The American Journal of Surgery 220 (2020) 170–177

Contents lists available at ScienceDirect

The American Journal of Surgery

journal homepage: www.americanjournalofsurgery.com

Risk factors for ileocolic anastomosis dehiscence; a cohort study

Thomas Golda [a, *, 1], Claudio Lazzara [a, b, 1], Carla Zerpa [a, c], Lucia Sobrino [a], Valeria Fico [d, a], Esther Kreisler [a], Sebastiano Biondo [a]

[a] Department of General and Digestive Surgery, Colorectal Unit, Bellvitge University Hospital, University of Barcelona, Barcelona, Spain
[b] Department of General and Digestive Surgery, Policlinico G. Martino, University of Messina, Messina, Italy
[c] Department of General and Digestive Surgery, Parc Tauli University Hospital, University Autonoma of Barcelona, Sabadell, Spain
[d] Department of General and Digestive Surgery, Agostino Gemelli University Hospital, Catholic University, Rome, Italy

ARTICLE INFO

Article history:
Received 11 September 2019
Received in revised form
25 October 2019
Accepted 10 November 2019

Keywords:
Anastomotic leak
Ileocolic anastomosis
Risk factor
Protective factor
Suture reinforcement

ABSTRACT

Background: Anastomotic leak (AL) after ileocolic anastomosis influences morbidity, mortality, length of hospitalization and costs. This study analyzes risk and protective factors for AL on ileocolic anastomoses.
Methods: We retrospectively analyzed our single institution patients' series undergoing elective ileocolic anastomosis for AL between 1/2008-12/2017. AL grade A/B (antibiotic treatment and/or radiological drainage) were summarized as mild, grade C (surgical re-intervention) corresponds to severe AL.
Results: We included 470 patients (mean age 70.8 years, 43.2% females). Overall AL rate was 9.4% (44 patients) with 6.0% severe and 3.4% mild AL. There was no difference in AL between hand sewn and stapled anastomoses. Multivariate analysis revealed preoperative serum albumin ($p = 0.004$), smoking habits ($p = 0.005$) and perioperative blood transfusion ($p = 0.038$) as risk factors for AL. Suture oversewing as anastomotic reinforcement resulted as independent protective factor ($p < 0.001$).
Conclusion: Poor nutritional status, smoking habits and perioperative blood transfusion are negative factors influencing on AL. Suture oversewing as anastomotic reinforcement associates with significantly less AL.

Introduction

Anastomotic leak (AL) after colorectal surgery is the most devastating complication. The huge range of its incidence (1–15.9%)[1–4] depends in part on the height of the anastomosis,[5,6] but also on the lack of standard definitions and confounding patients' inclusion criteria. Anastomotic failure is the main cause of increased morbidity, mortality, length of hospitalization and higher costs.[1] Reoperation constructing a temporary or definitive stoma is often necessary, affecting patients' quality of life,[2] increases mortality and seems to impair long-term oncological outcomes.[3,7] Despite compliance with surgical principles of tension-free tissue approximation and a correct blood supply of the anastomosis, the incidence of AL is still high. Several factors have been identified that influence AL rate, however confusion exists due to differences of colon and rectal resections.[4] AL rates after rectal resection are higher than in colon surgery, therefore results obtained in mixed cohorts always confirm the known risk factors for AL after rectal surgery,[5] but underestimate risk factors specific in colonic anastomoses. To date there is still scarce evidence on risk factors for AL after colonic surgery and even less evidence in protective factors. Identifying patients with factors known as high-risk for AL could help surgeons to optimize preoperative treatment, to tailor surgical strategy and/or to intensify the postoperative monitoring. The primary aim of this study was to identify pre-, peri- and postoperative risk and protective factors for AL after elective ileocecal resection, right and extended right colectomy with ileocolic anastomosis. Secondary objectives were to describe the influence of AL on the need for reoperation, length of hospital stay and mortality.

Methods

Study population

This observational study retrospectively analyzes all patients who underwent a primary ileocolic anastomosis after ileocecal

* Corresponding author. Bellvitge University Hospital, Department of General and Digestive Surgery, C/ Feixa Llarga s/n L'Hospitalet de Llobregat, 08907, Barcelona, Spain.
E-mail address: tgolda@bellvitgehospital.cat (T. Golda).
[1] T. Golda and C. Lazzara contributed equally to this study.

https://doi.org/10.1016/j.amjsurg.2019.11.020
0002-9610/

resection, right and extended right colectomy for cancer at the University Hospital of Bellvitge between January 2008 and December 2017. All patients' charts were reviewed for AL within 90 postoperative days. Data were prospectively entered into our colorectal unit database and then retrospectively revised. Inclusion criteria were: diagnosis of colon cancer, surgery in an elective setting with any applied hand sewn or stapled anastomosis in patients of any ASA (American Society of Anesthesiologists) grade (I-IV). Exclusion criteria were emergency surgery, diagnosis different from cancer, resection without anastomosis, multivisceral resection, creation of a temporary loop-ileostomy, palliative surgery and performance of an ileocolic anastomosis during a re-intervention due to a complicated postoperative course.

Bowel preparation consisted in all cases in light diet and an enema the night before surgery. All patients were given preoperative antibiotic prophylaxis with a cephalosporin (or ciprofloxacin in case of cephalosporin allergy) and metronidazole. Perioperative treatment (progressive diet introduction, deep vein thrombosis prophylaxis with a low molecular weight heparin) was the same for all patients; a standardized ERAS program (Enhanced Recovery After Surgery) including prehabilitation was established after the study period. Perioperative period includes one preoperative day, the day of surgery and the first postoperative day. After hospital discharge, all patients were followed at our outpatient center.

Definition and categories of AL

AL is defined as recommended by *the International Study Group of Rectal Cancer* as "a defect of the intestinal wall at the anastomotic site, leading to a communication between the intra and the extraluminal compartments".[8] Clinical suspicion of AL included abdominal tenderness, septicemia, or evidence of gas or fecal discharge from the drainage. Routine radiological imaging was not performed postoperatively unless AL was suspected. In that case, a computed tomography or an enema with hydro-soluble contrast was done. Patients with AL were divided into the three grades (A, B and C), described by Rahbari et al.[8] according to the severity of the leakage and the therapeutic management. For analysis, we summarized grade A + B as clinically mild and grade C as severe.

