anastomotic site was selected by the surgeon using typical standard of care assessment. However, intraoperative IGA has been recently introduced into our regular clinical practice. The use of the ECPS to perform the anastomosis was the only modification.

In addition to the clinical consequences suffered by the patients, AL may lead to a 65–81% increase in hospital costs [18]. Patients who had postoperative AL incurred an additional hospital cost of 34.900–54.300€ [19, 20]. The new device is around 35% more expensive than the previous manual version. Nevertheless, if the reduction in AL rate is confirmed, this increase in the cost of the stapler could be compensated by a reduction in hospital expenses.

Finally, we acknowledge the limitations in the present study. We used a retrospective and uncontrolled single-centre design with a small sample size. Patients were operated in different time frames (MCS before and EPCS after June 2019), albeit by the same surgeons with over 10 years experience in colorectal surgery. This leads to inherent bias particularly in the ECPS group, restricting the ability to draw conclusions. Propensity score matching was used to obtain homogeneous and comparable groups and address some of these limitations though other AL related variables may not have been included. This study attempts to assess the impact of the ECPS stapler on the risk of AL as a primary outcome, presents valuable data relevant to clinical practice and possible improvement of outcomes. It is a single-center preliminary experience and the results must be interpreted with caution. To assess the real impact of the novel ECPS on AL rate, we are currently planning a multicenter international controlled trial with the same inclusion and exclusion criteria as the present study (540 patients, randomized on a 1:1 basis to anastomosis performed with ECPS or MCS, alpha 0.05, beta 80%). Participating centres will be high volume accredited colorectal centers with homogeneous perioperative care protocols.

Conclusions

Our initial experience with ECPS shows that it could have a positive impact in reducing AL rates in left-sided colorectal anastomosis. Multicenter controlled trials are needed to obtain stronger evidence and justify a change in clinical practice.

Author contributions VP-M: conception and design, drafting the article and final approval of the manuscript. JM-A: acquisition of data, analysis and interpretation of data, revising critically the content and final approval of the version to be published. DM-V: design, revising the study critically for important content and final approval and final approval of the version to be published. SG-B: design, revising the manuscript critically for important intellectual content and final approval of the version to be published. IM-O: acquisition of data, revising critically the content and final approval of the version to be published. RG-M: acquisition of data, revising critically the content and final approval of the version to be published. CC-L: revising of data, analysis and interpretation and final approval of the manuscript. AE-M: conception and design, revising the manuscript critically for

important intellectual content and final approval of the version to be published.

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Availability of data and material Not applicable.

Compliance with ethical standards

Conflict of interest Pla-Martí V. reports consultancy for Johnson and Johnson and has received honorarium for speaking at symposia by Johnson and Johnson and Medtronic. Moro-Valdezate D. has received honorarium for speaking at symposia by Johnson and Johnson. The rest of the authors declare no conflict of interest.

Ethical approval All procedures performed in the study were conducted according with the ethical standards of the institution and with the 1964 Helsinki declaration and later amendments or comparable ethical standards.

Informed consent All patients signed the institution informed consent for colorectal surgery. No specific consent for this type of study is required.

Code availability Not applicable.

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