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The impact of surgical delay on resectability of colorectal cancer: an international prospective cohort study

COVIDSurg Collaborative*

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What does this paper add to the literature?

Prospective cohort study of 5453 patients with a decision for curative colorectal cancer surgery. Surgical delays of up to twelve weeks were not associated with worse rates of complete resection. Any reduction in long-term survival attributable to delays is likely to be due to micro-metastatic disease and should be the focus of postoperative surveillance programmes.

Aim:

The SARS-CoV-2 pandemic has provided a unique opportunity to explore the impact of surgical delays on cancer resectability. This study aimed to compare resectability for colorectal cancer patients undergoing delayed versus non-delayed surgery.

Methods:

International prospective cohort study of consecutive colorectal cancer patients with a decision for curative surgery (January-April 2020). Surgical delay was defined as an operation taking place more than 4 weeks after treatment decision, in a patient who did not receive neoadjuvant therapy. A subgroup analysis explored effects of delay in elective patients only. The impact of longer delays was explored in a sensitivity analysis. The primary outcome was complete resection, defined as curative resection with a R0 margin.

Results:

Overall, 5453 patients from 304 hospitals in 47 countries were included, of which 6.6% (358/5453) did not receive their planned operation. Of the 4304 operated patients without neoadjuvant therapy, 40.5% (1744/4304) were delayed beyond four weeks. Delayed patients were more likely to be older, male, more comorbid, have higher BMI, have rectal cancer and early-stage disease. Delayed patients had higher unadjusted rates of complete resection (93.7% vs 91.9%, p=0.032) and lower rates of emergency surgery (4.5% vs 22.5%, p<0.001). After adjustment, delay was not associated with a lower rate of complete resection (OR 1.18, 95%CI 0.90-1.55, p=0.224), which was consistent in elective patients only (OR 0.94, 95%CI 0.69-1.27, p=0.672). Longer delays were not associated with poorer outcomes.

Conclusion:

One in fifteen colorectal cancer patients did not receive their planned operation during the first wave of COVID-19. Surgical delay did not appear to compromise resectability, raising the hypothesis that any reduction in long-term survival attributable to delays is likely to be due to micro-metastatic disease.

Introduction

Globally, colorectal cancer is the third most commonly diagnosed cancer type, and the second largest cause of cancer death.[1] The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has affected all aspects of healthcare, and has led to variable delays to the delivery of colorectal cancer surgery across the globe.[2,3] It is estimated that over 28 million operations were cancelled in the initial three months of disruption alone.[4,5] This creates a unique 'natural experiment' to explore the effects of treatment delay on outcomes of colorectal cancer surgery.

Although there is no international guidance on the optimal timing of for colorectal cancer resection, it is generally perceived as a time-critical intervention. In the UK, the National Health Service sets a target of 4-weeks from a treatment decision to definitive treatment in cancer care, but global practice and policy varies significantly. A number of modelling studies and systematic reviews have explored the impact of delays in long term survival in colorectal cancer, but it is unclear whether this is related to poorer initial cancer control (i.e., lower rates of complete resection) or micro-metastatic disease spread.[6]

Understanding the effects of surgical delay during the SARS-CoV-2 pandemic will help inform future prioritisation of surgical waiting lists during post-pandemic recovery, and postoperative surveillance by the multidisciplinary team.

This study aimed to explore the association between delayed surgery for colorectal cancer in patients not undergoing neoadjuvant therapy and surgical resectability during the SARS-CoV-2 pandemic.

Methods

Study design and setting

This was an international prospective cohort study which included consecutive patients with a decision for elective curative surgery from the multidisciplinary team meeting, tumour board or equivalent. Any hospital worldwide undertaking elective colorectal cancer surgery was eligible for inclusion in this analysis. Each participating site recruited consecutive eligible patients for a period of three months following the emergence of COVID-19 in their local area (first notification of SARS-CoV-2, ranging between January and April 2020). Each site obtained ethical approval according to local regulations, and the CovidSurg-Cancer study (overall inclusion by cancer type available in Supplementary Table 12) was pre-registered with ClinicalTrials.gov (identifier: NCT04384926).

Patient inclusion, pathways and follow-up

All patients with a decision for curative cancer surgery, or that would have normally been offered curative surgery in the pre-pandemic setting but an alternative treatment was offered due to COVID-19 were included. Patients were excluded from this study if they had (1) planned palliative surgery, (2) a suspected cancer that was later found to be benign on histopathology, (3) a suspected benign tumour that was later found to be cancerous, or (4) received endoscopic treatment only (e.g., transanal endorectal microsurgery (TEMS)).

From all the included patients, part of them did receive their planned curative surgery but some ended up not receiving it during the study period. For patients who were operated, follow-up data was collected at 30-days after surgery. For patients who remained non-operated, their last known status was recorded. All follow-up was completed by the 31st of August 2020 with a minimum follow-up of 3 months for all included patients. The characteristics of non-operated patients were described and reasons for the non-performance of the planned surgery were reported. This allows a comprehensive understanding of the whole sample and an informed discussion on how treatment pathways that were in place during the study influenced the patient groups that we are comparing.

From all the operated patients, some require surgical resection alone and some require neoadjuvant therapy (chemo and/or radiotherapy prior to surgery). Due to differences in disease biology, and potentials effects of treatment intervals in patients undergoing neoadjuvant therapy, the patients who received neoadjuvant therapy were excluded from the main analysis, as their disease behaviour is expected to be fundamentally different. However, tumour location and the type of neoadjuvant treatment were reported in the supplement for completeness.

Delay to surgery

The main analysis on surgical delays focused on patients who received their planned surgery with curative intent, without having received neoadjuvant therapy. Delay to surgery was defined according to number of weeks from the date of the decision for curative surgery up to the date when the patient received surgery. For the primary analysis, patients who were operated more than four weeks after their decision for surgery were classified as delayed and those who were operated within four weeks were defined as non-delayed. This four-week cut-off was informed by UK National Institute for Clinical Excellence (NICE) guidance and standards for timely delivery of cancer care.[7]

Outcomes

The primary outcome measure for the study was complete resection, defined as disease amenable to surgical removal at the time of surgery with a negative circumferential resection margin (R0, no microscopic or macroscopic disease within 1mm of the circumferential resection margin). Patients whose disease became unresectable during the study period or whose surgical resection was achieved with positive resection margins (R1 or R2) were classified as having an incomplete resection.