- **Severe AL**: patients who needed surgical treatment due to sepsis or peritonitis (Grade C);
- **Mild AL**: patients with perianastomotic localized collection treated only with antibiotic therapy and/or radiologically (ultrasound or computed tomography) guided drainage (Grade A and B).

Data collection

The colorectal surgery unit runs a prospective clinical database of all colorectal patients. Variables entered in the database comprise patient's demographic data, smoking habits (no smokers, smokers and ex-smokers - patients who quit smoking at least 2 months before surgery), comorbidities and history of immunosuppression (immunosuppressive medication, non-intestinal active malignancy, end-stage renal failure, chronic corticosteroid treatment, congenital or acquired immunodeficiency). Patient's pre-operative data (ASA, BMI -body mass index-, serum albumin and hemoglobin level), diagnosis (colon cancer, inflammatory bowel disease, unresectable polyps, bowel occlusion or ischemia, localized peritonitis due to perforation after diverticulitis or colonoscopy, intestinal fistula and appendicopathy), tumor localization and type of surgery (ileocecal resection, right colectomy and extended right colectomy) were also prospectively registered. All patients received an extracorporeal ileocolic anastomosis, also in case of a laparoscopic approach. The type of anastomosis was decided by the operating surgeon: stapled, linear side-to-side or circular end-to-side with closure of the colon with a linear stapler; handsewn, side-to-side or end-to-side either as continuous suture or with interrupted stitches. Anastomotic reinforcement is defined as seromuscular oversewing suture either with a running suture or interrupted inverting stitches on the serosal layer of the entire anastomotic line.

We analyzed perioperative data (serum albumin, need of vasoactive drugs, blood transfusion) and postoperative data (time to the detection of AL, length of hospital stay, need for re-intervention, postoperative mortality) in relation to AL. Furthermore, we analyzed if there was a correlation between these variables and the severity of AL studying their influence on the severe and mild AL groups.

Statistical analysis

Quantitative data are presented as mean and standard deviation or median and interquartile range. Differences between groups were evaluated using parametric or non-parametric tests as appropriate. Qualitative variables were analyzed using the Chi-Square test. Quantitative variables were analyzed using ANOVA or Kruskal-Wallis test to compare more than 2 groups and T-student or Mann-Whitney *U* test to compare two groups. A multivariate logistic regression was performed to study AL. All variables which turned out to be significant in the univariate analysis were checked in the multivariate logistic regression model. The statistical analysis was performed using Software R 3.6 (R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was set at a p-value of <0.05.

Results

Patients' inclusion

The database search identified 824 patients undergoing any kind of ileocecal, right or extended right colectomy for various indications between 2008 and 2017. Three hundred fifty-four patients were excluded. Reasons for exclusion are reported in Fig. 1. A total of 470 consecutive patients, 203 women and 267 men, with a mean age of 70.8 years, were included in the study (Fig. 1). All analyzed patients underwent elective surgery with a confirmed pathological result of colon cancer. The pre-operative demographic characteristics of these patients are described in Table 1.

Surgical procedure

Standard right colectomy was the most frequent type of surgery, whereas extended right colectomy was performed in 57 patients (12.1%) and ileocecal resection in 13 patients (2.7%). A hand sewn anastomosis was performed in 234 patients (49.8%) whilst a stapled in 236 patients (50.2%). The median operating time was 178 min, without a statistical difference ($p = 0.105$) between patients without AL (180 min), mild (162 min) or severe (157 min) AL.

From 2011 on, a second seromuscular oversewing suture as reinforcement of the entire anastomosis was introduced and performed with increasing frequency until 2017. This oversewing suture reinforcement in any kind of ileocolic anastomosis was progressively applied by all surgeons of the colorectal unit covering at least 94% of all ileocolic anastomoses in the last three years of the study with a total of 268 patients (57.0%). Suture oversewing reinforcement consisted in a running suture (104 patients) or interrupted inverting stitches (164 patients). All intraoperative

