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Outcomes from elective colorectal cancer surgery during the SARS-CoV-2 pandemic

COVIDSurg Collaborative*

A complete list of the investigators is included in Appendix

Corresponding author: Mr Aneel Bhangu, NIHR Global Health Research Unit on Global Surgery, Heritage Building, University of Birmingham, Mindelson Way, Birmingham, UK, B15 2TH. Correspondence to: A.A.Bhangu@bham.ac.uk. ORCID ID: 0000-0001-5999-4618

Co-author: Dr Elizabeth Li, NIHR Clinical Research Fellow, University of Birmingham, Birmingham, UK.

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Abstract

Aim: This study aimed to describe the change in surgical practice and the impact of SARS-CoV-2 on mortality after surgical resection of colorectal cancer during the initial phases of the SARS-CoV-2 pandemic.

Method: This was an international cohort study of patients undergoing elective colon or rectal cancer resection, without preoperative suspicion of SARS-CoV-2. Centres entered data from their first recorded case of COVID-19 until 19 April 2020. The primary outcome was 30-day mortality. Secondary outcomes included anastomotic leak, postoperative SARS-CoV-2, and a comparison with a pre-pandemic European Society of Coloproctology cohort data.

Results: From 2073 patients in 40 countries, 1.3% (27/2073) had a defunctioning stoma and 3.0% (63/2073) had an end stoma instead of an anastomosis only. 30-day mortality was 1.8% (38/2073), the incidence of postoperative SARS-CoV-2 was 3.8% (78/2073), and the anastomotic leak rate was 4.9% (86/1738). Mortality was lowest in patients without a leak or SARS-CoV2 (14/1601, 0.9%), and highest in patients with both a leak and SARS-CoV-2 (5/13, 38.5%). Mortality was independently associated with an anastomotic leak (adjusted odds ratio 6.01, 95% confidence interval 2.58-14.06), postoperative SARS-CoV-2 (16.90, 7.86-36.38), male sex (2.46, 1.01-5.93), age >70 years (2.87, 1.32-6.20), and advanced cancer stage (3.43, 1.16-10.21). Compared to pre-pandemic data, there were fewer anastomotic leaks (4.9% versus 7.7%), an overall shorter length of stay (6 versus 7 days), but higher mortality (1.7% versus 1.1%).

Conclusion: Surgeons need to further mitigate against both SARS-CoV-2 and anastomotic leak when offering surgery during current and future COVID-19 waves based on patient, operative, and organisational risks.

What does this paper add to the literature?

Mortality associated with anastomotic leak and postoperative SARS-CoV-2 during the COVID-19 pandemic was extremely high. A relatively small change in stoma practice was seen. Surgeons need to robustly mitigate against both SARS-CoV-2 and anastomotic leak when offering surgery during future waves of COVID-19 , based on patient, operative, and organisational factors.

Introduction

During the early phases of the COVID-19 pandemic, there was uncertainty as to the impact of perioperative SARS-CoV-2 on surgical patients and a growing scarcity of intensive care capacity [1, 2]. Guidelines emerged which recommended changing anastomotic practice in favour of forming defunctioning stomas or end stomas in patients who would have previously only had an anastomosis [3-6]. The first anticipated benefit was to diminish the severity and volume of postoperative anastomotic leaks during a time when the impact of the novel coronavirus was unknown [7]. The second was to reduce the requirement for intensive care when hospital resources were being redirected to the pandemic response [8]. The third was to reduce complications that lead to increased length of hospital stay, in order to release bed space and minimise risks of nosocomial infection [9, 10].

Subsequent data have confirmed the detrimental effect of perioperative SARS-CoV-2, showing a 51.2% rate of postoperative pulmonary complications and a 30-day mortality rate of 23.8% [11]. Despite outbreaks, cancer surgery must continue in order to prevent an overwhelming number of delayed operations, a possible increase in emergency procedures and a significant decline in population health [12].

The extent of new stoma formation during the first phases of the pandemic and the subsequent patient related outcomes are unknown. In addition, the impact of anastomotic leaks and postoperative SARS-CoV-2 infection on mortality was unknown. This study aimed to fill these knowledge gaps and to produce patient level outcome data that would inform patient selection and informed consent.

Methods

Study design

This was a planned specialty analysis of adult patients undergoing elective colonic and rectal cancer resection in a prospective international multicentre cohort study of patients undergoing elective surgery without preoperative suspicion of SARS-CoV-2 [13]. Study approvals for participating hospitals were secured by Local Principal Investigators before entry into the study and data collection. The study protocol was either registered as a clinical audit with institutional review, or a research study obtaining ethical committee approval dependent on local and national requirements. Data were collected online and stored on a secure server running the Research Electronic Data Capture (REDCap) web application [14], based in the University of Birmingham, UK. Any hospital performing elective colon or rectal cancer surgery in countries affected by the COVID-19 pandemic were eligible for participation. Hospitals were required to collect data on consecutive eligible patients from the date of their first recorded case of COVID-19 until April 19th, 2020.

Patients and procedures

All adult patients, aged 18 years and over, who underwent elective colonic or rectal cancer resectional surgery with curative intent, were eligible. Palliative operations, including those where the tumour was left in situ (e.g. formation of end stoma without resection or bypass procedures) were excluded. Consecutive eligible patients were identified from multidisciplinary team meetings, operating lists and outpatient or telemedicine clinics. Day of surgery was defined as day zero, with patients followed up for 30 days postoperatively using routine follow-up pathways. Patients who had an operation for suspected cancer which subsequently was shown to be a pre-invasive lesion after histological examination (e.g. high-grade dysplasia, carcinoma in situ) were still included in this study. However, patients who had an operation for a suspected cancer but who had a histologically benign lesion were excluded. Elective surgery was defined as any surgery booked in advance of a planned admission to hospital [15].

Patients who were suspected or confirmed to have SARS-CoV-2 infection at the time of surgery, either through nasopharyngeal swab and quantitative Reverse Transcription Polymerase Chain Reaction, CT thorax, or clinical symptoms consistent with COVID-19, were excluded from these analyses.