Secondary outcomes were also compared between patients undergoing delayed and non-delayed surgery. These included the 30-day postoperative mortality rate, 30-day major postoperative complication rate (defined as Clavien-Dindo grade III to V complications),[8] stage change from baseline (clinical) to pathology (according to the AJCC 8th edition of Tumour Node Metastasis (TNM) staging system [9], defined as upstaged for any increase in stage, downstaged for any decrease in stage and no

change for patients remaining at the same stage group), detection of new metastatic disease (clinically, intraoperatively or on radiological imaging that was not present at the time of decision for surgery) and the rate of emergency surgery (i.e., as all patients had an initial plan for elective surgery at study entry, emergency surgery can be interpreted as a cancer-related complication requiring emergency intervention). The indications for emergency surgery were presented.

Data variables

Baseline information was collected for each patient at the point of entry to the study. This included age, sex, American Society of Anaesthesiologists (ASA) physical status classification, Eastern Cooperative Oncology Group (ECOG) performance score, Revised Cardiac Risk Index (RCRI), Body Mass Index (BMI, defined as underweight if <18.5 kg/m^2, normal if 18.5-24.9 kg/m^2, overweight if 25-29.9 kg/m^2) or obese if ≥30 kg/m^2), clinical (based on imaging and clinical observation at the time of decision for surgery) and pathological Tumour Node Metastasis (TNM) stage groups were collected according to the AJCC 8th edition, country income (grouped as high, upper-middle and low/low-middle income, as per the World Bank index classification based on gross national income per capita), surgical approach (open, laparoscopic or converted), anastomotic performance (with or without defunctioning stoma) and anastomotic method (handsewn or stapled).

Data handling and statistics

All the data collected was non-identifiable and uploaded to a secure online server hosted by the University of Birmingham, using the Research Electronic Data Capture (REDCap) system. Data management and analysis used RStudio version 4.0.3 with the “readr”, “tidyverse”, “dplyr”, “gmodels”, “Hmisc”, and “finalfit” packages (R Foundation for Statistical Computing). Unadjusted categorical data were compared using either the Chi-square test with Fisher’s exact modification where required. A P-value <0.05 was considered statistically significant. Logistic regression models were used to explore the association between delay to surgery and complete resection, adjusting for clinically plausible patient and disease factors selected *a priori*. All missing data were recorded and reported in the tables and figures.

Reflecting differences in treatment timelines and capacity across different resource settings, we performed a sensitivity analysis exploring longer delays of 6-, 8- and 12-weeks from treatment decision to surgery, and the primary outcome measure.

Given that patients undergoing emergency surgery could have shown distinct clinical features at the time of decision for surgery that made them more likely to receive an urgent intervention, a pre-planned subgroup analysis was performed for patients undergoing planned (elective) surgery only. Further subgroup analyses were performed looking exclusively at colon cancers, rectal cancers, early disease and advanced disease. For this purpose, early disease stage was defined as organ confined, non-nodal, non-metastatic (T1-3 N0 M0) and advanced disease was defined as reaching the serosa, nodal or metastatic disease (T4, N+ or M1). A sensitivity analysis of the adjusted and unadjusted results was conducted to explore the impact of longer delays in resectability: zero to four, five to eight, nine to twelve and more than twelve weeks from decision to surgery.

Results

In total, 5453 patients eligible for elective curative colorectal cancer surgery were included from 304 hospitals in 47 countries. This corresponds to 24.4% of all the patients included in the COVID-Surg Cancer study (the remaining being patients with other cancer types).[10] Of these 66.3% (3616/5453) had colon cancer and 33.7% (1837/5453) had rectal cancer. The clinical colorectal cancer stage was advanced in 63.6% (3466/5453) of the patients and early in 36.4% (1987/5453). Around two thirds of the patients were ASA grade 1-2 (66.7% [3619/5453]) and one third were ASA grade 3-5 (33.2% [1809/5453]). The majority of the patients were from high income countries (84.3% [4599/5453]) of patients, with 9.2% (500/5453) being from upper-middle income countries and 6.4% (351/5453) from lower-middle or low-income countries.

Non-operated patients

From all the included patients, 6.6% (358/5453) did not receive their planned operation during the study period (Figure 1), of which 74.3% (266/358) were still planned to have curative surgery at the time of follow up. Patients who were not operated were more likely to have rectal cancer (52.5% vs 32.4%, p<0.001), worse performance status (5.9% vs 2.9% were ECOG 3-4, p<0.001), lower BMI (9.3% vs 3.5% were underweight, p<0.001), higher stage disease (14.6% vs 10.3% had clinical Stage IV, p=0.004), and be from a low/lower-middle income country (18.2% vs 5.6%, p<0.001) (Supplementary Table 1). The reasons why patients did not receive their planned operation is detailed in Supplementary Table 2, with the most common reasons being an MDT decision to avoid surgery due to patient risk (72.6% [260/358]), disease progression (29.1% [104/358]) and patient being unable to travel to hospital during the pandemic (26.3% [94/358]).

Operated patients

Of the 5095 operated patients, 15.5% (791/5095) received neoadjuvant therapy and 85.4% (4304/5095) underwent surgery without neoadjuvant treatment. The majority of the patients receiving neoadjuvant therapy had rectal cancer (81.8% [647/791]). Neoadjuvant therapy regimens by cancer location are shown in Supplementary Figure 1.

From the 4304 patients who received an operation without neoadjuvant therapy, 59.5% (2559/4303) had surgery within four weeks of treatment decision and 40.5% (1744/4304) were delayed beyond four weeks. Delayed patients were more likely to be older (53.0% vs 46.3% aged over 70 years, p<0.001), male (58.7% vs 54.6%, p=0.008), more comorbid (37.7% vs 30.9% were ASA 3-5, p<0.001), have a lower performance status (46.4% vs 53,4% were ECOG 0), be from a higher income country (90.1% vs 83.7% were from high income countries), have a higher BMI (22.5% vs 17.4% were obese), have a rectal cancer (26.9% vs 20.8%, p<0.001) and early stage disease (41.9% vs 32.8% were clinical stage I). Full demographics are shown in Table 1.