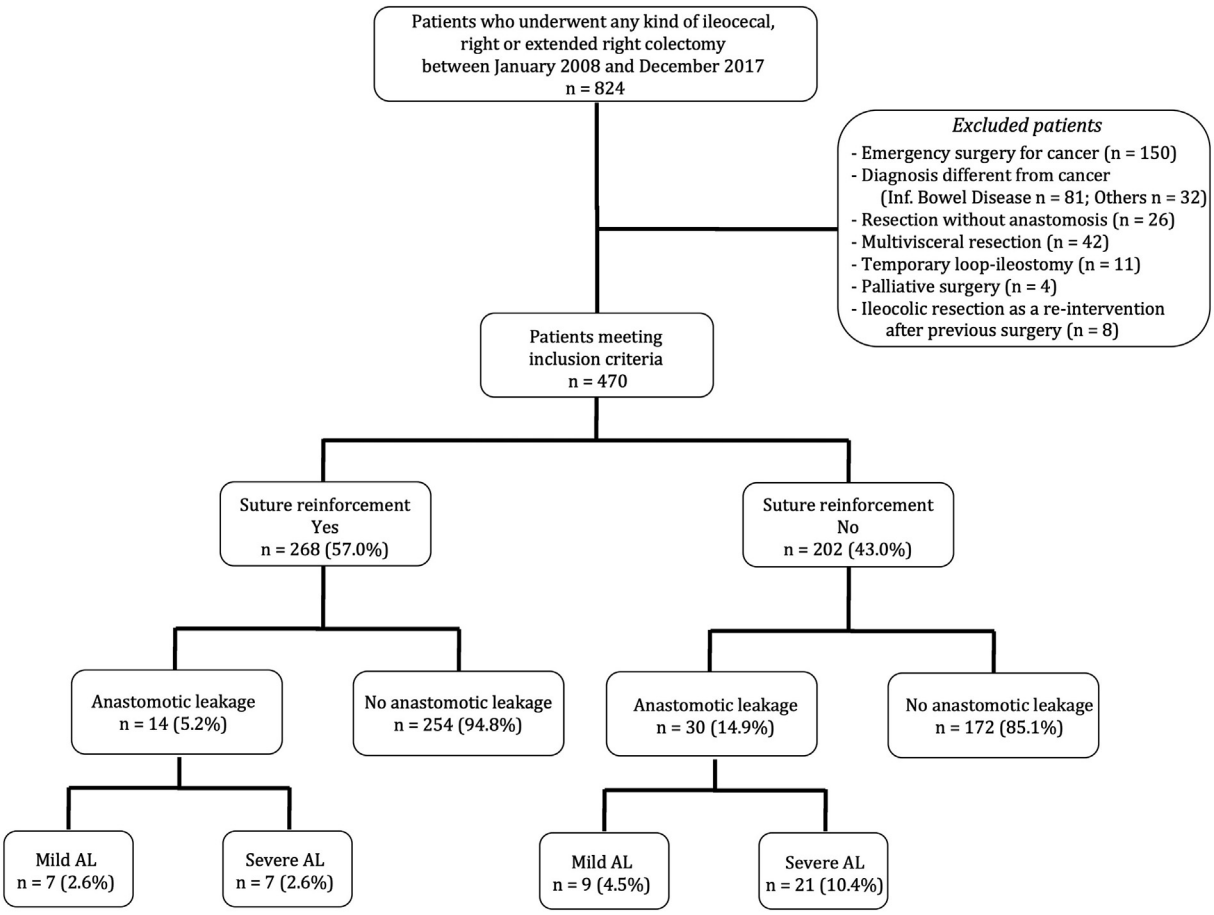

Fig. 1. Flow Chart of all eligible patients according to their evolution.

Table 1
Demographic data of patients with colonic cancer included in the analysis; Data are expressed as number of patients, n (%) or mean (SD).

		[Total] n = 470
Gender		
	Female	203 (43.2%)
	Male	267 (56.8%)
Age (years)		70.8 (10.5)
ASA score		
	I	5 (1.0%)
	II	222 (47.2%)
	III	227 (48.3%)
	IV	16 (3.5%)
Diabetes mellitus		
	No	348 (74.0%)
	Yes	122 (26.0%)
Chronic Obstructive Pulmonary Disease		
	No	370 (78.7%)
	Yes	95 (20.3%)
	Not known	5 (1.0%)
Smoking habits		
	Smoker/Ex-Smoker	224 (47.7%)
	No Smoker	243 (51.7%)
	Not known	3 (0.6%)
Chronic corticosteroid use		
	No	432 (91.9%)
	Yes	32 (6.8%)
	Not known	6 (1.3%)
Preoperative albumin (g/l)		40.1 (5.53)

ASA: American Society of Anesthesiologists.

technical data are detailed in Table 2.

AL rates

In the study period, the overall AL rate was 9.4% with 3.4% in the mild group and 6.0% in the severe group. The number of overall anastomotic leaks decreased from 2008 (15.8%) to 2017 (5.4%). Fig. 2 shows the reduction in overall and severe AL rate related to the reinforcement of the anastomosis, significant both in the univariate ($p < 0.001$, Table 2) and multivariate ($p < 0.001$, Table 4) analysis. The incidence of severe and mild AL dropped in 2017 to 0% and 5.4%, respectively. Reinforcement did not show any discriminant relation to mild or severe AL (Table 5). The mean time to detect a mild AL was 11.0 days postoperatively, severe AL was detected four days earlier (7th day, $p = 0.028$).

Postoperative findings

The median length of postoperative hospital stay was 12.8 days. Postoperative blood transfusion was required overall in 95 patients. In patients without AL, necessity of postoperative blood transfusion, vasoactive drug therapy and the length of hospital stay was less than in the AL group; subgroup analysis revealed the same for mild versus severe AL. The postoperative mortality rate (14 patients: 9 for respiratory complications, 2 for cardiovascular failure and 3 due to multiorgan failure related to septic shock) was significantly lower in the group without AL and increased accordingly to mild and severe AL (Table 3)

Table 2
Univariate analysis on the association of surgical details with anastomotic leak (mild and severe) in all elective procedures for colonic cancer. Data are expressed as number of patients, n (%) or mean (SD).

	[TOTAL] n=470	No AL n=426 (90.6%)	Mild AL n=16 (3.4%)	Severe AL n=28 (6.0%)	p-value[a]
Type of surgery					0.805
Ileocecal resection	13 (2.8%)	13 (100%)	0 (0%)	0 (0%)	
Right colectomy	400 (85.1%)	363 (90.8%)	14 (3.5%)	23 (5.7%)	
Extended right colectomy	57 (12.1%)	50 (87.7%)	2 (3.5%)	5 (8.8%)	
Operating time (minutes)	178 (63.1)	180 (64.4)	162 (40.4)	157 (47.6)	0.105[b]
Anastomosis technique					0.447
Manual (hand-sewn)	234 (49.8%)	216 (92.3%)	7 (3.0%)	11 (4.7%)	
Stapled	236 (50.2%)	210 (89.0%)	9 (3.8%)	17 (7.2%)	
Type of anastomosis					0.716
Side-to-side manual	211 (44.9%)	195 (92.5%)	6 (2.8%)	10 (4.7%)	
Side-to-side stapled	118 (25.1%)	106 (89.8%)	7 (6.0%)	5 (4.2%)	
End-to-side stapled	118 (25.1%)	104 (88.1%)	2 (1.7%)	12 (10.2%)	
End-to-side manual	23 (4.9%)	21 (91.4%)	1 (4.3%)	1 (4.3%)	
Reinforcement					**<0.001**
No	202 (43.0%)	172 (85.1%)	9 (4.5%)	21 (10.4%)	
Yes	268 (57.0%)	254 (94.8%)	7 (2.6%)	7 (2.6%)	

AL: anastomotic leakage
[a] chi-squared test.
[b] *Anova Test*

Factors, related to AL

Table 4 shows the univariate and multivariate analysis of variables associated with AL. In the univariate analysis COPD, smoking habits and preoperative serum albumin were patient-specific factors associated with AL. Perioperative factors, associated with AL were: operating time, perioperative blood transfusion and anastomotic reinforcement.

Multivariate analysis showed current or past smoking habits, value of preoperative serum albumin, perioperative blood transfusion and anastomotic reinforcement as independent factors associated with AL. In contrast, history of COPD and operating time lost their statistical significance. AL neither was related to the type of surgery nor to the anastomotic technique (manual versus stapled), nor to the type of anastomosis performed (linear stapled side-to-side, circular stapled end-to-side, hand sewn side-to-side or end-to-side).