Data variables

Baseline patient characteristics included age, sex and American Society of Anaesthesiologists (ASA) physical status classification [16]. Age was collected as deciles of years as a categorical variable. ASA was analysed as grades 1-2 versus grades 3-5. Disease characteristics included baseline tumour, node, metastases (TNM) stage prior to surgery, or neoadjuvant treatment. The TNM stage was used to calculate the patients' baseline cancer disease stage. Disease stages were grouped for analysis as stage I or stage II versus stage III or stage IV. For patients with cancers involving the rectum, data on neoadjuvant radiotherapy and the duration of therapy (long course or short course radiotherapy) were also analysed. Operative variables collected included the operative procedure performed, if a defunctioning or end stoma was formed, the operative approach (minimally invasive, minimally invasive converted to open, or open), the specialty and grade of the lead surgeon (consultant or trainee, colorectal or general surgeon), and whether a stapled or hand sewn technique was used for the anastomosis where applicable. We did not specify the precise nature of minimally invasive surgery as there are many variants, but we know from previous international studies that >95% of minimally invasive operations are laparoscopic [17, 18]. For analysis, operative procedures were grouped anatomically into right resection, left resection, rectal resection and total/subtotal/panproctocolectomies. A full list of operative procedures is included in Supplementary Table 1.

Outcomes

The primary outcome measure was mortality within the 30 days following surgery. Secondary outcome measures were anastomotic leak, admission to critical care (including high dependency areas), postoperative SARS-CoV-2 infection, and total length of hospital stay up to 30 days after surgery. Postoperative SARS-CoV-2 infection was defined as a positive swab or CT thorax in line with locally implemented protocols, or a clinical diagnosis of symptoms in keeping with COVID-19 in patients where no swab test or CT scan was available.

Change in anastomotic practice due to COVID-19

Data were collected on the intraoperative decision on stoma formation. Where patients had a stoma, surgeons were asked if this was their “normal practice” or a “change in practice due to COVID-19”. The group with stoma created as a change in practice were labelled “COVID-end-stoma” or “COVID-defunctioning-stoma” for tables and analyses. If the patient had a stoma formed and the surgeon indicated a “change in practice due to COVID-19”, they were asked to list all the reasons that applied to that case for this change (Supplementary Figure 1).

Pre-pandemic data

Pre-pandemic data on colorectal cancer surgery were obtained from published European Society of Coloproctology (ESCP) 2015 Right Hemicolectomy Audit [19-21] and the 2017 Left Colon, Sigmoid and Rectal Resections Audit data [18, 22]. Data from 5792 patients from 54 countries undergoing segmental resection for a colonic or rectal cancer were used for comparison to the equivalent cohort undergoing surgery during the pandemic. This data provided a contemporaneous and detailed comparison of case selection and outcomes during the pandemic and pre-pandemic periods. Data were not presented in these studies for total or subtotal colectomy, so no comparison was made with these operation types. TNM staging data were not available from the 2015 Right Hemicolectomy Audit and therefore comparison was not made in that field.

Statistical analysis

The study was conducted according to guidelines set by the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement for observational studies [23]. Chi-squared ($\chi 2$) test were used to compare differences in categorical data apart from when cell sizes were small, where Fisher's exact tests were used. Continuous non-parametric data were presented as medians and interquartile ranges and median differences between groups were compared using the Mann-Whitney U test. Missing data were included in summary tables.

For the primary outcome of 30-day mortality, a multilevel logistic regression was used to evaluate the impact of postoperative SARS-CoV-2 and anastomotic leak on death after surgery, summarised using odds ratios (OR) with 95% confidence intervals (95% CI). Country was included in the model as a random effect. The model also included clinically plausible preoperative and intraoperative factors in order to adjust for covariates and reduce risk of confounding factors (Age, sex, ASA grade, disease stage and operation type). Chi-squared tests and Fisher's exact tests were using to compare outcomes for those with a COVID-Stoma and those who did not. Similar methods were used to compare pandemic data with published pre-pandemic data. Analysis were performed used Stata SE version 16.1, (StataCorp, Texas, United States of America).

Results

Patients and disease characteristics

This analysis included 2073 patients undergoing resection of a colonic or rectal cancer in 270 hospitals from 40 countries (*Supplementary table 2*). Of these patients, 1236 (59.6%) were men (*Table 1*). Overall, 1420 patients (68.7%) were ASA grade 1-2 and 1288 (62.1%) patients had a disease stage I-II. Of 947 patients who had an operation involving the rectum (including panproctocolectomies), 89 (9.4%) patients received short course and 206 (21.8%) received long course neoadjuvant radiotherapy.

Of the 2073 patients, 785 (37.9%) had an open approach and 1186 (57.2%) had a minimally invasive approach. 102 (4.9%) had attempted minimally invasive surgery with conversion to an open operation. Of patients who had an anastomosis, 85.6% (1474/1722) had a stapled anastomosis. The lead surgeon in the majority of operations was a colorectal consultant (1522/2060, 73.9%), with a trainee as lead operator in 10.5% of procedures (217/2060).

Change in anastomosis (COVID-stoma) and outcomes

The overall rate of stoma formation was 34.2% (708/2073), which was more frequent than the rate of 27.2% in the pre-pandemic era (1573/5792). The change in practice of patients having a COVID-stoma was small; 4.3% (90/2073) of all patients (*Table 2*). Of patients with a new COVID-stoma, 70% (63/90) had an end stoma, which is far higher than the pre-pandemic rate for end stoma formation of 43.6% (686/1573) (*Table 5*). Colorectal trainees were more likely to be the named lead surgeon when defunctioning COVID-stomas were formed (8.3% [11/133]) when compared to colorectal consultants (0.9% [13/1521]) and general surgical consultants (0.6% [2/322]) *Table 2*. This contrasts with the pre-pandemic era when a colorectal trainee was the named lead surgeon in 4.4% (97/2218) of procedures where a stoma was formed. More COVID-end-stomas were formed in patients undergoing rectal resections, in those who had an open approach to surgery and in those who received either no neoadjuvant therapy or long course neoadjuvant radiotherapy (*Table 2*). This is also reflected in an increase in the number of end stoma formations in rectal resections during the pandemic era (27.3%, 255/935) when compared to the pre-pandemic era (23.7%, 613/2579) and a decrease of formation of anastomosis without defunctioning stoma during the pandemic (37.4%, 350/935) compared to pre-pandemic (42.8%, 1103/2579). The proportion of COVID-stomas compared to all stomas is shown in *Supplementary table 3*.

Of all rectal resections, 7.4% (69/935) received a COVID-stoma (Figure 1), representing 76.7% of all COVID-stomas (n=90). In right colonic resections, 11 COVID-stomas were formed (1.5% of 724 right resections), 9 were formed in left colonic resections (2.5% of 367 left resections), and one COVID-stoma was formed from the total/subtotal/panproctocolectomies group (2.1% of 47, Table 2).

