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Alimentary Tract

The impact of colectomy and restorative procedure on pouch function after ileo-pouch-anal anastomosis in ulcerative colitis. The icon fun study on behalf of the Italian Society of Colon and Rectal Surgery (SICCR) Inflammatory Bowel Diseases committee

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ABSTRACT

Background: Available guidelines lack in indications on surgical standard in Ulcerative Colitis (UC)

Aims: To determine the role of surgical strategies of colectomy and proctectomy with pouch-anal anastomosis (IPAA) on functional outcomes in a nationwide population multicenter study. The secondary aims consisted of perioperative outcomes and complications.

Methods: Data on 379 patients who underwent total abdominal colectomy and proctectomy with ileo-pouch-anal-anastomosis (IPAA) with or without diverting ileostomy were retrospectively collected in a red cap multicenter-database searching for variables that could impact on pouch outcomes as cuffitis, pouchitis, anastomotic stenosis, pouch stenosis, failure or pathological Low-Anterior-Resection-Syndrome (LARS) score.

Results: Mesocolic dissection sealing vessels at major trunks and from medial to lateral are associated with better outcomes. Laparoscopy is associated with lower rate of cuffitis over time ($p = 0.028$). Mesentery lengthening is associated with higher pouchitis rate ($p = 0.015$) and earlier failure ($p < 0.0001$). Hand-sewn IPAA results in early anastomotic stenosis ($p = 0.00011$). The Transanal-Transsection and Single-Stapling Anastomosis (TTSS) showed to be protective against pouchitis. Extended dissection of adhesions correlates with lower rate of pouchitis-episodes ($p = 0.0057$).

Conclusions: The study highlights advantages of laparoscopy. New techniques such as TTSS promise further improvements. Mesentery lengthening correlates with high risk of pouch-failure and pouchitis, hand-sewn anastomosis increased risk of stenosis.

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See Appendix A.

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1. Introduction

Total proctocolectomy with ileo-pouch-anal-anastomosis (IPAA) is the treatment of choice for Ulcerative Colitis (UC) non responder to medical treatment [1,2].

Colectomy represents the “first step” of surgery in UC and Acute Severe Ulcerative Colitis (ASUC) being the main indication in acute setting [3].

A recent nationwide survey, completed by Italian IBD referral centres, showed that there is no consensus about the technique of dissection, vascular ligation, treatment of the omentum and management of rectal stump [4]. Disagreement exist about level of major vessels ligation, dissection of the mesocolon (lateral to medial or vice versa), starting approach from right or left colon, management of omentum or rectal stump. The laparoscopic approach, which should represent the gold standard as stated by recent guidelines, [3] has proven to be chosen for ASUC in 70 % of cases. Data are lacking about the role that such variability could have in jeopardizing or facilitating the second surgical step, in terms of adhesions or mesocolon retracted or inflamed (if not removed during colectomy) or complex rectal stump.

Proctectomy and pouch creation represent the “second step” in patients for whom a restorative treatment is feasible [5,3].

The restorative procedure could also be conducted in several ways, ranging from the approach (laparoscopy or laparotomy) to rectal dissection, to pouch shape or choice of anastomosis configuration [6].

The aim of this multicenter study was to assess the role of different surgical techniques adopted during colectomy and during restorative proctectomy on pouch functional results after stoma closure.

2. Methods

The Impact of COlectomy and restorative procedure oN pouch FUNction after ileo-pouch-anal anastomosis in Ulcerative Colitis (ICON FUN study) is a retrospective study based on data obtained from Red Cap prospectively maintained database of several Italian IBD Centres. The study was designed to compare operative results and functional outcomes of patients treated by colectomy, proctectomy and ileo-pouch-anal anastomosis; seventeen Italian Centers were invited and 10 of those accepted to participate: Policlinico Sant’Orsola – Malpighi [Bologna, Italy], Dipartimento di Scienze Biomediche, Humanitas University [Rozzano-Milano, Italy], Fondazione Policlinico Universitario Agostino Gemelli IRCCS – Università Cattolica S. Cuore – [Roma, Italy], Ospedale di Santa Maria delle Croci di Ravenna [Ravenna-Italy], ASST Rhodense- Ospedale Monumento ai Caduti [Rho-Milano, Italy], Università Federico Secondo [Napoli, Italy], Policlinico Universitario di Torvergata, [Torvergata-Roma, Italy], SOC Chirurgia Generale Ospedale di Pordenone [Pordenone, Italy], IRCCS Sacro Cuore Don Calabria Negrar di Valpolicella, [Verona-Italy], Ospedale Mauriziano ‘Umberto I’, [Torino, Italy].

2.1. Study population and inclusion/exclusion criteria

All consecutive patients with diagnosis of UC who underwent colectomy, proctectomy and pouch-anal anastomosis from January 2017 to December 2022 were included.

The only exclusion criterion was Crohn Disease.

Patients under the age of 18 and patients who denied the informed consent to the data processing were excluded.

2.2. Definitions and data of interest

Patients who were considered for this study were those who underwent colectomy (first stage) proctectomy and pouch creation with pouch anal anastomosis (IPAA) with or without ileostomy, and stoma closure were included. When the surgeon avoided creating the stoma a “two stage modified” procedure was performed.

Pre-operative characteristics, intra-operative findings and surgical procedures, post-operative morbidity, and long-term functional outcomes were collected and in case of missing data single centre’s investigator was contacted in order to fulfil all missing field.

At all the participating centres, the indication for surgery was scheduled after a multi-disciplinary meeting (MDM) and complete diagnostic work-up.