Factors showing significance for AL in the multivariate analysis were tested for an association to severe versus mild AL. This analysis could not detect an association of the identified risk factors with the severity (mild or severe) of AL (Table 5).

Discussion

Analysis of factors related to AL in ileocolic anastomoses showed that serum albumin level smoking habits and perioperative blood transfusion, independently influence AL. In addition, reinforcement of the entire anastomosis either with single seromuscular interrupted stitches or a continuous oversewing suture proved to be a protective factor significantly reducing AL rates.

The incidence of AL in colorectal surgery differs largely between series.[5,9–11] We found a globally elevated AL rate of 9.4% which is higher than previously described.[10,12–14] Due to the inconsistency of AL definition and the time of diagnosis, studies may underestimate AL rates.[15] This study includes all AL detected within 90 postoperative days. Moreover, this study considers not only the clinically evident grade C anastomotic leakage but also a contained collection adjacent to the anastomosis (grade A + B).[8] As to eliminate confounding factors, we decided to exclude from analysis cases of surgery in the emergency setting[16,17] that could have reduced the study's power in identifying risks factors for AL and we focused our attention on patients treated for colonic cancer in an elective setting.[18]

Recently, ileocolic anastomoses have been shown to have a higher risk of AL compared to other sites of an intestinal anastomosis.[15–18] Segelman et al.[18] found a 13.2% of AL after ileocolic (sigmoid or rectum) anastomosis, explaining this result as possible consequence of the altered perfusion of the remaining colon. Hyman et al.[15] discussed the role of the terminal ileum: despite the fact that the ileum is usually well perfused and free of tension, it may has “too narrow and/or thin walls” for stapler placement. Another possible explanation could be that in high volume and University Hospitals, experienced surgeons usually perform a primary anastomosis also in sub-optimal conditions challenging ileocolic anastomoses more than colorectal ones, frequently covered by a diverting stoma.[17]

Technique is obviously a crucial point when analyzing anastomotic failure. Recently various studies on AL rates have been published, but results are diverse regarding the role of technique.

The present study did neither find significant differences between hand sewn and stapled anastomoses nor in the subgroup analysis of the different ileocolic anastomotic techniques applied. The ESCP snapshot study on ileocolic anastomoses identified in the adjusted analysis stapled anastomosis to be at higher risk of AL than the hand sewn.[19] However, focusing on inflammatory bowel disease, there was no difference between the two techniques.[20] A recent Swedish population based study found also a significant higher AL in stapled ileocolic anastomoses than in hand sewn ones.[21] On the other side, a Cochrane review on ileocolic anastomoses found stapled anastomoses associated with significantly fewer AL.[22] A recent multicenter Spanish study confirms the results from this study for ileocolic anastomoses showing no differences in AL between hand sewn (8.0%) and stapled techniques (8.9%, $p = 0.46$).[10]

Perioperative variables are considered as potential risk factors for AL. An altered albumin synthesis correlates with sepsis, inflammation and malnutrition as a known risk factor for AL.[23] Preoperative nutritional status, expressed as serum albumin level, is important in the proliferative and remodelling phase of the healing process, influencing collagen synthesis and fibroblast proliferation.[24–26] Our findings aline with studies on low overall protein levels as a possible risk factor for AL.[10,21,25,26]

In the present series, perioperative blood transfusion was also identified as independent risk factor for AL and in line with