There were slight but non-significant differences in patients who had a COVID-stoma compared to those who did not (*Table 3*), including a slight increase in anastomotic leak (7.4% versus 4.9%) and intensive care usage (29.9% versus 22.5%) and slight decrease in mortality (1.1% versus 1.9%). There was shorter length of stay in the group with COVID-stoma (4.5 days versus 6.0 days). Similarly, no difference in outcomes was observed in patients undergoing COVID-stoma when stratified by cancer location (*Supplementary Table 4).*

Reasons for COVID-stoma formation

The reason for change in practice was explored in patients who had a COVID-stoma (stoma formation as a direct result of COVID-19 (n=90). Surgeons were permitted to give more than one reason for change. There were a total of 147 responses. The most common reasons reported for formation of COVID-stoma were "recommendation from specialty associations" (44%, 64/147, *Supplementary Figure 1)* and "to avoid possible complications requiring critical care" (39%, 57/147). "Wish to reduce length of inpatient stay" was given in 10% (14/147) and "fear of patient suffering COVID-19 postoperatively" was given in 6% (9/147) of responses. Only 2% (3/147) cited "Lack of access to postoperative intensive care" and one cited "very difficult working conditions of full PPE" as the reasons for COVID-stoma.

Outcomes after surgery

Overall 38 (1.8%) patients died within 30 days after surgery, 78 (3.8%) patients developed postoperative SARS-CoV-2, and 86 (4.9%) patients had an anastomotic leak. Mortality rates are presented in *Figure 2*, and show an increasing relationship with both anastomotic leak and SARS-CoV-2 infection. In risk adjusted analyses, significant predictors of 30-day mortality were postoperative SARS-CoV-2, anastomotic leak, male sex, age over 70 years, cancer disease stage IV, and having a total/subtotal/panproctocolectomy (see *Table 4* for adjusted odds ratios).

Case selection during the pandemic

Pandemic data were compared with pre-pandemic data from ESCP published cohort data in *Table 5.* There were few differences between patient characteristics across different operations. Overall, during the pandemic, patients selected for surgery were fitter (with lower ASA), more stomas were formed, and a stapled technique was used more frequently than hand sewn anastomosis (*Table 5*). Outcomes following surgery during the pandemic included fewer anastomotic leaks and admissions to critical care, however, mortality was higher during the pandemic than in pre-pandemic era (*Table 5*).

Of patients who had an anastomotic leak, mortality was 8.6%, (6/70) in the pandemic data. In the pre-pandemic data, the mortality in those who had a leak was 6.6% (26/395).

Discussion

Mortality associated with an anastomotic leak and postoperative SARS-CoV-2 during the first waves of the COVID-19 pandemic was extremely high. A small change in stoma practice was observed, with less than 5% of patients receiving a COVID-stoma when they would usually have had an anastomosis only. Although those patients did not suffer any adverse outcomes, those measures alone did not reduce the overall complication rates seen in this study. In comparison to published mortality data following perioperative SARS-CoV-2 infection alone, the relative risk of death was almost 60% higher in combination with anastomotic leak (24.1% versus 34.8%) [11].

Comparison to previous ESCP cohort data identifies some of the selection bias that took place during these phases of the pandemic. There was an increased use of stapled anastomosis, fewer admissions to intensive care, and shorter length of stay. These all suggest efforts by surgeons and patients to reduce duration of surgery, resource usage, and hospital stay. Rectal cancer patients undergoing surgery seemed to be fitter compared to data from the ESCP audits, with a higher proportion of patients with ASA grades 1-2 . Slightly fewer patients underwent neoadjuvant therapy compared to pre-pandemic patients, which suggests a greater element of delayed surgery or 'watch and wait' strategies during the pandemic. Outcomes from patients who had neoadjuvant therapies and were either delayed or did not have surgery are awaited. There may be a 'post-pandemic' increased flow of patients, both needing surgery and needing monitoring, who will require additional support from already strained surgical systems.

This study had limitations. Firstly, this was an observational study of the first phase of the pandemic, where guideline implementation was incomplete. Data on implementation of guidelines by each hospital or country was not captured in this study. Secondly, the absolute change in practice presented was small, so firm conclusions cannot be drawn around safety of wider adoption of risk-averse practices. Thirdly, comparison to the pre-pandemic ESCP audit dataset may be biased through undetected patient, hospital, and country level differences that could preclude direct comparison, therefore the results must be interpreted with caution and firm conclusions should not be drawn. Fourthly, data were not presented on patients who had surgery delayed due to COVID-19 or had an alternative treatment strategy. We therefore present an incomplete picture of the care of colorectal cancer patients during the pandemic. Fifth, change in practice to COVID-stoma was reported by the surgeon and is therefore subjectively reported. We attempted to overcome this by comparing the total stoma rate to pre-pandemic rates, showing an increased rate of stoma formation during the pandemic. Sixth, despite guidance and concerns around aerosolisation, this study showed that laparoscopic approaches continued. The reasons for this, including surgeon and patient attitudes, deserve further exploration by way of addition qualitative research. Finally, although case selection and more elective stomas can potentially reduce post-operative risks, further robust strategies are needed to mitigate against morbidity and mortality and further exploration is required.

Clear data and safe strategies are needed to continue to provide safe surgery during future pandemic waves. This study highlights several patient, operative, and organisational factors that may bring benefit and need further testing. At a patient level, selection of fitter patients, who will benefit most from curative surgery during peaks of pandemics, is logical. This has been previously recommended to both conserve critical care capacity and avoid exposing high risk patients to nosocomial SARS-CoV-2 transmission [3, 9]. At an operative level, avoidance of leaks seems paramount. Forming stomas alone is not necessarily the solution, as they carry their own risks and morbidity. Selecting lower risk patients for anastomosis, use of defunctioning stomas, and more liberal use of end stomas in high risk patients might be best supported through formal risk stratification for anastomotic leak [23, 24]. At an organisational level, the prevention of postoperative SARS-CoV-2 related infections is paramount. This seems best approached by identifying preoperative, presymptomatic carriers (i.e. preoperative swab testing), and by providing COVID-19-free surgical pathways. Both of these areas require further evidence to best define exactly which measures they include (e.g. number of swabs, role of computed tomography of the thorax, components of COVID-19-free pathways). With an estimated 3,000,000 cancer operations postponed around the world [12], and more accruing during second waves, efficient measures to safely discharge patients early and protect them from risk of in-hospital transmission should continue.