Data on age, gender, American Society of Anaesthesiology physical status classification system score (ASA), body mass index (BMI), smoke habits, familiarity, Haemoglobin level (Hb), Albumin level, C Reactive Protein (CRP), Mayo endoscopic score, The Montreal Classification for UC [7] previous medications with biologics and number of therapeutic shifts, as well as daily stool frequency were collected. Complications were classified using the Clavien-Dindo Classification. Class I and II complications were considered ‘minor’, class III and IV ‘major’, and death was classified as class V [8].

Post-operative follow-up was based on clinical evaluation at 3, 6 and 12 months post surgery, or depending on patients’ clinical conditions. Endoscopy was performed 12 months after surgery or in the case of suspected pouch inflammatory condition.

Data were collected before each surgical step.

2.3. Endpoint and outcome measures

2.3.1. Colectomy

The primary aim of the ICON FUN study was to assess if different surgical approaches during colectomy could have had an impact on pouch outcomes such as developing cuffitis, pouchitis, anastomotic stenosis, pouch stenosis.

The secondary aims consisted of perioperative surgical outcomes, complication rates, surgical time.

2.3.2. Proctectomy and pouch creation

The primary aim of the ICON FUN study was to assess if different surgical approaches during proctectomy could have an impact on pouch outcomes such as developing of cuffitis, pouchitis, anastomotic stenosis, pouch stenosis, pathological Low Anterior Resection Syndrome (LARS) score or pouch failure (need for pouch removal with permanent end ileostomy or ileostomy creation).

The LARS score is a fast and useful “patient reported” measure of function outcomes used to evaluate the severity of bowel dysfunction after rectal surgery by scoring the major symptoms of the syndrome: incontinence (flatus and liquid stool), frequent bowel movements, stool fragmentation/clustering, and urge. First evaluation of LARS has been assessed at first follow up examination 3 months after stoma closure.

The scores from each of the five questions are summed up to obtain a total score ranging from 0 to 42. LARS can be categorized into three groups: no LARS (0–20 points), minor LARS (21–29 points), or major LARS (≥ 30) [9].

The secondary aims consisted of perioperative surgical outcomes, complication rates, surgical time.

2.4. Statistical analysis

Continuous variables were expressed as median and interquartile range (IQR) and compared using two-tailed, unpaired, Mann-Whitney U test. Categorical variables were expressed as absolute value and proportions and compared using Fisher’s exact.

Logistic regression model using Firth’s bias reduction method was performed to assess the odds ratio of variables associated with pouch outcomes after the first surgical step (colectomy). Analysis was stratified by different operative strategies (laparoscopy or laparotomy, site of start approach, level of stich of major vascular trunks, mesocolic dissection, need for conversion).

Time-to-event estimates for surgical outcomes were calculated using the Kaplan Meier function and compared using the Log-rank test. Cox proportional hazard regression analysis was used to set up a predictive model simultaneously exploring the effects of the independent variables on surgical outcome in relation to time. Time to event analysis was stratified by different surgical factor (laparoscopy or laparotomy, two stage or three stage procedure, need for mesentery lengthening, dissection of adhesions, type of anastomosis).

LARs score was expressed as median and IQR and compared using Kruskal-Wallis rank sum test.

Results were expressed with 95% confidence intervals [95% CI] and the level of significance was set at $p \leq 0.05$. Statistical analysis was performed using R version 4.3.0 (R Foundation for statistical computing, Vienna, Austria).

2.5. Ethical

The study has been reported according the Strengthening The Reporting of Observational Studies in Epidemiology (STROBE) [7].

The Study was conducted according to the ethical standards of the Declaration of Helsinki [2013 version]; the study protocol was approved by the ethical committee of the promoting Centre, and subsequently by all local ethical committees of participating centres. All patients provided written informed consent before receiving any surgical procedure and for data auditing.

3. Results

Data on 410 patients who underwent surgery for UC in the study period (colectomy first and restorative proctectomy with or without ileostomy in a second time) were available from the participating centres; 31 (7,5%) of those were removed because of missing data. Hence, 379 (92,5%) patients were included in the analysis.

Median follow up was 43 months [IQR 26–58].

Table 1 shows baseline characteristics of all patients included in the study, including surgical strategies at the first surgery (colectomy) and surgical strategy at the second time (proctectomy and pouch creation). Operative times are also reported.

3.1. Baseline characteristics

There were 223 (58,8%) men and 156 (41,2%) women. Patients of each centre did not show differences in terms of gender, ASA score, haemoglobin level, BMI, albumin level, CRP, smoking habits, Mayo, Montreal e and s, previous use of biologic and number of lines. Patients from one centre were significantly older than others subsequently, the median age at surgery differed in the various centres from 34 [28–40] to 59 [41,4–71] years, respectively.

The duration of surgery (colectomy and proctectomy) has proven to be variable among different centres and, moreover, the mean surgical time for the laparoscopic colectomy was 200 min [IQR 163 –240] versus surgical time for open colectomy 140 min [IQR 120 –167], $p < 0,001$.

The mean surgical time for the laparoscopic proctectomy and pouch creation was 328 min [IQR 223,5–300] versus surgical time for open proctectomy 240 min [IQR 192,5–280], $p = 0,032$.

The baseline characteristics table shows distribution of independent and dependent variables of colectomy and proctectomy for each single centre.

Table 2 shows technical aspects and outcomes of Colectomy and Proctectomy.

3.2. Colectomy

Different intraoperative choices were analysed to assess if one or more of those could impact significantly on pouch outcomes such as: cuffitis, pouchitis, pouch stenosis or pouch failure.

The start approach from the right colon was associated with the stenosis of pouch anal anastomosis (Odds ratios 4,4) [CI 1,84–10,52] $p = 0,001$.