Outcomes of delayed surgery

Delayed patients did not have lower rates of complete resection, compared to non-delayed patients. In the unadjusted analysis, delayed patients were more likely to have resectable disease (93.7% vs 91.9%, p=0.032) and less likely to develop new metastases (6.2% vs 10.1%, p<0.001) than non-delayed patients. Changes in disease stage from baseline to pathological staging were more common in delayed patients, including both upstaging and downstaging (Table 2). Delayed patients were also less likely to have had emergency surgery (4.5% vs 22.9%, p<0.001), while waiting for their planned surgery, mainly due to obstructive symptoms. Other indications for emergency surgery in this cohort are shown in Supplementary Table 3. There were no significant differences in 30-day major postoperative complications (9.3% vs 9.8%, p=0.648) or postoperative mortality rates (1.5% vs 2.2%, p=0.126). After adjustment for case mix, delay was not associated with significantly lower rates of complete resection (OR 1.18 [95% CI=0.90-1.55, p=0.224]) (Figure 2). The full adjusted model can be found in Supplementary Table 4.

Subgroup analysis

In the subgroup analysis of patients undergoing elective surgery only, delay was not associated with lower rates of complete resection (OR=0.94 [0.69-1.27, p=0.672]) (Logistic regression model available in Supplementary Figure 2). Demographic trends of delayed patients were also similar to the main analysis (Supplementary Table 5). When looking at colon and rectal cancers in isolation, a delay of four weeks

was not associated with a reduced rate of complete resection in colon (OR=1.33 [0.95-1.87, p=0.101]) or rectal cancer OR=0.91 [0.58-1.44, p=0.692]). Delay was not associated with poorer resectability in patients with early disease only (OR=1.20 [0.67-2.18, p=0.537]), or advanced disease only (OR=1.11 [0.81-1.52, p=0.517]). Full logistic regression models for the subgroup analysis are shown in Supplementary Tables 6 to 9.

Sensitivity analysis of longer surgical delays

In a sensitivity analysis exploring the association of longer delays and complete resection, 59.5% (2559/4304) of patients were operated in 0-4 weeks, 25.3% (1089/4304) in 5-8 weeks, 8.9% (384/4304) in 9-12 weeks and 6.3% (271/4304) >12 weeks from decision to surgery (all demographics available in Supplementary Table 10). Longer delays were not associated with worse resectability outcomes in unadjusted (Supplementary Table 11) or adjusted analyses (Table 3). Compared to patients undergoing surgery within 4 weeks of treatment decision, the odds of complete resection were not significantly different at 5-8 weeks from treatment decision (OR 1.16, 95% CI 0.86-1.59, p=0.344), at 9-12 weeks (OR 1.40, 0.85-2.41, p=0.206) or beyond 12 weeks (OR 1.03, 0.62-1.80, p=0.920).

Discussion and conclusions

During the first wave of the SARS-CoV-2 pandemic, one in fifteen patients did not receive their planned operation for colorectal cancer. In those who did undergo surgery, delays of more than four weeks did not appear to be associated with reduced rates of complete resection. This was robust to several sensitivity and subgroup analyses. Although there are inherent biases in this study design, including selection bias in those that were exposed to treatment delay, this study represents a unique natural experiment to better understand the pathobiology of survival after colorectal cancer surgery.

Whilst long term oncological outcome data is not yet available for this cohort, these data provide important insight into the potential mechanism for the relationship between long-term survival and treatment delay. Although the previous studies show controversial findings on the impact of delay to oncological outcomes[11-14], a systematic review looking at long term survival for patients undergoing colorectal cancer surgery 1 month and 3 months after the diagnosis showed a reduction in overall and disease free survival with surgical delays.[15] Another multi-specialty review of delays in multimodal cancer treatment showed a negative impact on long term oncological outcomes.[6] This study suggests that a delay to surgery does not affect short-term patho-oncological outcomes. It raises the hypothesis that any decrease in long-term survival observed is unlikely to be due to initial cancer control and may be related to micro-metastatic disease spread. Patients whose surgery is delayed might therefore benefit from closer follow-up strategies for early detection of relapse and metastatic disease. Further research is required to understand the effectiveness of enhanced follow-up pathways on long-term survival, alongside with its performance in different tumour biology patterns (uncaptured in this study).

The clinical features of non-operated patients suggest clinical selection based on a perceived high risk of surgical complications, given that these patients had worse performance status, were more likely to be underweight and had more advanced disease. Although these decisions probably aimed to protect frail patients from the additional risk conveyed by perioperative SARS-CoV-2 infection, they might have exposed some patients with advance disease to a risk of progression to palliative disease. Changes in the management of colorectal cancer during the COVID-19

pandemic have been described by several research groups, including reduction of the number of patients receiving surgery and shorter treatment regimens. [16-18] This study provides further insight on the drivers of these clinical decisions and on which patients might have been more impacted by them.

Advanced (non-organ confined) and rectal cancers were also more likely to be operated promptly, as opposed to early and colon cancers which were more likely to be delayed. This suggests that additional features of the disease were perceived by surgical teams as justifying early surgery, which might explain why non-delayed patients had higher non-adjusted rates of progression to unresectable disease and new metastasis. Changes in disease stage observed in this study include both higher rates of both upstage and downstage with increased delay. As delayed patients were more likely to have advanced disease, this might reflect lower reliability of clinical staging and imaging studies in advanced cancers, particularly when nodal disease is present.[19]

The performance of elective colorectal cancer surgery within four weeks of treatment decision might not be feasible in many settings worldwide, even in a pre-pandemic setting[20,21]. Additionally, there might be variation in the usual timeframes from decision to surgery across settings, depending on local practices and pathways (e.g. pre-operative assessment efficiency, existence of routine pre-habilitation programmes). This study looked at longer delays of eight and twelve weeks which showed no association with resectability impairment either, ensuring the generalisability of the findings.

Symptoms of obstruction, perforation or bleeding in patients awaiting elective surgery might have prompted earlier surgery, explaining why emergency surgery was more common in non-delayed patients (undergoing surgery within four weeks of treatment decision). Although we presented the reasons for emergency surgery in this cohort of patients awaiting planned resection, some could have had symptoms of obstruction or other acute complication at the time of treatment decision, to whom a delay beyond four weeks would not be clinically acceptable. To address the selection bias that these clinical findings might have had in the length of delay from decision to surgery, we performed a subgroup analysis of patients undergoing

elective surgery only, that again showed no difference in resectability with surgical delays.