References

1. Ranney ML, Griffeth V, Jha AK. Critical supply shortages—the need for ventilators and personal protective equipment during the Covid-19 pandemic. New England Journal of Medicine. 2020;382(18):e41.

2. Xie J, Tong Z, Guan X, Du B, Qiu H, Slutsky AS. Critical care crisis and some recommendations during the COVID-19 epidemic in China. Intensive care medicine. 2020:1-4.

3. American College of Surgeons. COVID 19: Elective Case Triage Guidelines for Surgical Care. Available from: https://www.facs.org/-/media/files/covid19/guidance_for_triage_of_nonemergent_surgical_procedures.ashx. Accessed 27th March 2020

4. The Royal College of Surgeons of Edinburgh. Intercollegiate General Surgery Guidance on COVID-19. Available from: https://www.rcsed.ac.uk/news-public-affairs/news/2020/march/intercollegiate-general-surgery-guidance-on-covid-19-update. Accessed 27th March 2020

5. Aj B, Brown C, Abdelrahman T, Rl H, Rj E, Ansell J, et al. International surgical guidance for COVID-19: Validation using an international Delphi process-Cross-sectional study. International Journal of Surgery. 2020;79:309-316.

6. Association of Coloproctology of Great Britian and Ireland. Urgent Intercollegiate General Surgery Guidance on COVID-19. Available from:

https://www.acpgbi.org.uk/news/urgent-intercollegiate-general-surgery-guidance-on-covid-19/. Accessed 27th March 2020

7. Lisi G, Campanelli M, Spoletini D, Carlini M. The possible impact of COVID-19 on colorectal surgery in Italy. Colorectal Disease. 2020 Jun;22(6):641-642.

8. Willan J, King AJ, Jeffery K, Bienz N. Challenges for NHS hospitals during covid-19 epidemic. British Medical Journal. 2020 Mar 20;368:m1117.

9. COVIDSurg Collaborative. Global guidance for surgical care during the COVID-19 pandemic. The British Journal of Surgery. 2020 Aug;107(9):1097-1103.

10. Wang Y, Wang Y, Chen Y, Qin Q. Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures. Journal of Medical Virology. 2020;92(6):568-76.

11. Covidsurg Collaborative. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. The Lancet. 2020;396(10243):27-38.

12. CovidSurg Collaborative. Elective surgery cancellations due to the COVID-19 pandemic: global predictive modelling to inform surgical recovery plans. British Journal of Surgery. 2020 May 12:10.1002/bjs.11746

13. CovidSurg Collaborative. Elective Cancer Surgery in COVID-19-Free Surgical Pathways During the SARS-CoV-2 Pandemic: An International, Multicenter, Comparative Cohort Study. Journal of Clinical Oncology. 2020 Oct 6:JCO2001933.

14. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. Journal of biomedical informatics. 2009;42(2):377-81.

15. National Confidential Enquiry into Patient Outcome and Death. The NCEPOD Classification of Intervention 2004. Available from: https://www.ncepod.org.uk/classification.html. Accessed 27th March 2020.

16. American Society of Anesthesiologists. ASA Physical Status Classification System 2019. Available from: https://www.asahq.org/standards-and-guidelines/asa-physical-status-classification-system. Accessed 27th March 2020.

17. The European Society of Coloproctology collaborating groups. The impact of conversion on the risk of major complication following laparoscopic colonic surgery: an international, multicentre prospective audit. Colorectal Disease. 2018;20(S6):69-89.
18. The European Society of Coloproctology collaborating group. Safety of primary anastomosis following emergency left sided colorectal resection: an international, multi-centre prospective audit. Colorectal Disease. 2018;20(S6):47-57.
19. European Society of Coloproctology Collaborating Group. The impact of stapling technique and surgeon specialism on anastomotic failure after right-sided colorectal resection: an international multicentre, prospective audit. Colorectal Disease. 2018;20(11):1028-40.
20. European Society of Coloproctology Collaborating Group, Battersby N, Bhangu A, Chaudhri S, El-Hussuna A, Frasson M, et al. Relationship between method of anastomosis and anastomotic failure after right hemicolectomy and ileo-caecal resection: an international snapshot audit. Colorectal Disease. 2017;19(8):e296-e311.
21. European Society of Coloproctology Collaborating Group. Predictors for Anastomotic Leak, Postoperative Complications, and Mortality After Right Colectomy for Cancer: Results From an International Snapshot Audit. Diseases of the Colon & Rectum. 2020;63(5):606-18.
22. The European Society of Coloproctology collaborating group. An international multicentre prospective audit of elective rectal cancer surgery; operative approach versus outcome, including transanal total mesorectal excision (TaTME). Colorectal Disease. 2018;20(S6):33-46.
23. Sammour T, Lewis M, Thomas ML, Lawrence MJ, Hunter A, Moore JW. A simple web-based risk calculator (www.anastomoticleak.com) is superior to the surgeon's estimate of anastomotic leak after colon cancer resection. Techiques in Coloproctology. 2017;21(1):35-41.
24. Frasson M, Flor-Lorente B, Rodríguez JLR, Granero-Castro P, Hervás D, Alvarez Rico MA, et al. Risk Factors for Anastomotic Leak After Colon Resection for Cancer. Annals of Surgery. 2015;262(2):321-30.

Table 1: Patients and disease characteristics stratified by operation

		Right side resection n=724		Left side resection n=367		Rectal resection n=935		Total / subtotal panproctocolectomy n=47	
Sex									
	Female	343	47.4%	135	36.8%	343	36.7%	16	34.0%
	Male	381	52.6%	232	63.2%	592	63.3%	31	66.0%
ASA									
	1-2	454	62.7%	244	66.5%	686	73.4%	36	76.6%
	3-5	269	37.2%	123	33.5%	244	26.1%	11	23.4%
	Missing	1		0		5		0	
Age									
	<50	42	5.8%	25	6.8%	96	10.3%	11	23.4%
	50-69	268	36.9%	187	51.0%	495	52.9%	16	34.0%
	≥70	414	57.3%	155	42.2%	344	36.8%	20	42.6%
Disease stage									
	I - II	512	70.7%	216	71.1%	482	51.5%	33	70.2%
	III	181	25.0%	78	21.3%	385	41.2%	9	19.1%
	IV	31	4.3%	28	7.6%	68	7.3%	5	10.6%
Neoadjuvant radiotherapy*									
	Short course					89	9.5%	0	0
	Long course					205	21.9%	1	2.9%
	None					641	68.6%	33	97.1%
Approach									
	Laparoscopic	395	54.6%	231	62.9%	540	57.8%	19	40.4%
	Open	298	41.1%	109	29.7%	355	38.0%	24	8.5%
	Conversion	31	4.3%%	27	7.4%	40	4.3%	4	8.5%
Anastomosis technique									
	Staped	527	77.3%	298	89.2%	619	92.1%	30	88.2%
	Hand sewn	155	22.7%	36	10.8%	53	7.9%	4	11.8%
	No anastomosis	37		30		255		13	
	Missing	5		3		8		0	
Seniority									
Colorectal consultant		488	67.5%	263	71.7%	732	78.3%	38	80.8%
Colorectal trainee		61	8.4%	14	3.8%	55	5.9%	3	6.4%
General surgery consultant		126	17.4%	65	17.7%	124	13.3%	6	12.8%
General surgery trainee		43	6.1%	23	6.3%	18	1.9%	0	0
Missing		5		2		6		0	