The mesocolic dissection from lateral to medial was associated with an increased risk of cuffitis (Odds ratios 2,42 [CI: 1,16–5,04] $p = 0,021$).

The subcutaneous placement of the rectal stump seems to be associate to increased risk of anastomotic stenosis (Odds Ratio 1.16 [CI: 0.06–23.93] $p = 0,05$).

Table 3 shows variables associated with pouch outcomes and complications after colectomy.

3.3. Proctectomy and pouch anal anastomosis

Fig. 1 reports the 60 months Kaplan and Meier time-to-event estimates for long term pouch survival and pouch outcomes globally and considering surgical strategies (three time or two steps modified), surgical approach (laparoscopy or laparotomy), need for application of mesentery lengthening techniques, type of rectal dissection technique (Knight and Griffen, TA-IPAA, TTSS, handsewn pouch-anal anastomosis after mucosectomy), need for dissection of adhesions (no dissection, dissection of more or less than 15 min). No significant differences were present between three stage procedures or two stage modified procedures.

Laparoscopic approach was associated with lower rate of cuffitis over time ($p = 0,028$) and with lower LARS (mean LARS 5 [IQR 2–20] $p = 0,02$), see Table 4.

The necessity of mesentery lengthening was associated with higher rate of pouchitis ($p = 0,015$) and earlier pouch failure ($p < 0,0001$).

All patients who underwent pouch-anal anastomosis following mucosectomy developed early anastomotic stenosis ($p = 0,00011$).

The TTSS technique showed to be protective against pouchitis but the difference over time was not statistically significant ($p = 0,096$).

Dissection for adhesions for more than 15 min was significantly associated with lower rate of pouchitis episodes ($p = 0,0057$).

A Cox's proportional hazard model (Table 5) was performed to identify the independent risk factors for pouch complications. The risk of developing cuffitis was significantly higher after open procedures if compared with laparoscopic approach (HR:2.16 [95%CI: 1.07–4.37], $p = 0,03$). The risk of developing cuffitis was significantly lower after the TTSS approach (HR: 0.27 [95%CI 0.09–0.79] $p = 0,01$). The risk of developing pouchitis was significantly higher after systematic application of techniques for mesentery lengthening (HR 1,59 [95% CI 1,02–2,47] $p = 0,03$) and decreases if a dissection of adhesions is performed (HR 0,50 [95%CI 0,28–0,87] $p = 0,01$). The risk of pouch anal anastomosis stenosis was significantly associated to hand sewn anastomosis following mucosectomy. (HR 22.84 [95%CI 2,58–202.38] $p = 0,005$) In addition the risk of pouch failure (necessity of pouch removal of creation of ileostomy) is significantly associated with a need for mesenteric lengthening (HR 9.29 [95%CI: 2.35–36.78] $p = 0,001$).

4. Discussion

Results of Icon Fun study confirmed the variability still existing among Italian IBD referral centres about surgical strategy regarding colectomy. Different operative choices were analysed to assess if one or more could impact significantly on pouch outcomes such

Table 1

Patients characteristics.

	Total Number of Patients 379	
Age (years). median [IQR] ¹	42	[29 – 56]
Gender. number (%)		
Male	223	(58.8%)
Female	146	(41.2%)
Smoking Habit. number (%)		
Active	26	(6.9%)
Previous	74	(19.5%)
Family History of IBD. number (%)	33	(8.7%)
Body Mass Index. median [IQR] ¹	22	[19 – 24.2]
ASA ² score. median [IQR] ¹	2	[2]
Haemoglobin (g/L). median [IQR] ¹	11.5	[10 – 13]
Albumin (g/L). median [IQR] ¹	33	[27 – 38]
C Reactive Protein (f/L). median [IQR] ¹	28.2	[10 – 80]
Bowel movements (per day). median [IQR] ¹	8	[5 – 11]
Mayo Endoscopic Score ² . number (%)		
0, 1, 2, 3.	7 (1.8%), 21 (5.6%), 105 (27.7%), 246 (64.9%)	
Montreal Classification, disease extent ⁴ . number (%). E1, E2, E3.	23 (6.1%), 136 (35.9%), 220 (58%)	
Montreal Classification, disease activity ⁵ . number (%). S0, S1, S2, S3.	6 (1.6%), 18 (4.7%), 138 (36.4%), 217 (57.3%)	
Preoperative Biological Therapy (30days). number (%)	302	(79.7%)
Surgical Approach. number (%)		
Open	51	(13.5%)
Laparoscopy	328	(86.5%)
Conversion rate. number (%).	13	(4%)
Surgical Strategy. number (%)		
Three stages	334	(88.1%)
Modified two stages	45	(11.9%)
Duration of surgery (minutes). median [IQR] ¹		
Open Colectomy	140	[120 – 167.5]
Laparoscopic colectomy	200	[163 – 240]
Open Proctectomy	240	[192.5 – 280]
Laparoscopic Proctectomy	265	[223.5 – 300]
Complications (Clavien-Dindo Classification ⁶). number (%)		
Colectomy		
0–2	356	(94%)
>3	23	(6%)
Proctectomy		
0–2	369	(97.4%)
>3	10	(2.6%)
Stoma reversal		
0–2	314	(98.7%)
>3	4	(1.3%)

¹ IQR: Interquartile Range.² American Society of Anaesthesiology Physical Status Classification System.³ Mayo Endoscopic Score. 1: inactive disease; 2: mild disease; 3: moderate disease; 4: severe disease.⁴ Montreal classification of disease extension: E1: ulcerative proctitis; E2: left-sided colitis; E3: Extensive colitis.⁵ Montreal classification of disease activity: S0: clinical remission; S1: mild disease; S2: moderate disease; S3: severe disease. ⁶ Clavien-Dindo classification of post-operative complications: 0–2: normal postoperative course or any deviation requiring pharmacological treatment, including parenteral nutrition and blood transfusion; >3 any complication requiring surgical, endoscopic, or radiologic intervention, life threatening complications requiring intensive care management, and patient death.

as: cuffitis, pouchitis, pouch stenosis, pouch failure or poor function estimated with low anterior resection syndrome score (LARSs-core).