This study has several important limitations. Longer-term follow-up of this cohort will be required to explore the true clinical impact of treatment delay for these patients. The second is the risk of selection bias in the comparison of delayed and non-delayed patients. We attempted to overcome this through multivariable modelling and several subgroup and sensitivity analysis, but the analysis may still be subject to residual bias from unmeasured confounders. Third, patients who remained non-operated may have had a poorer prognosis at baseline and/or may have been subject to disease progression and other cancer-related sequelae which could lead to underestimation of the impact of delay (7% of the cohort overall). Fourth, we were unable to explore the impact of treatment delay in patients with prior neoadjuvant therapy, who pose a biologically distinct treatment group. Finally, histological data was not collected and therefore we were unable to explore whether molecular subtypes or mutational status differed between the groups, and whether this impacted resection.

SARS-CoV-2 waves are not the only pressure that health systems face, and many factors can cause delays in the delivery of surgical care. These findings can inform clinical decision making, management of surgical waiting lists and patient informed consent before surgery. Guidance on management of colorectal cancer should also take these findings into account when designing follow-up strategies for patients who are operated for colorectal cancer. The possibility of performing cancer resection with a few weeks of delay without a negative impact on local control could be important for patients who may benefit from longer periods of pre-habilitation and pre-conditioning before surgery, in order to achieve a better fitness status and optimise perioperative outcomes.

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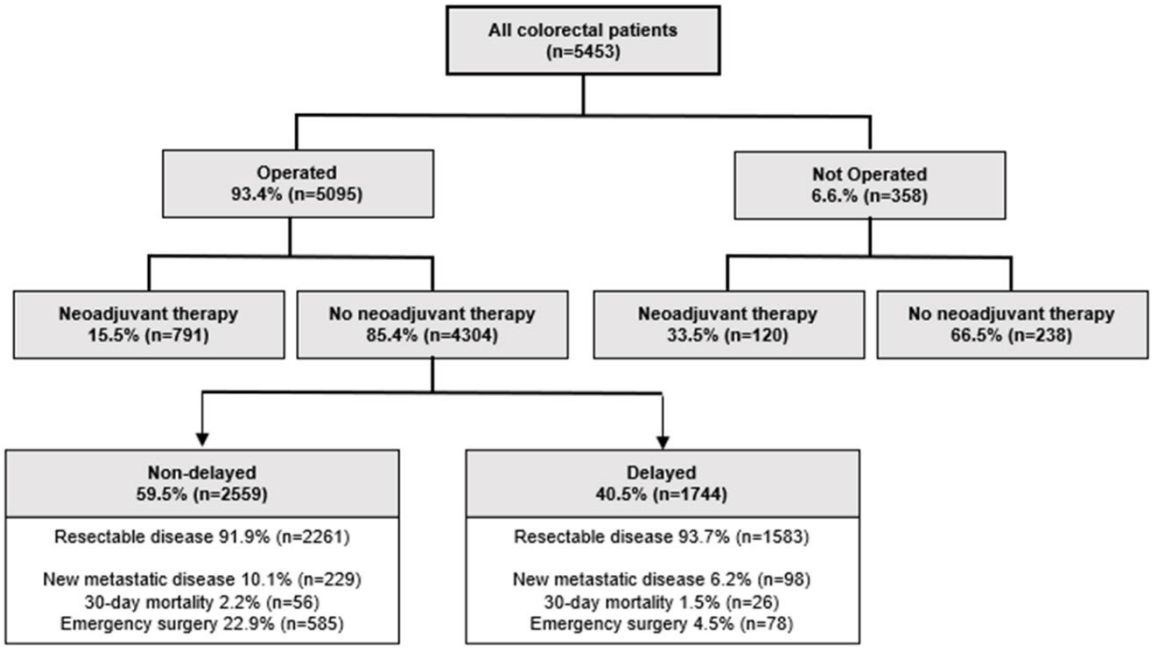
Figure 1: Flowchart of patient inclusion, with outcomes stratified by delay versus non-delay.



Delay was defined as a time from decision to treat to surgery of >4 weeks.

Table 1: Demographic features of patients having delayed and non-delayed surgery.

		Non-delayed (n=2559)	Delayed (n=1744)	P value
Site	Colon	2028 (79.2)	1274 (73.1)	<0.001
	Rectum	531 (20.8)	470 (26.9)	
Age	<70 years	1374 (53.7)	819 (47.0)	<0.001
	≥70 years	1185 (46.3)	925 (53.0)	
Sex	Female	1162 (45.4)	720 (41.3)	0.008
	Male	1397 (54.6)	1024 (58.7)	
ASA grade	1-2	1764 (69.1)	1084 (62.3)	<0.001
	3-5	789 (30.9)	657 (37.7)	
	Missing	6	3	
ECOG Score	0	1343 (53.1)	795 (46.4)	<0.001
	1-2	1101 (43.5)	867 (50.6)	
	3-4	85 (3.4)	50 (2.9)	
	Missing	30	32	
Revised Cardiac Risk Index	1-2	2382 (93.1)	1598 (91.6)	0.086
	≥3	177 (6.9)	146 (8.4)	
Body Mass Index	Underweight	92 (3.7)	45 (2.6)	<0.001
	Normal	1121 (44.7)	634 (37.1)	
	Overweight	858 (34.2)	646 (37.8)	
	Obese	437 (17.4)	385 (22.5)	
	Missing	51	34	
Stage group	Stage I	806 (32.8)	709 (41.9)	<0.001
	Stage II	560 (22.8)	365 (21.6)	
	Stage III	863 (35.1)	503 (29.7)	
	Stage IV	230 (9.4)	116 (6.9)	
	Missing	100	51	
Country Income	High income	2143 (83.7)	1571 (90.1)	<0.001
	Upper middle income	259 (10.1)	116 (6.7)	
	Low/lower-middle income	157 (6.1)	57 (3.3)	
Approach	Open	1203 (47.1)	800 (45.9)	0.733
	Minimally invasive	1216 (47.6)	850 (48.8)	
	Converted to open	137 (5.4)	92 (5.3)	
	Missing	3	2	
Anastomosis	Yes (with defunctioning stoma)	330 (13.1)	199 (11.6)	0.316
	Yes (without defunctioning stoma)	1716 (68.3)	1187 (69.1)	
	No	467 (18.6)	331 (19.3)	
	Missing	46	27	
Anastomotic method	Stapled	1646 (80.5)	1125 (81.2)	0.641
	Handsewn	398 (19.5)	260 (18.8)	
	Missing	515	359	