* Of patients who had an operation involving the rectum

Table 2: Additional number of stomas formed due to COVID-19 in relation to all patients undergoing surgery

	COVID-defunctioning-stoma / All operations	COVID-end-stoma / All operations
Overall		

New COVID-stomas	27 / 2073	1.3%	63 / 2073	3.0%
Sex				
Female	11 / 837	1.3%	24 / 837	3.1%
Male	16 / 1236	1.3%	39 / 1236	3.2%
ASA				
1-2	23 / 1420	1.6%	36 / 1420	2.5%
3-5	4 / 647	0.6%	26 / 647	4.0%
Age				
<50	3 / 174	1.7%	2/ 174	1.1%
50-69	15 / 966	1.6%	31 / 966	3.2%
≥70	9 / 933	1.0%	30 / 933	3.2%
Operation				
Right resection	1 / 724	0.1%	10 / 724	1.4%
Left resection	2 / 367	0.5%	7 / 367	1.9%
Rectal resection	24 / 935	2.5%	45 / 935	4.8%
Total / Subtotal /Panproctocolectomy	0 / 47	0	1 / 47	2.1%
Disease stage				
I - II	11 / 838	1.3%	31 / 838	3.4%
III	13 / 653	2.0%	30 / 653	4.6%
IV	3 / 133	2.3%	2 / 133	1.5%
Neoadjuvant radiotherapy*				
Short course	3 / 89	3.4%	1 / 89	1.1%
Long course	5 / 206	2.4%	9 / 206	4.4%
None	16 / 674	2.4%	35 / 674	5.2%
Approach				
Minimally invasive	11 / 1185	0.9%	18 / 1185	1.5%
Open	15 / 786	1.9%	42 / 786	5.3%
Minimally invasive converted to open	1 / 102	0.9%	3 / 102	2.9%
Anastomosis technique**				
Staped	25 / 1474	1.7%	N/A	N/A
Hand sewn	2 / 248	0.8%	N/A	N/A
Seniority				
Colorectal consultant	13 / 1521	0.9%	45 / 1521	3.0%
Colorectal trainee	11 / 133	8.3%	3 / 133	2.3%

General surgery consultant	2 / 322	0.6%	11 / 322	3.4%
General surgery trainee	1 / 84	1.2%	5 / 84	6.0%

Percentage (%) is the increased number of new stomas (COVID-stoma) formed during the COVID-19 pandemic out of total number of patients who had an operation in each group.

* Of patients who had an operation involving the rectum

** Of patients who had an anastomosis

Figure 1: Flowchart of type stoma-anastomosis configuration broken down by operative region and if patients had a change in stoma practice due to COVID-19 (COVID-stoma).