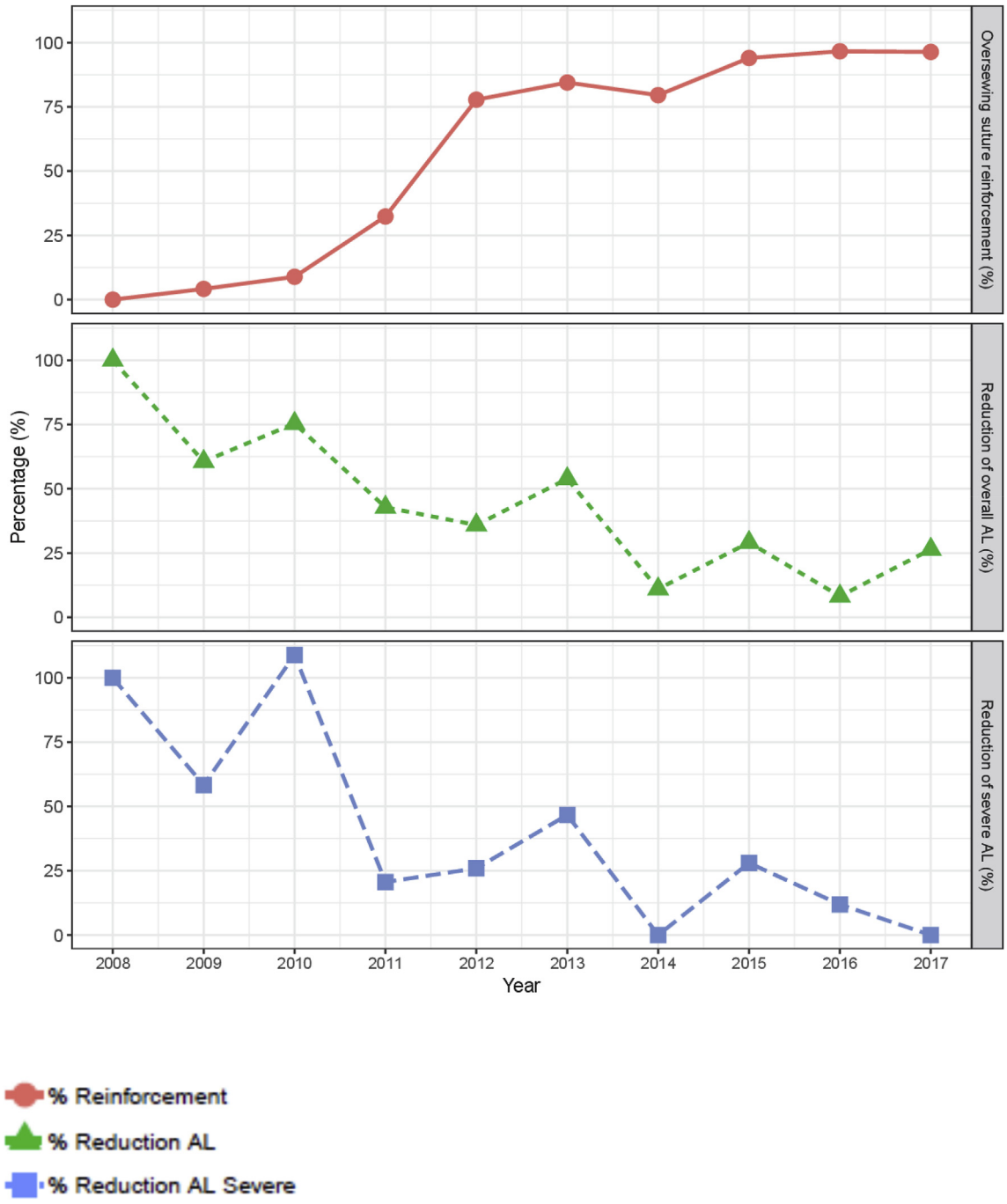

Fig. 2. Reduction of overall AL (dotted green line) and severe AL (dotted blue line) related to suture oversewing reinforcement (orange) over the study period in relation to the first year of the study (%). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

previous studies.[27] Clear reasons explaining this association are not completely known: preoperative anemia or loss of blood requiring blood transfusion may be correlated with hypoxia and hypovolemia undermining the anastomotic healing process.[28] Also immunosuppressive effects in the context of blood transfusion could impair the recently performed anastomosis.[29]

Current or past smoking habits showed also significant correlation to AL. As shown in other studies, tobacco use is a risk factor for AL due to various nicotine-related mechanisms.[9] Vasoconstriction with reduced perfusion, decreased tissue oxygenation and micro-thromboses caused by enhanced platelet adhesiveness may are relevant pathomechanisms.[30] Our findings, supported by previous literature results,[9,30] suggest that patients with active or recent smoking habits should be informed about the increased risk of AL.

The most remarkable finding of this study, however, is the AL protective effect of sero-muscular oversewing reinforcement of the anastomosis as either continuous suture or interrupted stiches (Tables 2 and 4, Fig. 2). The gastrointestinal (anastomotic) healing process has particular characteristics[31]; involving specific collagen subtypes, the gastrointestinal microbioma,[32] and especially the serosal layer strengthening the wound, are important factors.

Table 3
Univariate analysis on the association of postoperative data with anastomotic leak (mild or severe). Data are expressed as number of patients' n (%) or mean (SD).

	[TOTAL] n=470	No AL n=426	Mild AL n=16	Severe AL n=28	p-value[a]
Length of stay (days)	12.8 (12.1)	10.9 (8.7)	26.1 (17.2)	34.8 (23.1)	**<0.001** [b]
Postoperative blood transfusion					**<0.001**
No	359 (76.4%)	348 (81.7%)	7 (43.8%)	4 (14.3%)	
Yes	95 (20.2%)	63 (14.8%)	8 (50.0%)	24 (85.7%)	
Not known	16 (3.4%)	15 (3.5%)	1 (6.2%)	0 (0.0%)	
Postop AL detection (days)	8.5 (5.7)		11.0 (6.9)	7.07 (4.5)	**0.028** $
Postop albumin (g/l)	33.5 (48.7)	34.2 (51.3)	28.6 (3.8)	26.0 (5.07)	0.647
Need for vasoactive drug treatment					**<0.001**
No	418 (88.9%)	401 (94.1%)	12 (75.0%)	5 (17.9%)	
Sí	41 (8.7%)	15 (3.5%)	3 (18.8%)	23 (82.1%)	
Not known	11 (2.4%)	10 (2.4%)	1 (6.2%)	0	
Mortality					**<0.001**
No	456 (97.0%)	421 (98.8%)	15 (93.8%)	20 (71.4%)	
Yes	14 (3.0%)	5 (1.2%)	1 (6.2%)	8 (28.6%)	

AL: anastomotic leakage.
[a] chi-squared test.
[b] *Anova Test. $ Student's t-test*

Table 4
Univariate and multivariate analysis to identify Independent Risk Factors for overall AL (Logistic Regression). Association of demographic characteristics and surgical details with anastomotic leak (overall). Data are expressed as number of patients' n (%) or mean (SD).

			Univariate		Multivariate	
	No AL N = 426	AL N = 44	OR CI95%	p-value*	OR CI95%	p-value**
Gender						NS
Female	185 (91.1%)	18 (8.9%)	Ref.	Ref.		
Male	241 (90.3%)	26 (9.7%)	1.11 [0.59; 2.12]	0.756		
Age, years	60.6 (10.6)	72.5 (9.3)	1.02 [0.99; 1.05]	0.256		NS
ASA						NS
I-II	209 (92.1%)	18 (7.93%)	Ref.	Ref.		
III	204 (89.9%)	23 (10.1%)	1.31 [0.68; 2.53]	0.419		
IV	13 (81.2%)	3 (18.8%)	2.75 [0.56; 9.72]	0.187		
Diabetes mellitus						NS
No	312 (89.7%)	36 (10.3%)	Ref.	Ref.		
Yes	110 (94.0%)	7 (6.0%)	0.56 [0.22; 1.23]	0.158		
Chronic Obstructive Pulmonary Disease						NS
No	343 (92.7%)	27 (7.3%)	Ref.	Ref.		
Yes	78 (82.1%)	17 (17.9%)	2.77 [1.41; 5.31]	**0.004**		
Smoking habits						
No Smoker	228 (93.8%)	15 (6.2%)	Ref.	Ref.	Ref.	Ref.
Smoker/Ex-Smoker	195 (87.1%)	29 (12.9%)	2.25 [1.18; 4.43]	**0.013**	2.652 (1.37; 5.34)	**0.005**
Chronic corticosteroid use						NS
No	390 (90.3%)	42 (9.7%)	Ref.	Ref.		
Yes	30 (93.8%)	2 (6.2%)	0.66 [0.10; 2.32]	0.566		
Preop albumin (g/dl)	40.3 (5.4)	37.7 (5.6)	0.93 [0.88; 0.98]	**0.004**	0.927 (0.88; 0.97)	**0.004**
Perioperative blood trasfusion						
No	378 (92.4%)	31 (7.58%)	Ref.	Ref.	Ref.	Ref.
Yes	48 (78.7%)	13 (21.3%)	3.31 [1.57; 6.67]	**0.002**	2.252 (1.02; 4.77)	**0.038**
Type of Surgery						NS
Ileocecal resection	13 (100%)	0 (0.0%)	–	–		
Right colectomy	363 (90.8%)	37 (9.2%)	Ref.	Ref.		
Extended right colectomy	50 (87.7%)	7 (12.3%)	1.39 [0.54; 3.14]	0.466		
Operating time (min)	180 (64.4)	159 (44.7)	0.99 [0.99; 1.00]	**0.034**		NS
Anastomosis technique						NS
Manual (hand-sewn)	216 (92.3%)	18 (7.7%)	Ref.	Ref.		
Stapled	210 (89.0%)	26 (11.0%)	1.48 [0.79; 2.83]	0.221		
Type of anastomosis						NS
Side to side manual	195 (92.4%)	16 (7.6%)	Ref.	Ref.		
Side to side stapled	106 (89.8%)	12 (10.2%)	1.38 [0.61; 3.04]	0.427		
End to side stapled	104 (88.1%)	14 (11.9%)	1.64 [0.76; 3.52]	0.207		
End to side manual	21 (91.3%)	2 (8.7%)	1.23 [0.17; 4.81]	0.802		
Reinforcement						
No	172 (85.1%)	30 (14.9%)	Ref.	Ref.	Ref.	Ref.
Yes	254 (94.8%)	14 (5.2%)	0.32 [0.16; 0.61]	< **0.001**	0.294 (0.14; 0.57)	< **0.001**