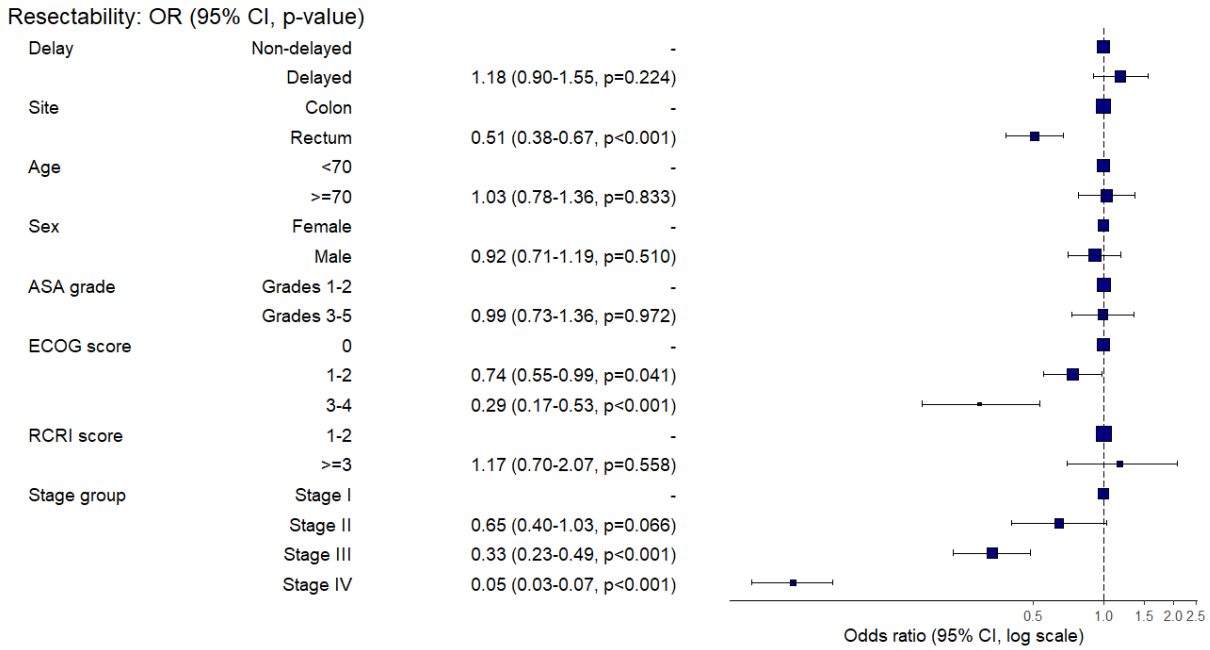
Delay was defined as a time from decision to treat to surgery of >4 weeks. Data reported as n (%). Percentages expressed of column total. P values calculated using Chi-square test. ASA=American Society of Anaesthesiologists classification, ECOG=Eastern Cooperative Oncology Group.

Table 2: Unadjusted outcomes compared between delayed and non-delayed patients.

		Non-delayed (n=2559)	Delayed (n=1744)	P value
Resectability	Complete resection	2261 (91.9)	1583 (93.7)	0.032
	Incomplete resection	199 (8.1)	106 (6.3)	
	Missing	99	55	
Resection margins	Positive	107 (4.4)	74 (4.4)	1
	Negative	2310 (95.6)	1599 (95.6)	
	Missing	142	71	
Progression to unresectable disease	Yes	127 (5.0)	40 (2.3)	<0.001
	No	2432 (95.0)	1703 (97.7)	
	Missing	0	1	
New metastatic disease	Yes	229 (10.1)	98 (6.2)	<0.001
	No	2036 (89.9)	1472 (93.8)	
	Missing	294	174	
Stage change (from baseline to pathology)	Downstaged	393 (18.1)	335 (22.0)	0.001
	No change	1236 (56.9)	775 (50.8)	
	Upstaged	543 (25.0)	416 (27.3)	
	Missing	387	218	
30-day mortality	Died	56 (2.2)	26 (1.5)	0.126
	Alive	2502 (97.8)	1718 (98.5)	
	Missing	1	0	
30-day major postoperative complications	Yes	251 (9.8)	163 (9.3)	0.648
	No	2307 (90.2)	1581 (90.7)	
	Missing	1	0	
Urgency	Emergency	585 (22.9)	78 (4.5)	<0.001
	Elective	1973 (77.1)	1663 (95.5)	
	Missing	1	3	

Delay was defined as a time from decision to treat to surgery of >4 weeks. Data reported as n (%). Percentages expressed of column total. P values calculated using Chi-square test. pCR = complete pathological response.

Figure 2: Multivariate logistic regression model exploring the association between delay to surgery and resectability, adjusting for patient and disease factors.



Number in dataframe = 3966, Number in model = 3966, Missing = 0, AIC = 1786.9, C-statistic = 0.776. Full model presented in Supplementary Table 4. Delay was defined as a time from decision to treat to surgery of >4 weeks. Data reported as odds ratio (95% confidence interval, P value). OR>1 means higher odds of resectability for delayed patients, OR<1 means lower odds of resectability for delayed patients. ASA=American Society of Anaesthesiologists classification, ECOG=Eastern Cooperative Oncology Group, RCRI=Revised Cardiac Risk Index