Following pouch creation, a lot of patients reported significant increase in the number of faecal discharges, mostly during the night. Other typical symptoms may be incontinence, soiling, clustering, fragmentation or urgency. While most patients gain a new “lifestyle” much better than before surgery, a minority of those develop disabling symptoms compromising their quality of life. A standardization in carrying out functional follow up is lacking at the present time and every IBD unit adopt different protocols, tools or questionnaires without a consensus. In a recent narrative review of current literature, Vernon et al. underlined the big variability of validated scores used to assess the quality of life after IPAA surgery, such as *CGQOL* (Cleveland Global Quality of Life), *PFS* (Pouch Functional Score), *OS* (Oresland Score), *IBDQ* (Inflammatory Bowel Disease Questionnaire), *SF-36* (36-Item Short Form Health Survey), *WCGS* Wexner Continence Grading Scale [10]. The

Ileoanal Pouch Syndrome score (IPSS) has recently been introduced tailoring on pouch surgery by patient-reported outcomes, based on 7-bowel related symptoms and 7 consequences [11]. Complained symptoms are quite similar to those experienced by patients who develop LARS. After low or very low anterior resection a large percentage (ranging from 25 to 70) of patients complains symptoms including faecal urgency, frequent bowel movements, incontinence, soiling. This constellation of symptoms refers to the LARS. The aetiology is multifactorial starting from potential sphincter injury, alteration of anorectal motility, neuropathy, lumbar plexopathy whose symptoms are increased by pelvic sepsis [12,9].

The LARS score Italian version is validated for low rectal surgery and shows to be simple and fast whilst reflecting the quality of life for patients post IPAA surgery [13]. For those reasons we choose the LARS score as quality of life assessment for this study.

The ten participating centres offered a large cohort of patients with similar characteristics with the exception of one which treated a significantly older group. Previously, IPAA was not rec-

Table 2
Technical aspects and outcomes.

		Total Number of Patients 379	
Colectomy.			
Starting dissection from: number (%).	Left colon	309	(81.5%)
	Right colon	64	(16.9%)
	Transverse colon	3	(0.8%)
	Undeclared	3	(0.8%)
Mesenteric dissection. number (%).	Medial to lateral	272	(71.8%)
	Lateral to medial	103	(27.2%)
	Undeclared	4	(1.1%)
Mesenteric resection. Number (%)	Central	17	(4.5%)
	Pericolic	345	(91%)
	Undeclared	17	(4.5%)
	Proximal ligation	78	(20.6%)
Vascular control (left colon). number (%).	Distal ligation	298	(78.6%)
	Undeclared	3	(0.8%)
	Proximal ligation	88	(23.2%)
Vascular control (transverse colon). number (%).	Distal ligation	288	(76%)
	Undeclared	3	(0.8%)
	Subcutaneous ¹	94	(24.8%)
Rectal stump closure. number (%).	Intraperitoneal	249	(65.7%)
	Undeclared	36	(9.5%)
	Removed	106	(28%)
Omentum. number (%).	Preserved	269	(71%)
	Undeclared	4	(1%)
	Handsewn	3	(0.8%)
Pouch construction.			
Dissection of adhesions (more 15 min). number (%).		92	(24.3%)
Mesentery lengthening. number (%).		125	(33%)
IPAA ¹ technique. number (%).	Knight-Griffen	225	(59.4%)
	TA-IPAA	68	(17.9%)
	TTSS	83	(21.9%)
	Handsewn	3	(0.8%)
Length of rectal cuff. median [IQR] ²		3	[1 – 4]
Pouch outcomes			
Cuffitis. number (%).		32	(8.4%)
Pouchitis. number (%).		95	(25.1%)
IPAA stenosis. number (%).		23	(6.1%)
Pouch stenosis. number (%).		16	(4.2%)
Pouch failure. number (%).		12	(3.2%)
LARS score. median [IQR] ²		5	[2 – 22]

¹ Ileal-Pouch-Anal Anastomosis.

² Rectal stump stitched to the anterior abdominal wall, including mucous fistula.

ommended for patients older than 60 years due to poor functional outcomes. In a paper published by Colombo et al. the authors evaluated a cohort of 77 patients older than 65 years in comparison with 154 control younger patients. Postoperative complications and pouch failure were similar between the groups, with low rate of pouchitis, pouch failure with necessity of redo-pouch or permanent defunctioning. Elderly patients required more pharmacological treatment for complications (44% versus 28.5% Clavien-Dindo Grade II) and experienced more serious complications (20% versus 4.7% Grade IV and V) than younger patients and longer length of stay. Laparoscopy was associated with a shorter duration of surgery ($p = 0.0001$), and length of stay ($p = 0.0001$), and the same complication rate as open [14].

A systematic review published by K.E. Pederson et al. including 13 papers observed, after a median follow up of 62 months, rate of pouchitis, incontinence and pouch failure not statistically different between a group of patients aged from 50 to 65 years versus patients aged more than 65. Increasing age did not increase the rate of short and long term adverse events, including pouch failure. Those data suggest that the decision for IPAA construction should not be based on age alone [15].