**Wald's Test.
AL: anastomotic leakage.
OR: Odds ratio.

Table 5
Association of the identified risk factors with the severity of the anastomotic leakage (mild and severe). Data are expressed as number of patients' n (%) or mean (SD).

	Mild AL n = 16	Severe AL n = 28	p-value[a]
Chronic Obstructive Pulmonary Disease			0.279
No	12 (44.4%)	15 (55.6%)	
Yes	4 (23.5%)	13 (76.5%)	
Smoking habits			0.176
No Smoker	8 (53.3%)	7 (46.7%)	
Smoker/Ex-Smoker	8 (27.6%)	21 (72.4%)	
Preop albumin (g/dL)	38.8 (3.7)	37.1 (6.4)	0.300 $
Perioperative blood transfusion			0.738
No	12 (38.7%)	19 (61.3%)	
Yes	4 (30.8%)	9 (69.2%)	
Reinforcement			0.343
No	9 (30.0%)	34 (70.0%)	
Yes	7 (50.0%)	7 (50.0%)	

AL: anastomotic leakage.
[a] chi-squared test. $ Student's t-test.

In recent years suture line reinforcement products have been developed to improve anastomotic healing outcomes.[33] Bio-absorbable (fibrin glue)[34] and semiabsorbable (bovine pericardial patches)[35] products have been studied, particularly in obesity surgery. None of these could demonstrate to be a protective factor to prevent AL. Also autologous patches like an omentum flap have been used as a buttressing agent. Analyzing a population of 112 colorectal patients, Tocchi et al. obtained less AL in the omentoplasty group (3.8% vs 11.8% of AL).[36]

In our series, a sero-muscular reinforcement with serosal approximation of the anastomosis decreased significantly AL rates. More importantly, the more ileocolic anastomoses were reinforced the less severe AL rates (grade C) were seen (Fig. 2). In 2008, 63 patients underwent an ileocolic anastomosis, without any patient receiving reinforcement and the AL rate was 15.8% (30.8% of which were radiologically documented collections successfully treated with antibiotics). Due to the high AL rate reported in 2008, the chief of the colorectal surgery department (S.B.) suggested to all surgeons of the department a seromuscular oversewing suture reinforcement of the ileocolic anastomosis with an institutional standardized technique as either running suture or interrupted inverting stitches on the serosal layer of the entire anastomotic line. Three surgeons of the colorectal unit started to implement this technique and due to the progressive reduction of the AL rate, this easy applicable technique is now widely implemented and accepted within the department of surgery for any kind of ileocolic anastomosis. In 2017, an ileocolic anastomosis was performed in 55 patients, with an anastomotic reinforcement in 96.4% (53 patients). Overall, in this group, **3** patients presented AL (5.4%) and all were mild AL with no need for reoperation. Of these three patients, two anastomoses had been reinforced (Fig. 2).

However, the role of suture line reinforcement in gastrointestinal surgery is conflicting in literature. Karam et al.,[37] who specifically evaluated the role of reinforcement in ileocolic anastomosis or ileostomy closure, found a strong reduction of anastomotic leak in reinforced patients (0% of 1862 patients), however without a group of comparison. Widmar et al. also described a protective effect of oversewing the anastomotic line in Crohn's disease patients undergoing an ileocolic resection.[38] Contrary, other studies do not support oversewing the anastomotic staple line to decrease the AL rate in ileocolic anastomosis.[39,40] Our findings seem to be in part contrary to the findings of the ESCP snapshot study on right sided colorectal resections[40] analyzing the sub-group of antiperistaltic side-to-side ileocolic anastomoses. It may be that oversewing just the apical staple line of the "Barcelona" anastomosis is not sufficient in preventing anastomotic dehiscence. In our experience, the cross-stapling in the apical line discourages the use of this technique.

Secondary objectives of the present study were to analyze the relationship of the aforementioned variables with the severity of AL (severe or mild). As widely documented in literature, we found that the presence of AL, and especially severe AL, is an independent risk factor that worsens patients' hemodynamic status, increases morbidity and mortality.[12,13,41–43]

The identification of various preoperative (patient-related) and operative (technical-related) variables as potential risk factors for AL enables identifying high-risk patients and allows to choose the best surgical strategy to prevent AL or to mitigate its severe clinical consequences.

Focusing only on ileocolic anastomoses in a homogeneous cohort of patients with a confirmed diagnosis of cancer strengthens this analysis. Analyzing different types of ileo-colic anastomoses in an inhomogeneous cohort of patients could have been an important confounder and as so a limitation of the study. Other limitations are its single center design and its retrospective nature. However, all the variables of the present series were prospectively collected before the design of the study and all were included in the analysis. Cases were not selected but consecutive in order to reduce the possible bias and to document their impact on the objectives.