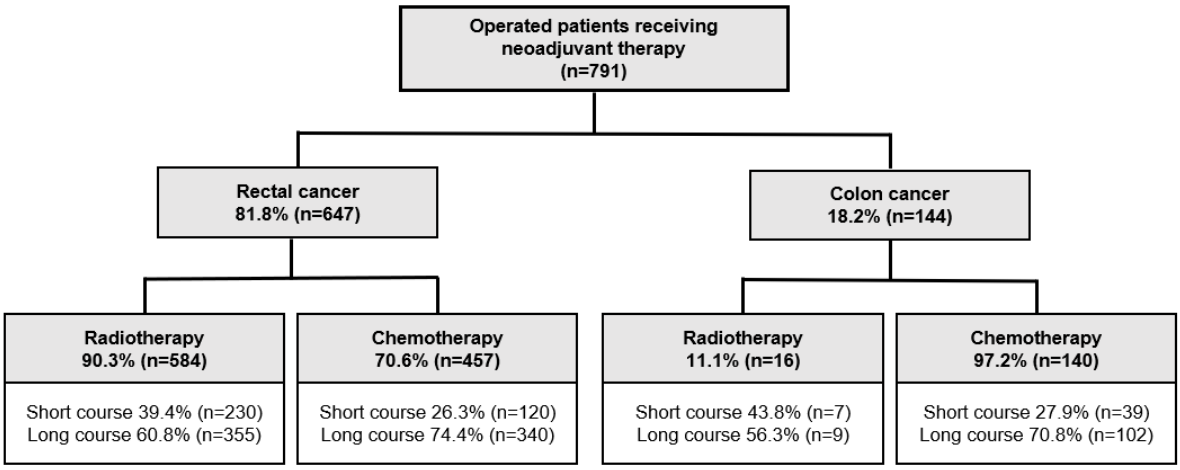
Table 3: Multivariate logistic regression model exploring the association between stratified delay to surgery and resectability, adjusting for patient and disease factors.

		Non-resectable (n=297)	Resectable (n=3669)	OR (univariable)	OR (multivariable)
Delay	0-4 weeks	193 (8.2)	2154 (91.8)	-	-
	5-8 weeks	66 (6.5)	955 (93.5)	1.30 (0.98-1.74, p=0.079)	1.16 (0.86-1.59, p=0.344)
	9-12 weeks	19 (5.3)	338 (94.7)	1.59 (1.01-2.67, p=0.060)	1.40 (0.85-2.41, p=0.206)
	>12 weeks	19 (7.9)	222 (92.1)	1.05 (0.66-1.76, p=0.855)	1.03 (0.62-1.80, p=0.920)
Site	Colon	200 (6.6)	2846 (93.4)	-	-
	Rectum	97 (10.5)	823 (89.5)	0.60 (0.46-0.77, p<0.001)	0.51 (0.38-0.68, p<0.001)
Age	<70	158 (7.9)	1850 (92.1)	-	-
	≥70	139 (7.1)	1819 (92.9)	1.12 (0.88-1.42, p=0.358)	1.03 (0.78-1.36, p=0.828)
Sex	Female	127 (7.3)	1604 (92.7)	-	-
	Male	170 (7.6)	2065 (92.4)	0.96 (0.76-1.22, p=0.749)	0.91 (0.70-1.18, p=0.491)
ASA grade	1-2	187 (7.1)	2437 (92.9)	-	-
	3-5	110 (8.2)	1232 (91.8)	0.86 (0.67-1.10, p=0.226)	0.99 (0.73-1.36, p=0.964)
ECOG grade	0	129 (6.4)	1874 (93.6)	-	-
	1-2	144 (7.9)	1690 (92.1)	0.81 (0.63-1.03, p=0.090)	0.74 (0.55-0.98, p=0.039)
	3-4	24 (18.6)	105 (81.4)	0.30 (0.19-0.50, p<0.001)	0.29 (0.17-0.53, p<0.001)
RCRI grade	1-2	278 (7.6)	3387 (92.4)	-	-
	≥3	19 (6.3)	282 (93.7)	1.22 (0.77-2.03, p=0.421)	1.18 (0.71-2.08, p=0.544)
Stage group	Stage I	39 (2.7)	1418 (97.3)	-	-
	Stage II	35 (4.0)	838 (96.0)	0.66 (0.41-1.05, p=0.078)	0.65 (0.40-1.03, p=0.066)
	Stage III	102 (7.8)	1205 (92.2)	0.32 (0.22-0.47, p<0.001)	0.34 (0.23-0.49, p<0.001)
	Stage IV	121 (36.8)	208 (63.2)	0.05 (0.03-0.07, p<0.001)	0.05 (0.03-0.07, p<0.001)

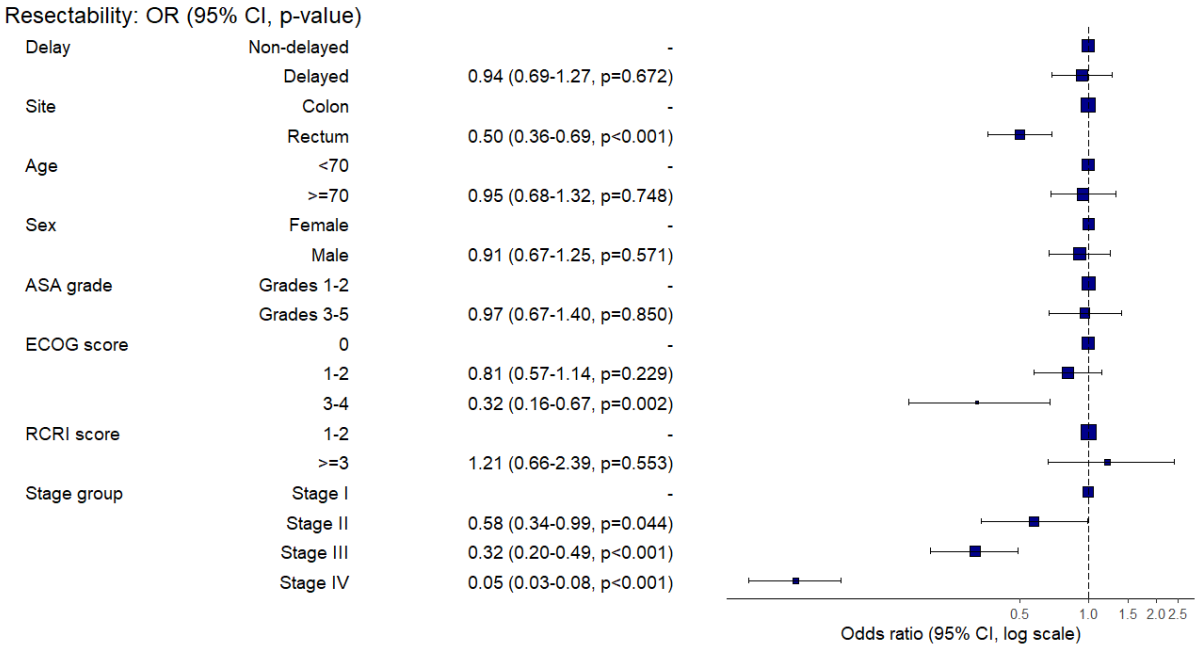
Number in dataframe = 3966, Number in model = 3966, Missing = 0, AIC = 1790.1, C-statistic = 0.776. Delay was measured from decision to treat to surgery. Data reported as odds ratio (95% confidence interval, P value). OR>1 means higher odds of resectability for delayed patients, OR<1 means lower odds of resectability for delayed patients. ASA=American Society of Anaesthesiologists classification, ECOG=Eastern Cooperative Oncology Group, RCRI=Revised Cardiac Risk Index