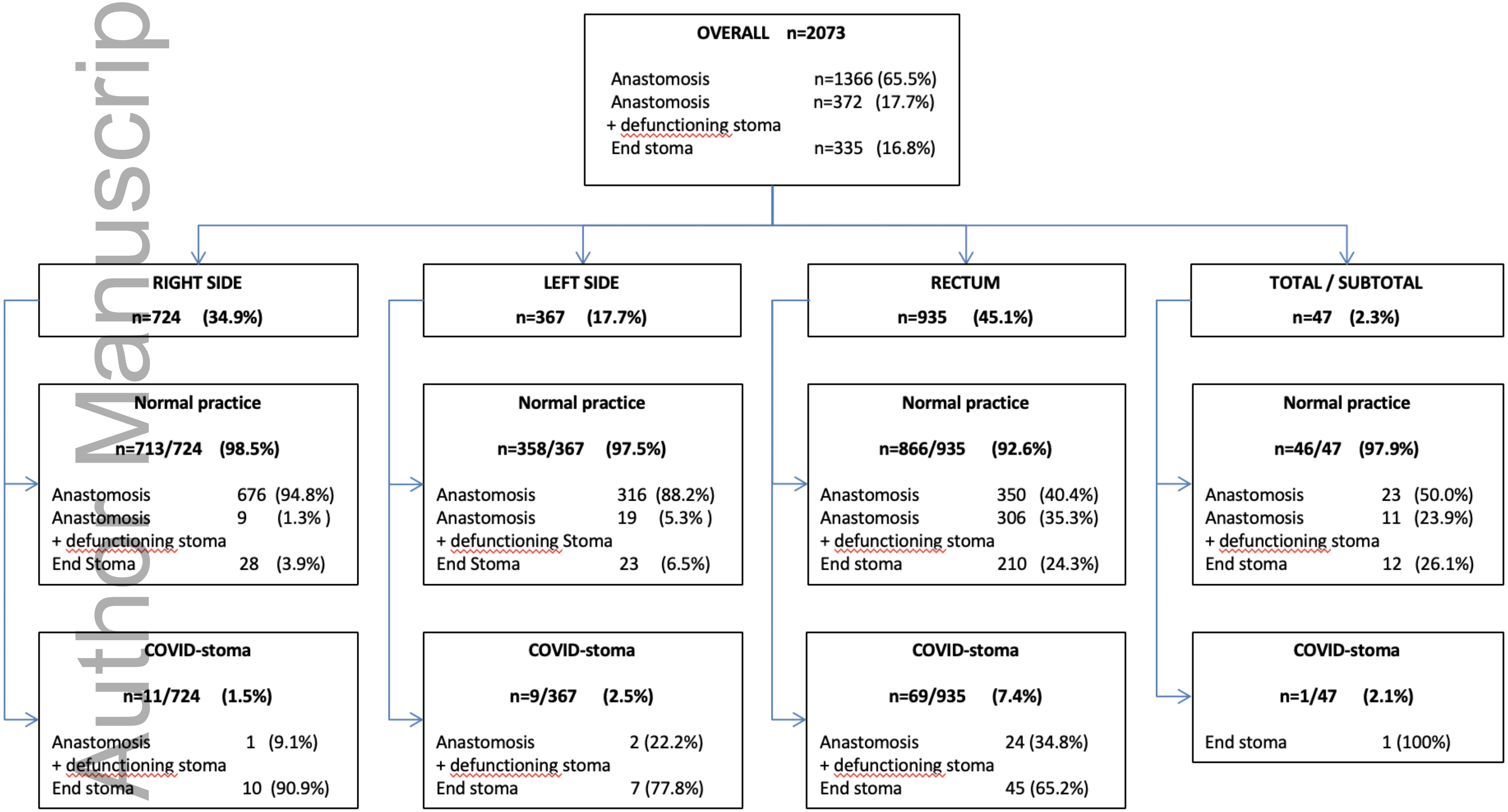


Figure 2: Flowchart of mortality related to postoperative SARS-CoV-2 and if an anastomotic leak occurred.

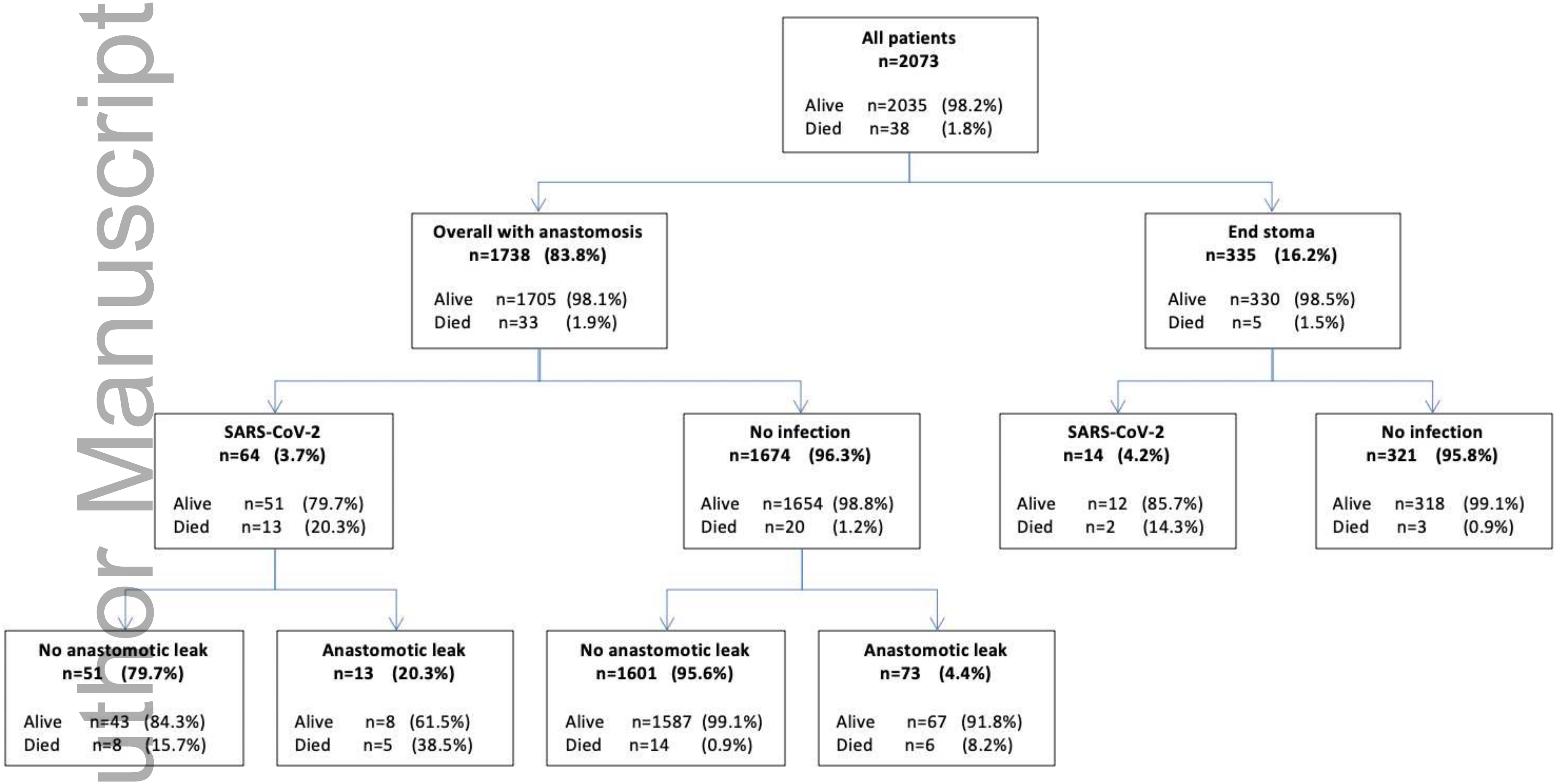


Table 3: Outcomes stratified by additional stoma formation due to COVID-19 (COVID-stoma).

	Normal practice		COVID-stoma		p
	n	%	n	%	
Anastomotic leak *					
No	1627	94.9%	25	92.6%	0.390
Yes	84	4.9%	2	7.4%	
Intensive care					
No	1537	77.5%	64	71.1%	0.157
Yes	446	22.5%	26	29.9%	
Death					
No	1946	98.1%	89	98.9%	1.000
Yes	37	1.9%	1	1.1%	
Postoperative SARS-CoV-2					
No	1909	96.3%	86	95.6%	0.579
Yes	74	3.7%	4	4.4%	
Length of stay (days)					
(median, IQR)	6	(4-8)	4.5	(4-6.5)	0.270

* Of patients who had an anastomosis

Table 4: Adjusted and unadjusted regression model of predictors for 30-day mortality