Conclusion

In conclusion, this stud**y** focusing on a homogeneous cohort of patients treated for colon cancer in elective surgery revealed that poor nutritional status, smoking habits and perioperative blood transfusion are factors influencing negatively anastomotic dehiscence. Oversewing suture reinforcement of the anastomosis associates with a significantly reduced AL risk. Randomized and multicentric studies are required to definitely determine the role of the anastomotic reinforcement as a protective factor reducing AL in ileocolic anastomoses.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

All authors disclose no conflicts.

Acknowledgments

The authors thank Mr. Bernat Miguel, Data Manager of the

Colorectal Unit, General and Digestive Surgery, Bellvitge University Hospital and IDIBELL, University of Barcelona, for the statistical analysis.

References

1. Westreenen HL Van, IJpma FF, Wevers KP, et al. Reoperation after colorectal surgery is an independent predictor of the 1-year mortality rate. *Dis Colon Rectum*. 2011;54:1438–1442. https://doi.org/10.1097/DCR.0b013e31822c64f1.
2. Nesbakken A, Nygaard K, Lunde OC. Outcome and late functional results after anastomotic leakage following mesorectal excision for rectal cancer. *Br J Surg*. 2001;88:400–404. https://doi.org/10.1046/j.1365-2168.2001.01719.x.
3. Marra F, Steffen T, Kalak N, et al. Anastomotic leakage as a risk factor for the long-term outcome after curative resection of colon cancer. *Eur J Surg Oncol*. 2009;35:1060–1064. https://doi.org/10.1016/j.ejso.2009.02.011.
4. Mäkelä JT, Kiviniemi H, Laitinen S. Risk factors for anastomotic leakage after left-sided colorectal resection with rectal anastomosis. *Dis Colon Rectum*. 2003 May;46(5):653–660. https://doi.org/10.1007/s10350-004-6627-9.
5. Trencheva K, Morrissey KP, Wells M, et al. Identifying important predictors for anastomotic leak after colon and rectal resection: prospective study on 616 patients. *Ann Surg*. 2013;257:108–113. https://doi.org/10.1097/SLA.0b013e318262a6cd.
6. Law WL, Chu KW. Anterior resection for rectal cancer with mesorectal excision: a prospective evaluation of 622 patients. *Ann Surg*. 2004;240:260–268. https://doi.org/10.1097/01.sla.0000133185.23514.32.
7. Yamamoto T, Spinelli A, Suzuki Y, et al. Risk factors for complications after ileocolonic resection for Crohn's disease with a major focus on the impact of preoperative immunosuppressive and biologic therapy: a retrospective international multicentre study. *U Eur Gastroenterol J*. 2016;4:784–793. https://doi.org/10.1177/2050640615600116.
8. Rahbari NN, Weitz J, Hohenberger W, et al. Definition and grading of anastomotic leakage following anterior resection of the rectum: a proposal by the International Study Group of Rectal Cancer. *Surgery*. 2010;147:339–351. https://doi.org/10.1016/j.surg.2009.10.012.
9. Sørensen LT, Kirkeby LT, Skovdal J, et al. Smoking and alcohol misuse are major risk factors of anastomotic leakage in colorectal surgery. *Gastroenterology*. 2006;114:A43. https://doi.org/10.1016/s0016-5085(98)80174-1.
10. Frasson M, Flor-Lorente B, Rodríguez JLR, et al. Risk factors for anastomotic leak after colon resection for cancer: multivariate analysis and nomogram from a multicentric, prospective, national study with 3193 patients. *Ann Surg*. 2015;262:321–330. https://doi.org/10.1097/SLA.0000000000000973.
11. Choi HK, Law WL, Ho JWC. Leakage after resection and intraperitoneal anastomosis for colorectal malignancy: analysis of risk factors. *Dis Colon Rectum*. 2006;49:1719–1725. https://doi.org/10.1007/s10350-006-0703-2.
12. Kube R, Mroczkowski P, Granowski D, et al. Anastomotic leakage after colon cancer surgery: a predictor of significant morbidity and hospital mortality, and diminished tumour-free survival. *Eur J Surg Oncol*. 2010;36:120–124. https://doi.org/10.1016/j.ejso.2009.08.011.
13. Krarup P-M, Jorgensen LN, Andreasen AH, et al. A nationwide study on anastomotic leakage after colonic cancer surgery. *Colorect Dis: Off J Assoc Coloproctol G B Irel*. 2012;14:e661–e667. https://doi.org/10.1111/j.1463-1318.2012.03079.x.
14. Leichtle SW, Mouawad NJ, Welch KB, et al. Risk factors for anastomotic leakage after colectomy. *Dis Colon Rectum*. 2012;55:569–575. https://doi.org/10.1097/DCR.0b013e3182423c0d.
15. Hyman N, Manchester TL, Osler T, et al. Anastomotic leaks after intestinal anastomosis: it's later than you think. *Ann Surg*. 2007;245:254–258. https://doi.org/10.1097/01.sla.0000225083.27182.85.
16. Veyrie N, Ata T, Muscari F, et al. Anastomotic leakage after elective right versus left colectomy for cancer: prevalence and independent risk factors. *J Am Coll Surg*. 2007;205:785–793. https://doi.org/10.1016/j.jamcollsurg.2007.06.284.
17. Marinello FG, Baguena G, Lucas E, et al. Anastomotic leakage after colon cancer resection: does the individual surgeon matter? *Colorect Dis: Off J Assoc Coloproctol G B Irel*. 2016;18:562–569. https://doi.org/10.1111/codi.13212.
18. Segelman J, Mattsson I, Jung B, et al. Risk factors for anastomotic leakage following ileosigmoid or ileorectal anastomosis. *Colorect Dis: Off J Assoc Coloproctol G B Irel*. 2018;20:304–311. https://doi.org/10.1111/codi.13938.
19. 2015 European Society of Coloproctology collaborating group. The relationship between method of anastomosis and anastomotic failure after right hemicolectomy and ileo-caecal resection: an international snapshot audit. *Colorect Dis: Off J Assoc Coloproctol G B Irel*. 2017. https://doi.org/10.1111/codi.13646.