In the present study the start approach from the right colon was associated with the stenosis of pouch anal anastomosis.

The approach from the right colon at colectomy was chosen in 64 cases (16.8%) of patients, being a small portion of the sample. In a paper from M. S. Vlug the authors analysed the effect of devascularization starting at the ileocolic artery as the first approach during colectomy, measuring the blood level of fatty acid

binding proteins (FABT), a marker of mucosa injury and ischemia, pre and postoperatively. The level of FABP in patients who underwent colectomy starting from ileocolic artery were significantly increased in postoperative days when compared with patients who underwent a left sided start approach. Moreover, similar outcomes were observed in patients treated with the same strategies but without IB. The study concluded that colectomy starting with ileocolic artery, caused a devascularization associated with prolonged intestinal mucosal ischemia [16]. It is not clear if such situation could cause a significant clinical inflammatory response, especially if in an emergency setting, and whether this may jeopardize the vascularization of the small bowel or of the rectal cuff.

The mesocolic dissection from lateral to medial was to be associated with increased risk of cuffitis and a worst LARS score. This approach was chosen in 103 patients (27.1%). The lateral to medial dissection could lead to seal the mesocolon close to the bowel, leaving in situ lymphatic tissue and vessels with same implication of above-mentioned ischemia. The dissection of mesocolon from lateral to medial is less adopted by laparoscopic surgeons with good expertise and worst results could be attributable to small volume of patients with acute presentation or, at the opposite, to presentation of patients with very serious acute conditions. It is widely believed that non-dedicated gastroenterologists send patients to referral centres just at the time of dramatic clinical worsening with life threatening conditions. At the same time a quote of patients operated on in peripheral hospitals for acute colitis surely exists. Those patients, once the burden of colitis is over, are taken in care for the restorative surgery from referral centres.

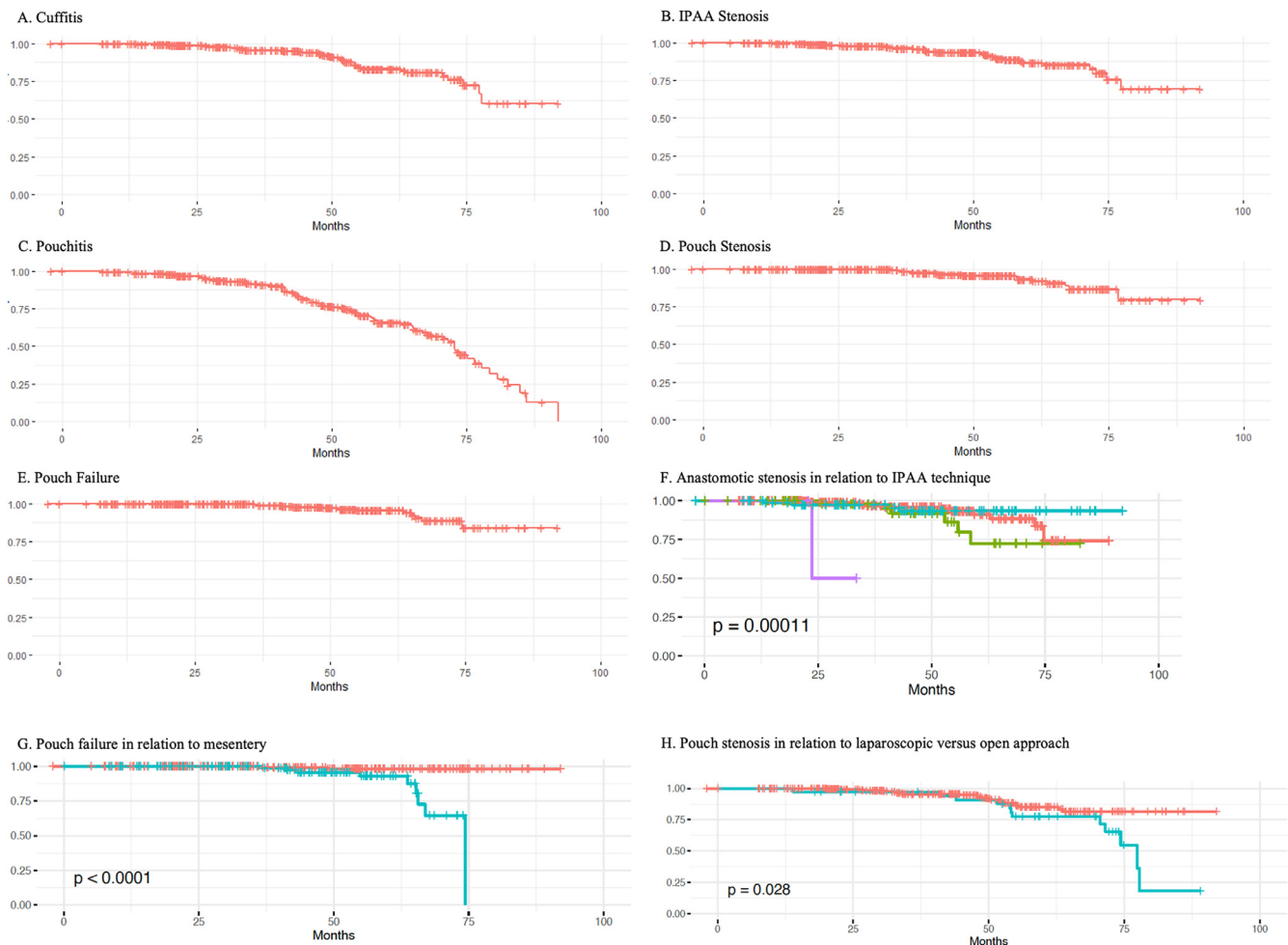


Fig. 1. Kaplan-Meier's time to event estimates.