				Univariable		Multivariable		
		Mortality		Odds ratio	95% confidence interval	Odds ratio	95% confidence interval	p
Anastomotic leak	No	27 / 1954	1.4%	-		-		
	Yes	11 / 93	11.8%	9.21	4.32 - 19.64	6.01	2.58 - 14.06	**<0.001**
SARS-CoV-2	No	23 / 1995	1.2%	-		-		
	Yes	15 / 78	19.2%	20.41	10.17 - 41.00	16.90	7.86 - 36.38	**<0.001**
Age	<70	13 / 1140	1.1%	-		-		
	>70	25 / 933	2.7%	2.39	1.21 - 4.69	2.87	1.32 - 6.20	**0.008**
Sex	Female	7 / 837	0.8%			-		
	Male	31 / 1236	2.5%	3.05	1.34 - 6.96	2.46	1.01 - 5.93	**0.045**
ASA*	1 - 2	19 / 1420	1.3%	-		-		
	3 - 5	19 / 647	2.9%	2.23	1.17 - 4.24	1.57	0.76 - 3.26	0.223
Disease stage	I - II	17 / 1288	1.3%			-		
	III	15 / 653	2.3%	1.76	0.87 - 3.54	2.00	0.91 - 4.20	0.088
	IV	6 / 132	4.6%	3.56	1.38 - 9.19	3.43	1.16 - 10.21	**0.026**
Operation	Right resection	9 / 724	1.2%	-		-		
	Left resection	6 / 367	1.6%	1.32	0.47 - 3.74	1.45	0.47 - 4.48	0.524
	Rectal resection	19 / 935	2.0%	1.65	0.74 - 3.66	1.60	0.65 - 3.93	0.302
	Total/subtotal/	4 / 47	8.5%	7.39	2.19 - 24.96	9.06	2.21 - 37.15	**0.002**

	panproctocolectomy			

* American Society of Anaesthesiologists (ASA) physical status classification [16]

Table 5: Comparison of patient and disease characteristics and outcomes of patients undergoing elective cancer operations currently (during pandemic) alongside composite data from the ESCP 2015 and 2017 audits (pre-pandemic).

Right	Pre-pandemic	During pandemic	p value
Sex			
Male	1151 (51.7%)	381 (52.6%)	0.676
Female	1074 (48.3%)	343 (47.4%)	
Age			
<50	104 (4.7%)	42 (5.8%)	0.312
50-69	876 (39.3%)	268 (37.0%)	
≥70	1245 (56.0%)	414 (57.2%)	
ASA			
1-2	1379 (62.0%)	454 (62.8%)	0.694
3-5	846 (38.0%)	269 (37.2%)	
Approach			
Minimally invasive	1211 (54.4%)	395 (54.7%)	**<0.001**
Open	813 (36.5%)	298 (41.0%)	
Conversion	201 (9.1%)	31 (4.3%)	
Operation			
Anastomosis	2194 (98.6%)	677 (93.5%)	**<0.001**
Anastomosis + defunction	6 (0.3%)	10 (1.4%)	
End stoma	25 (1.1%)	37 (5.1%)	
Anastomosis technique*			
Staped	1381 (62.8%)	527 (77.3%)	**<0.001**
Hand sewn	819 (37.2%)	155 (22.7%)	
Seniority			
Colorectal surgeon	1465 (58.3%)	488 (67.9%)	**<0.001**
Colorectal trainee	333 (13.2%)	61 (8.5%)	
General surgeon	467 (18.6%)	126 (17.5%)	
General surgical trainee	250 (9.9%)	44 (6.1%)	
Anastomotic leak*			
No	2056 (93.5%)	662 (96.4%)	**0.005**
Yes	144 (6.5%)	25 (3.6%)	
Intensive care			
No	1605 (72.1%)	578 (79.8%)	**<0.001**
Yes	620 (27.9%)	158 (20.2%)	

Left	Pre-pandemic	During pandemic	p value
Sex			
Male	589 (59.6%)	232 (63.2%)	0.228
Female	400 (40.4%)	135 (36.8%)	
Age			
<50	64 (6.5%)	25 (6.8%)	0.434
50-69	469 (47.4%)	187 (50.1%)	
≥70	456 (46.1%)	155 (42.1%)	
ASA			
1-2	617 (62.7%)	244 (66.5%)	0.198
3-5	367 (37.3%)	123 (33.5%)	
Disease stage			
I - II	468 (50.8%)	261 (71.1%)	**<0.001**
III	375 (40.6%)	78 (21.4%)	
IV	79 (8.6%)	28 (9.6%)	
Approach			
Minimally invasive	519 (53.6%)	231 (62.9%)	**0.001**
Open	356 (36.8%)	109 (29.7%)	
Conversion	93 (9.6%)	27 (7.4%)	
Operation			
Anastomosis	922 (93.3%)	316 (86.1%)	**<0.001**
Anastomosis + defunction	18 (1.8%)	21 (5.7%)	
End stoma	48 (4.9%)	30 (8.2%)	
Anastomosis technique*			
Staped	685 (72.9%)	298 (89.2%)	**<0.001**
Hand sewn	255 (27.1%)	36 (10.8%)	
Seniority			
Colorectal surgeon	705 (71.3%)	263 (72.1%)	**<0.001**
Colorectal trainee	88 (8.9%)	14 (3.8%)	
General surgeon	170 (17.2%)	65 (17.8%)	
General surgical trainee	26 (2.6%)	23 (6.3%)	
Anastomotic leak*			
No	869 (92.5%)	323 (95.9%)	**0.031**
Yes	71 (7.5%)	14 (4.1%)	

Rectum	Pre-pandemic	During pandemic	p value
Sex			
Male	1617 (62.7%)	592 (63.3%)	0.738
Female	962 (37.3%)	343 (36.7%)	
Age			
<50	210 (8.1%)	96 (10.3%)	0.061
50-69	1336 (51.8%)	495 (52.9%)	
≥70	1033 (40.1%)	344 (36.8%)	
ASA			
1-2	1685 (66.0%)	686 (73.8%)	**<0.001**
3-5	868 (34.0%)	244 (26.2%)	
Disease stage			
I - II	1421 (56.8%)	479 (51.5%)	**<0.001**
III	821 (32.8%)	383 (41.2%)	
IV	261 (10.4%)	68 (7.3%)	
Neoadjuvant radiotherapy			
Short course	177 (7.2%)	89 (9.5%)	**0.001**
Long course	679 (27.5%)	205 (21.9%)	
None	1611 (58.1%)	641 (68.6%)	
Approach			
Minimally invasive	1315 (54.2%)	540 (57.8%)	**<0.001**
Open	867 (35.8%)	355 (38.0%)	
Conversion	243 (10.0%)	40 (4.2%)	
Operation			
Anastomosis	1103 (42.8%)	350 (37.4%)	**0.012**
Anastomosis + defunction	863 (33.5%)	330 (35.3%)	
End stoma	613 (23.7%)	255 (27.3%)	
Anastomosis technique*			
Staped	1811 (92.1%)	619 (92.1%)	0.998
Hand sewn	155 (7.9%)	53 (7.9%)	
Seniority			
Colorectal surgeon	2078 (80.7%)	732 (78.8%)	0.087
Colorectal trainee	112 (4.4%)	55 (5.9%)	
General surgeon	355 (13.8%)	124 (13.4%)	