20. El-Hussuna A, Pinkney T, Zmora O, et al. Risk factors for unfavourable postoperative outcome in patients with Crohn's disease undergoing right hemicolectomy or ileocaecal resection. An international audit by ESCP and S-ECCO. *Colorect Dis: Off J Assoc Coloproctol G B Irel*. 2018;20. https://doi.org/10.1111/codi.13889.
21. Gustafsson P, Jestin P, Gunnarsson U, Lindforss U. Higher frequency of anastomotic leakage with stapled compared to hand-sewn ileocolic anastomosis in a large population-based study. *World J Surg*. 2015;39:1834–1839. https://doi.org/10.1007/s00268-015-2996-6.
22. Pyg C, Choy PYG FA. Cochrane Database of Systematic Reviews Stapled versus handsewn methods for ileocolic anastomoses (Review) Stapled versus handsewn methods for ileocolic anastomoses (Review). https://doi.org/10.1002/14651858.CD004320.pub3; 2011.
23. Ahrendt GM, Gardner K, Barbul A. Loss of colonic structural collagen impairs healing during intra-abdominal sepsis. *Arch Surg*. 1994;129:1179–1183. https://doi.org/10.1001/archsurg.1994.01420350077010.
24. Telem DA, Chin EH, Nguyen SQ, Divino CM. Risk factors for anastomotic leak following colorectal surgery: a case-control study. *Arch Surg*. 2010;145:371–376. https://doi.org/10.1001/archsurg.2010.40. discussion 376.
25. Iancu C, Mocan LC, Todea-Iancu D, et al. Host-related predictive factors for anastomotic leakage following large bowel resections for colorectal cancer. *J. Gastrointest. Liver Dis.: JGLD*. 2008;17:299–303.
26. IHJT De Hingh, De Man BM, Lomme RMLM, et al. Colonic anastomotic strength and matrix metalloproteinase activity in an experimental model of bacterial peritonitis. *Br J Surg*. 2003;90:981–988. https://doi.org/10.1002/bjs.4146.
27. Alves A, Panis Y, Trancart D, et al. Factors associated with clinically significant anastomotic leakage after large bowel resection: multivariate analysis of 707 patients. *World J Surg*. 2002;26:499–502. https://doi.org/10.1007/s00268-001-0256-4.
28. Schrock TR, Deveney CW, Dunphy JE. Factor contributing to leakage of colonic anastomoses. *Ann Surg*. 1973;177:513–518. https://doi.org/10.1097/00000658-197305000-00002.
29. Tartter PI. Blood transfusion and infectious complications following colorectal cancer surgery. *Br J Surg*. 1988;75:789–792. https://doi.org/10.1002/bjs.1800750822.
30. Jessen M, Nerstrøm M, Wilbek TE, et al. Risk factors for clinical anastomotic leakage after right hemicolectomy. *Int J Colorectal Dis*. 2016;31:1619–1624. https://doi.org/10.1007/s00384-016-2623-5.
31. Törkvist L, Månsson P, Raud J, et al. Role of CD18-dependent neutrophil recruitment in skin and intestinal wound healing. *Eur Surg Res*. 2001;33:249–254. https://doi.org/10.1159/000049714.
32. Jandhyala SM, Talukdar R, Subramanyam C, et al. Role of the normal gut microbiota. *World J Gastroenterol*. 2015;21:8836–8847. https://doi.org/10.3748/wjg.v21.i29.8787.
33. Ho YH, Ashour MAT. Techniques for colorectal anastomosis. *World J Gastroenterol*. 2010;16:1610–1621. https://doi.org/10.3748/wjg.v16.i13.1610.
34. Lee MGM, Provost DA, Jones DB. Use of fibrin sealant in laparoscopic gastric bypass fo the morbidly obese. *Obes Surg*. 2004;14:1321–1326. https://doi.org/10.1381/0960892042583824.
35. Kini S. A biodegradeable membrane from porcine intestinal submucosa to reinforce the gastrojejunostomy in laparoscopic Roux-en-Y gastric bypass: preliminary report. *Obes Surg*. 2001;11:469–473. https://doi.org/10.1381/096089201321209350.
36. Tocchi A, Mazzoni G, Lepre L, et al. Prospective evaluation of omentoplasty in preventing leakage of colorectal anastomosis. *Dis Colon Rectum*. 2000;43:951–955. https://doi.org/10.1007/bf02237357.
37. Karam C, Lord S, Gett R, Meagher AP. Circumferentially oversewn inverted stapled anastomosis. *ANZ J Surg*. 2018;88:E232–E236. https://doi.org/10.1111/ans.13803.
38. Widmar M, Cummings DR, Steinhagen E, et al. Oversewing staple lines to prevent anastomotic complications in primary ileocolic resections for Crohn's disease. *J Gastrointest Surg: Off J Soc Surg Aliment Tract*. 2015;19:911–916. https://doi.org/10.1007/s11605-015-2792-5.
39. Fleetwood VA, Gross KN, Alex GC, et al. Common side closure type, but not stapler brand or oversewing, influences side-to-side anastomotic leak rates. *Am J Surg*. 2017;213:590–595. https://doi.org/10.1016/j.amjsurg.2016.10.038.
40. Glasbey JC, Nepogodiev D, Battersby N, et al. The impact of stapling technique and surgeon specialism on anastomotic failure after right-sided colorectal resection: an international multicentre, prospective audit. *Colorect Dis: Off J Assoc Coloproctol G B Irel*. 2018;20:1028–1040. https://doi.org/10.1111/codi.14308.
41. Bakker IS, Grossmann I, Henneman D, et al. Risk factors for anastomotic leakage and leak-related mortality after colonic cancer surgery in a nationwide audit. *Br J Surg*. 2014;101:424–432. https://doi.org/10.1002/bjs.9395. discussion 432.
42. Krarup PM, Nordholm-Carstensen A, Jorgensen LN, Harling H. Association of comorbidity with anastomotic leak, 30-day mortality, and length of stay in elective surgery for colonic cancer: a nationwide cohort study. *Dis Colon Rectum*. 2015;58:668–676. https://doi.org/10.1097/DCR.0000000000000392.
43. Gessler B, Eriksson O, Angenete E. Diagnosis, treatment, and consequences of anastomotic leakage in colorectal surgery. *Int J Colorectal Dis*. 2017;32:549–556. https://doi.org/10.1007/s00384-016-2744-x.