The subcutaneous placement of the rectal stump was to be associated with increased risk of anastomotic stenosis. This result is hard to explain. The subcutaneous placement was adopted in 88 cases (23,2%).

Anastomotic IPAA stenosis have been reported in 21 patients (5,5%), most in the same centres that, in almost half patients, adopted the strategy to leave the rectal stump in subcutaneous tissue in suprapubic place [17]. A systematic review of rectal stump management during and after emergency total colectomy for acute severe ulcerative colitis published in 2019 analysed 476 patients and observed that the lowest reported pelvic sepsis rate was in patients with sub-cutaneous closure of the rectal stump and lowest wound infection rate was reported after intraperitoneal closure even if paying the highest rate of mortality. The authors concluded that subcutaneous placement of the rectal stump was associated with the lowest morbidity and mortality rate [18]. The current trend in referral centres is to leave a long rectal stump intraperitoneally, at the level of sacral promontory [19].

The open approach was associated with worst LARS and this evidence could reflect a low confidence with emergency colectomy in centres with also lower experience in pouch creation. Laparoscopic surgery even in emergency setting is highly recommended from ECCO guidelines and demonstrated to be safe and feasible worldwide [20,3]. The laparoscopic approach showed significantly longer surgical time when compared to open approach. Among different centres there was a vast variability in terms of duration of surgery. Currently the literature and guidelines are lacking in offering a standardized approach to colectomy for ASUC [4]. To

our knowledge just one paper has been published proposing a sequential approach in order to reduce operative time and complications of laparoscopic colectomy for such emergency surgery [21]. The authors showed results of a systematically applied "ten steps" standardized technique for laparoscopic colectomy (SACCO) with a significant reduction of operating time (144 vs. 224 min; $p < 0.0001$) when compared to the traditional laparoscopic approach. The SACCO technique presented a trend to fewer major complications (6.8% vs. 8.3%), less readmissions (2.3% vs. 13.5%; $p = 0.01$), and shorter postoperative hospital stay (7.2 vs. 8.8 days; $p = 0.003$) being a safe and reproducible surgical approach.

Concerning proctectomy and pouch creation no significant differences have been shown between three stages or two stages modified strategy.

Laparoscopic approach was associated with a lower rate of cuffitis over time. This result aligns with what emerged from analysis on colectomy and highlights that the laparoscopic approach is associated with better outcomes [6,3]. Laparoscopy is the preferred approach to colorectal resection. Significant evidence is available in the literature supporting this recommendation, with several papers [22] reporting benefits in terms of complications, functional outcomes, cosmesis, and quality of life and a single RCT including long-term results [23].

Laparoscopy should be offered for elective and emergent segmental and total colectomy and for reconstructive surgery. A referral centre for IBD should propose laparoscopic approach even in patients with previous abdominal surgery. The laparoscopic approach showed benefits over open surgery in IPAA with less blood

Table 3 Logistic regression model, using Firth's bias reduction method, to assess the odds ratio of variables associated with pouch outcomes and complications after colectomy.

	Cuffitis			Pouchitis			IPAA ¹ Stenosis			Pouch stenosis		
	OR ²	95% CI ³	p	OR ²	95% CI ³	p	OR ²	95% CI ³	p	OR ²	95% CI ³	p
	Starting dissection from:	1.49	0.63–3.55	0.3	1.21	0.66–2.21	0.51	4.4	1.8–10.5	0.001	0.43	0.08–2.33
Right colon	1.49	0.008–29.7	0.8	0.41	0.02–7.95	0.55	3.1	0.1–65.5	0.5	2.49	0.12–50.43	0.6
Transverse colon	2.4	1.1–5	0.02	0.67	0.38–1.17	0.1	1.7	0.7–4.1	0.24	0.27	0.05–1.48	0.07
Medial to lateral	0.6	0.15–2.34	0.34	0.34	0.13–0.91	0.03	2.4	0.14–41.71	0.4	0.24	0.06–1.01	0.09
Lateral to medial	0.55	0.2–1.55	0.2	0.55	0.29–1.04	0.8	1.8	0.75–4.6	0.2	0.9	0.28–3.1	0.9
Proximal ligation	1.7	0.6–4.3	0.3	1.3	0.7–2.3	0.3	0.5	0.2–1.2	0.1	1.93	0.5–7.5	0.3
Distal ligation	0.4	0.05–3.3	0.42	0.34	0.04–2.78	0.34	1.1	0.06–23.9	0.9	0.05	0–2.77	0.19
Proximal ligation (transverse colon).	0.11	0.01–0.87	0.07	0.6	0.08–4.6	0.6	0.3	0.03–6.55	0.41	0.41	0.02–8.4	0.6
Distal ligation	2.47	0.83–7.37	0.134	0.81	0.30–2.16	0.669	0.93	0.17–5.15	0.938	0.42	0.02–7.29	0.499
Mucous fistula	1.3	0.23–7.3	0.9	0.9	0.27–3.24	0.93	0.53	0.03–9.2	0.63	0.68	0.04–12	0.78
Subcutaneous												
Intraoperative												
Laparotomy												
Laparoscopy												
Conversion to laparotomy.												
No												
Yes												

¹ Ileal-Pouch-Anal Anastomosis.

² Odds Ratio.

³ Confidence Interval.

Table 4 Lars score.