Appendix A: Supplementary figures and tables

Supplementary Figure 1: Neoadjuvant therapy regimen by cancer location, in all operated patients receiving neoadjuvant treatment.



Supplementary Figure 2: Multivariate logistic regression model exploring the association between delay to surgery and resectability for patients receiving elective surgery, adjusting for patient and disease factors.



Number in dataframe = 3375, Number in model = 3375, Missing = 0, AIC = 1313.8, C-statistic = 0.768. Full model presented in Supplementary table 4. Delay was defined as a time from decision to treat to surgery of >4 weeks. Data reported as odds ratio (95% confidence interval, P value). OR>1 means higher odds of resectability for delayed patients, OR<1 means lower odds of resectability for delayed patients. ASA=American Society of Anaesthesiologists classification, ECOG=Eastern Cooperative Oncology Group, RCRI=Revised Cardiac Risk Index

Supplementary Table 1: Demographic features of patients receiving and not receiving an operation.

		Operated (n=5095)	Not Operated (n=358)	P value
Site	Colon	3446 (67.6)	170 (47.5)	<0.001
	Rectum	1649 (32.4)	188 (52.5)	
Age	<70 years	2726 (53.5)	209 (58.4)	0.083
	≥70 years	2369 (46.5)	149 (41.6)	
Sex	Female	2182 (42.8)	145 (40.5)	0.421
	Male	2913 (57.2)	213 (59.5)	
ASA grade	1-2	3413 (67.1)	206 (60.1)	0.009
	3-5	1672 (32.9)	137 (39.9)	
	Missing	10	15	
ECOG Score	0	2581 (51.3)	135 (39.8)	<0.001
	1-2	2298 (45.7)	184 (54.3)	
	3-4	148 (2.9)	20 (5.9)	
	Missing	68	19	
Revised Cardiac Risk Index	1-2	4728 (92.8)	327 (91.3)	0.358
	≥3	367 (7.2)	31 (8.7)	
BMI	Underweight	174 (3.5)	30 (9.3)	<0.001
	Normal	2111 (42.3)	120 (37.0)	
	Overweight	1756 (35.1)	111 (34.3)	
	Obese	955 (19.1)	63 (19.4)	
	Missing	99	34	
Stage group	Stage I	1572 (31.9)	92 (26.4)	0.004
	Stage II	1044 (21.2)	61 (17.5)	
	Stage III	1808 (36.7)	145 (41.5)	
	Stage IV	507 (10.3)	51 (14.6)	
	Missing	164	9	
Country Income	High income	4337 (85.1)	265 (74.0)	<0.001
	Upper middle income	472 (9.3)	28 (7.8)	
	Low/lower-middle income	286 (5.6)	65 (18.2)	

Data reported as n (%). Percentages expressed of column total. P values calculated using Chi-square test. ASA=American Society of Anaesthesiologists classification, ECOG=Eastern Cooperative Oncology Group.

Supplementary Table 2: Reasons why patients did not receive their operation.

	Number (%) (n=358)
Multidisciplinary team decision to cancel surgery due to patient risk	260 (72.6)
Disease progression	104 (29.1)
Patient unable to travel to hospital related to COVID-19	94 (26.3)
Patient choice to avoid surgery during COVID-19 pandemic	82 (22.9)
Watch and wait surveillance only	78 (21.8)
Performed local excision	75 (20.9)
No bed/critical care bed/OR/theatre space available	53 (14.8)
Change of recommendations in society guidelines related to COVID-19	38 (10.6)
Patient decision not related to COVID	11 (3.1)
Delayed due to COVID-19 infection	10 (2.8)
Collateral impact on services causing delay	6 (1.7)
Other medical/surgical condition presented whilst waiting for surgery causing delay	5 (1.4)
Patient unable to afford surgery	3 (0.8)
Remission leading to decision not to operate	2 (0.6)
Regression leading to change in plan and delay	1 (0.3)
Awaiting restaging and/or surgical plan	1 (0.3)

Data reported as n (%). Patients could have had multiple of these reasons to not receive an operation.

Supplementary Table 3: Reasons why patients received emergency surgery.

	Number (%) (n=663)
Gastrointestinal obstruction	396 (59.7)
Tumour progression	136 (20.5)
Bleeding	100 (15.1)
Organ perforation	64 (9.7)
Pain	58 (8.7)
Sepsis	28 (4.2)
Uncertain elective capacity	2 (0.3)

Data reported as n (%). Emergency surgery was any emergency surgery for colorectal cancer performed whilst awaiting the planned elective surgery, with or without resection.

Supplementary Table 4: Full multivariate logistic regression model exploring the association between delay to surgery and resectability, adjusting for patient and disease factors.