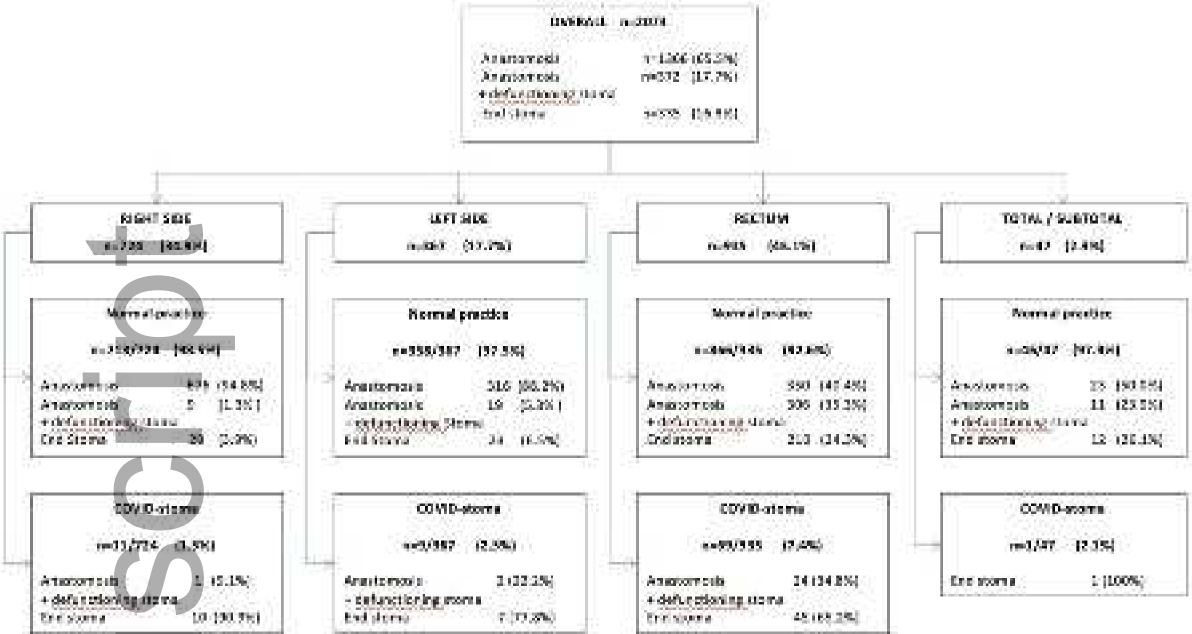
Death			
No	2188 (98.3%)	715 (98.8%)	0.155
Yes	37 (1.7%)	9 (1.2%)	
Length of stay (median)	7	6	**<0.001**
(days) (IQR)	(5-10)	(4-8)	

*Of patients who had an anastomosis

Note: disease stage data for right sided operations and data for total/subtotal/panproctocolectomy operations were not available from the ESCP data and have been excluded from comparison.

Intensive care			
No	693 (70.1%)	299 (81.5%)	**<0.001**
Yes	295 (29.9%)	68 (18.5%)	
Death			
No	982 (99.3%)	361 (98.4%)	0.254
Yes	7 (0.7%)	6 (1.6%)	
Length of stay (median)	7	6	**<0.001**
(days) (IQR)	(5-9)	(4-8)	

General surgical trainee	31 (1.2%)	18 (1.9%)	
Anastomotic leak*			
No	1786 (90.8%)	636 (93.5%)	**0.030**
Yes	180 (9.2%)	44 (6.5%)	
Intensive care			
No	1707 (66.2%)	692 (74.0%)	**<0.001**
Yes	870 (33.8%)	243 (26.0%)	
Death			
No	2559 (99.2%)	916 (98.0%)	0.261
Yes	20 (0.8%)	19 (2.0%)	
Length of stay (median)	8	7	**<0.001**
(days) (IQR)	(6-11)	(5-11)	



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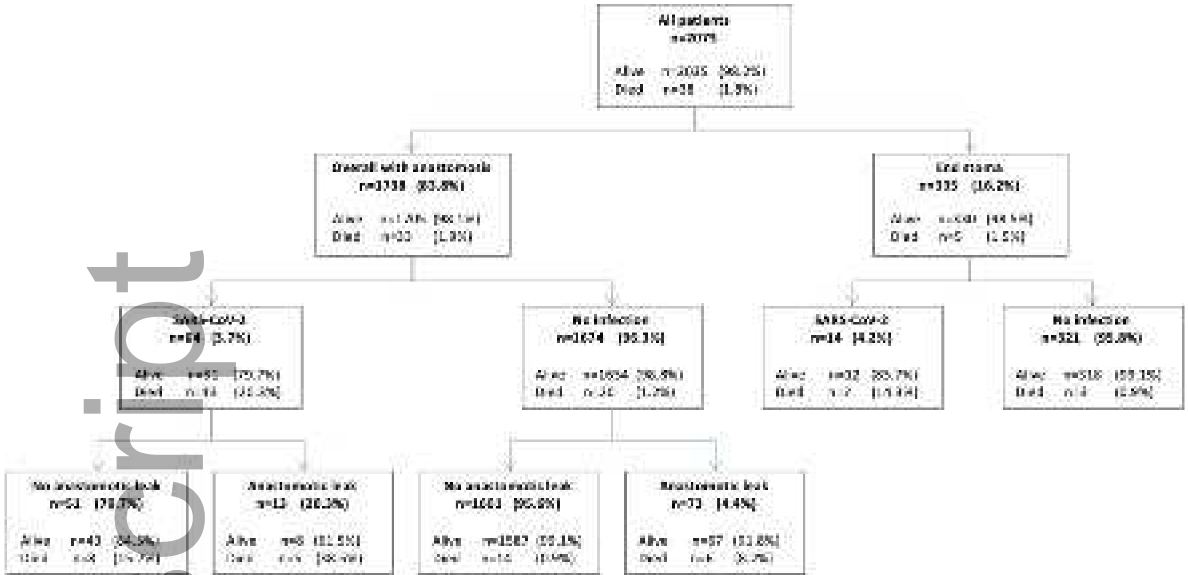

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