Pouch construction	LARS score		
	Mean	IQR ¹	p
Surgical Strategy			
Three stages	5.5	2–22	
Modified two stages	4.5	2–20	0.8
Mesentery lengthening			
Yes	4	2–26	
No	7	2–22	0.5
IPAA ² technique			
Knight-Griffen	8	2–22	
TA-IPAA	8	4–16	
TTSS	4	2–21	
Handsewn	20	11–28	0.57
Dissection of adhesions			
< 15 min	5	2–22	
> 15 min	9	2–24	0.8
Surgical Approach			
Open	13	2–27.5	
Laparoscopy	5	2–20	0.02

¹ IQR: Interquartile Range.

² Ileal-Pouch-Anal Anastomosis.

loss, decreased time until bowel movements and a regular diet, improved cosmesis, lower morbidity and fertility rate that may be superior to that achievable after open IPAA [24]. Same results have been recently published concerning male fertility [25]. Furthermore a laparoscopic approach, as stated by ECCO guidelines, has proven to be superior allowing to achieve a distal rectal dissection in order to obtain a cuff no longer than 2 cm [26,6].

The necessity of mesentery lengthening was associated with higher rate of developing pouchitis and earlier pouch failure. Techniques of mesentery lengthening are in abundance and wide-ranging from simple manoeuvres of dissection of the root of mesentery or stepladder incisions to ligation of superior mesenteric vessels.

Techniques which require major vessel sealing are dangerous and a recent paper underlined the high percentage of postoperative complications and risk of pouch ischemia or failure [27]. The authors reported postoperative outcomes showing an overall surgical complication rate of 20.6%, and reoperation rate of 6.1%. Two patients underwent a pouch excision due to postoperative ischemia, despite no evidence of poor blood supply being observed during the primary pouch surgery. An additional paper from Toshimitsu Araki reported different lengthening techniques performed on 120 patients such as division of ileocecal artery, superior mesenteric artery and preservation of the vascular arcade. Despite those techniques allowed to perform tension-free pouch-anal anastomosis in almost all patients, complications occurred in 19% of patients, more frequent in those receiving steroids [28]. The above-mentioned considerations could explain the increased risk of developing pouchitis or pouch problems ischemia related, probably worsened by a compromised venous flow.

All patients who underwent pouch-anal anastomosis following mucosectomy developed early anastomotic stenosis. The literature reports a rate of anastomotic strictures ranging from 10 to 17%. In a large, retrospective study, Kirat et al. reported the results on almost 500 patients from a single institution, showing better outcomes and quality of life in patients with stapled IPAA when compared with those who underwent an handsewn pouch-anal anastomosis. The rate of anastomotic stricture, septic complications and pouch failure was significantly higher. Anastomotic stenosis correlates with difficulties in emptying the pouch and increased frequency of nocturnal seepage, necessity of pad usage, reduced diet and social and work restrictions [29,30]. Fibrotic strictures are usually related to intraoperative or postoperative complications, such as is-

Table 5
Cox's proportional hazard ratio (HR) of pouch outcomes in relation to surgical technique of proctectomy and ileo-pouch-anal anastomosis (IPAA).

	Cuffitis			Pouchitis			IPAA Stenosis			Pouch Stenosis			Pouch Failure		
	HR ¹	95% CI ²	p	HR ¹	95% CI ²	p	HR ¹	95% CI ²	p	HR ¹	95% CI ²	p	HR ¹	95% CI ²	p
Surgical strategy															
Three stages															
Modified two stages	2.1	0.8–5.5	0.1	1.38	0.7–2.7	0.37	0.47	0.06–3.45	0.45						
Surgical approach															
Laparoscopy		1.07–4.37	0.03	0.63	0.34–1.1	0.01	1.19	0.48–2.98	0.7				0.33	0.04–2.55	0.3
Laparotomy	2.1														
Mesentery lengthening															
Yes															
No	0.72	0.32–1.65	0.43	1.59	1.02–2.47	0.03	0.97	0.42–2.25	0.9	2.21	0.76–6.38	0.1	9.29	2.35–36.8	0.001
IPAA ³ technique															
Knight-Griffen	0.44	0.1–1.4	0.1	1.5	0.9–2.5	0.15	1.5	0.6–3.7	0.41	0.5	0.06–3.9	0.5	3.67	0.98–13.7	0.054
TA-IPAA	0.27	0.1–0.8	0.01	0.7	0.4–1.1	0.12	0.5	0.1–1.43	0.18	1.5	0.51–4.28	0.4	1.2	0.29–5.16	0.78
TTSS	0			0			22.8	2.5–202	0.005						
Handsewn															
Dissection of adhesions	0.9	0.4–2.2	0.8	0.78	0.49–1.24	0.29	0.89	0.31–2.58	0.8	1.07	0.31–3.68	0.9	1.42	0.37–5.39	0.6
<15 min	1.1	0.5–2.7	0.7	0.5	0.28–0.87	0.01	2	0.78–5.4	0.1	0.88	0.22–3.55	0.8	0.25	0.23–2.39	0.2
>15 min															

¹ Hazard Ratio.

² Confidence Interval.

³ Ileal-Pouch-Anal Anastomosis.

chemia and anastomotic leak, abscess or fistula. Chronic inflammation, from cuffitis or Crohn's disease, may also result in stricturing. Diagnosis is based on clinical examination and pouchoscopy [31].

The transanal-transection and single stapling anastomosis (TTSS) technique showed to be protective against pouchitis even if the difference over time was not statistically significant. The TTSS approach was first proposed by A. Spinelli and met widespread acceptance as well as the transanal-total-mesorectal excision (TaTME) before, providing a bottom-up approach to rectal dissection, transection and anastomosis. The techniques have proven to be both safe and effective as long as it is adopted in centres with a high volume and expertise [32]. Notwithstanding, the TaTME has been abandoned by many surgeons because of intraoperative injuries due to challenging manoeuvres during the rectal dissection and concerns on long term oncological results. The TTSS has gained consensus, and concerning pouch surgery seems to have overcome the limitation of traditional double-stapling technique, being precise in cuff length, allowing a symmetrical section of the rectal stump perpendicular to his own axis. In a recent paper from Spinelli et al. the authors presented results of 130 patients, 46 undergoing double-stapling technique and 84 undergoing single-stapled ileo-pouch anal anastomosis. The rectal cuff length was shorter after TTSS technique and functional parameters demonstrated significantly lower urgency (8% versus 30%) [33].

Dissection for adhesions for more than 15 min was significantly associated with lower rate of pouchitis episodes. The lysis of the adhesions was always performed through open or minimally invasive technique started mobilizing the root of the mesentery from the head of the pancreas and dissecting other small bowel adhesions. Moreover, the right mesocolon, left in place after colectomy with the intent of ileocecal arch preservation, often adheres to the mesentery and its dissection pays some minutes more [34]. Another step of dissection is performed around the rectal stump in order to start the rectal mobilization taking off all adherent structures [20,35]. Obtaining an optimal mobilization could offer a “tension free” anastomosis with lower risk of ischemic events and better outcomes.

Globally, pouch complications of the entire study population, were lower when compared with numbers of literature.

Pouch stricture has remained relatively constant although increased experience in UC surgery and its incidence varies between 5% and 38% [36]. A meta-analysis published in 2005 with 9317 patients reported stricture complication following IPAA to be 9.2% [37]. In this series the rate of pouch strictures aligned around 4.2%.

One of the most common inflammatory outcome of IPAA is pouchitis, which affects 44% of all patients with follow up longer than 5 years [38]. The rate of pouchitis in this series of patients was 25 % at 60 months.

Cuffitis represents a common complication after IPAA surgery and increased after standardization of the stapled anastomosis with incidence rate more than 20% [39]. This inflammatory complication typically responds to topic therapy with mesalamine, however, refractory patients may necessitate surgical intervention with mucosectomy or re-do pouch anal-anastomosis with a risk up to 15% of pouch failure. The rate of cuffitis in this study populations was 8.4%.

The rate of IPAA patients affected by anastomotic stricture is reportedly 14% and the stricture is usually associated with local ischemia or anastomotic tension. All manoeuvres of mesentery lengthening are key step to avoid stricture formation minimizing the traction on the reservoir. The management of pouch-anal strictures should be conservative having mechanical dilation more than 80% success rate. The rate of anastomotic strictures in this series of patients is around 6%.

The 10-year risk of pouch failure is reported to be approximately 6% [40].

Our series showed a rate of pouch failure of 3.2% even if estimated on a shorter follow up (60 months). Pouch failure derives from the mixture of infectious, inflammatory, or mechanical complications such as pelvic sepsis due to an anastomotic leak resulting in sinus or fistula [37]. Inflammatory complications include pouchitis, cuffitis, and Crohn's disease. Mechanical causes of failure result in obstruction and/or pouch dysfunction.

Limitations of this study are mainly represented by its retrospective nature with some missing data and difficulty in data reporting. To our knowledge this is the first publication describing surgical strategies and results of IBD centres in Italy, offering a snapshot on current trend of UC surgical treatment.

5. Conclusions

The IconFun study confirmed variability still existing among Italian IBD centres about surgical strategies for colectomy. Emergency colectomy showed better results in high volume centres with more standardized steps such as mesocolic dissection from medial to lateral and approach to left colonic vessels first. Laparoscopic approach was associated with better functional outcomes. Mesentery lengthening correlated with high risk of pouch failure and pouchitis. Hand-sewn anastomosis increased the risk of anastomotic stenosis and pouch failure.

It should be useful to establish guidelines on emergency surgery in case of acute severe ulcerative colitis in order to standardize the first time of UC surgery. A "tension free" IPAA, with the help of accurate dissection of adhesions and mobilization of the mesentery could improve functional results. TTSS technique proved heightened results in terms of pouchitis rates but further investigations are needed.

Data availability statement

The dataset generated and analysed during the current study are available from the corresponding author on reasonable request.

Declaration of competing interest

All the authors declare to not have any financial interest directly related to the work and to not have any conflict of interest. No funds were used for the research titled **The Impact of COlectomy and restorative procedure oN pouch FUNction after ileo-pouch-anal anastomosis in Ulcerative Colitis**. The ICON FUN study on behalf of the Italian Society of Colon and Rectal Surgery (SICCR) Inflammatory Bowel Diseases committee. Michela Mineccia and co-authors: Alessandro Ferrero, Matteo Rottoli, Antonino Spinelli, Luigi Sofò, Gianpaolo Ugolini, Giuliano Barugola, Giacomo Ruffo, Andrea Braini, Gaetano Luglio, Giuseppe Sica, Gianluca M. Sampietro, Paolo Massucco, Federico Fazio, Serena Perotti, Giovanni Castagna, Benedetta Petrello, Elena Brusa, Argentina Tiano, Giacomo Calini, Tommaso Violante, Stefano Cardelli, Michele Carvello, Stefano De Zanet, Nicolas Avellaneda, Franco Sacchetti, Mauro Giambusso, Giacomo Salina, Nicola Cracco, Angela Variola, Alessia Todeschini, Francesco Tumminelli, Antonio Miele, Francesca Tropeano, Michele Cricri, Brunella Pirozzi, Valeria Usai, Caterina Baldi, Carlo Alberto Manzo.

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