		Non-resectable (n=297)	Resectable (n=3669)	OR (univariable)	OR (multivariable)
Delay	Non-delayed	193 (8.2)	2154 (91.8)	-	-
	Delayed	104 (6.4)	1515 (93.6)	1.31 (1.02-1.68, p=0.035)	1.18 (0.90-1.55, p=0.224)
Site	Colon	200 (6.6)	2846 (93.4)	-	-
	Rectum	97 (10.5)	823 (89.5)	0.60 (0.46-0.77, p<0.001)	0.51 (0.38-0.67, p<0.001)
Age	<70 years	158 (7.9)	1850 (92.1)	-	-
	≥70 years	139 (7.1)	1819 (92.9)	1.12 (0.88-1.42, p=0.358)	1.03 (0.78-1.36, p=0.833)
Sex	Female	127 (7.3)	1604 (92.7)	-	-
	Male	170 (7.6)	2065 (92.4)	0.96 (0.76-1.22, p=0.749)	0.92 (0.71-1.19, p=0.510)
ASA grade	1-2	187 (7.1)	2437 (92.9)	-	-
	3-5	110 (8.2)	1232 (91.8)	0.86 (0.67-1.10, p=0.226)	0.99 (0.73-1.36, p=0.972)
ECOG grade	0	129 (6.4)	1874 (93.6)	-	-
	1-2	144 (7.9)	1690 (92.1)	0.81 (0.63-1.03, p=0.090)	0.74 (0.55-0.99, p=0.041)
	3-4	24 (18.6)	105 (81.4)	0.30 (0.19-0.50, p<0.001)	0.29 (0.17-0.53, p<0.001)
RCRI grade	1-2	278 (7.6)	3387 (92.4)	-	-
	≥3	19 (6.3)	282 (93.7)	1.22 (0.77-2.03, p=0.421)	1.17 (0.70-2.07, p=0.558)
Stage group	Stage I	39 (2.7)	1418 (97.3)	-	-
	Stage II	35 (4.0)	838 (96.0)	0.66 (0.41-1.05, p=0.078)	0.65 (0.40-1.03, p=0.066)
	Stage III	102 (7.8)	1205 (92.2)	0.32 (0.22-0.47, p<0.001)	0.33 (0.23-0.49, p<0.001)
	Stage IV	121 (36.8)	208 (63.2)	0.05 (0.03-0.07, p<0.001)	0.05 (0.03-0.07, p<0.001)

Number in dataframe = 3966, Number in model = 3966, Missing = 0, AIC = 1786.9, C-statistic = 0.776. Delay was defined as a time from decision to treat to surgery of >4 weeks. Data reported as odds ratio (95% confidence interval, P value). OR>1 means higher odds of resectability for delayed patients, OR<1 means lower odds of resectability for delayed patients. ASA=American Society of Anaesthesiologists classification, ECOG=Eastern Cooperative Oncology Group, RCRI=Revised Cardiac Risk Index

Supplementary Table 5: Demographic features of patients having delayed and non-delayed, elective surgery only.

		Non-delayed (n=1973)	Delayed (n=1663)	P value
Site	Colon	1511 (76.6)	1213 (72.9)	0.013
	Rectum	462 (23.4)	450 (27.1)	
Age	<70 years	1050 (53.2)	778 (46.8)	<0.001
	≥70 years	923 (46.8)	885 (53.2)	
Sex	Female	886 (44.9)	672 (40.4)	0.007
	Male	1087 (55.1)	991 (59.6)	
ASA grade	1-2	1390 (70.6)	1031 (62.1)	<0.001
	3-5	579 (29.4)	629 (37.9)	
	Missing	4	3	
ECOG Score	0	1118 (57.3)	763 (46.7)	<0.001
	1-2	784 (40.2)	825 (50.5)	
	3-4	49 (2.5)	47 (2.9)	
	Missing	22	28	
Revised Cardiac Risk Index	1-2	1845 (93.5)	1520 (91.4)	0.019
	≥3	128 (6.5)	143 (8.6)	
Body Mass Index	Underweight	61 (3.2)	44 (2.7)	<0.001
	Normal	860 (44.5)	607 (37.2)	
	Overweight	670 (34.7)	610 (37.4)	
	Obese	341 (17.7)	372 (22.8)	
	Missing	41	30	
Stage group	Stage I	697 (36.8)	683 (42.3)	0.002
	Stage II	407 (21.5)	354 (21.9)	
	Stage III	641 (33.8)	472 (29.2)	
	Stage IV	151 (8.0)	105 (6.5)	
	Missing	77	49	
Country Income	High income	1721 (87.2)	1512 (90.9)	0.002
	Upper middle income	168 (8.5)	102 (6.1)	
	Low/lower-middle income	84 (4.3)	49 (2.9)	
Approach	Open	786 (39.9)	743 (44.7)	0.01
	Minimally invasive	1080 (54.8)	829 (49.9)	
	Converted to open	104 (5.3)	89 (5.4)	
	Missing	3	2	
Anastomosis	Yes (with defunctioning stoma)	260 (13.5)	181 (11.1)	<0.001
	Yes (without defunctioning stoma)	1413 (73.2)	1152 (70.4)	
	No	258 (13.4)	304 (18.6)	
	Missing	42	26	
Anastomotic method	Stapled	1373 (82.2)	1084 (81.4)	0.613
	Handsewn	298 (17.8)	248 (18.6)	
	Missing	302	331	

Delay was defined as a time from decision to treat to surgery of >4 weeks. Data reported as n (%). Percentages expressed of column total. P values calculated using Chi-square test. ASA=American Society of Anaesthesiologists classification, ECOG=Eastern Cooperative Oncology Group.

Supplementary Table 6: Multivariate logistic regression model exploring the association between delay to surgery and resectability in colon cancer patients, adjusting for patient and disease factors.

		Non-resectable (n=200)	Resectable (n=2846)	OR (univariable)	OR (multivariable)
Delay	Non-delayed	142 (7.6)	1720 (92.4)	-	-
	Delayed	58 (4.9)	1126 (95.1)	1.60 (1.18-2.21, p=0.003)	1.33 (0.95-1.87, p=0.101)
Age	<70 years	100 (6.8)	1375 (93.2)	-	-
	≥70 years	100 (6.4)	1471 (93.6)	1.07 (0.80-1.43, p=0.645)	1.06 (0.75-1.48, p=0.753)
Sex	Female	93 (6.8)	1276 (93.2)	-	-
	Male	107 (6.4)	1570 (93.6)	1.07 (0.80-1.43, p=0.647)	0.95 (0.70-1.30, p=0.767)
ASA grade	1-2	121 (6.2)	1842 (93.8)	-	-
	3-5	79 (7.3)	1004 (92.7)	0.83 (0.62-1.12, p=0.228)	0.94 (0.65-1.37, p=0.740)
ECOG grade	0	78 (5.3)	1400 (94.7)	-	-
	1-2	104 (7.1)	1354 (92.9)	0.73 (0.53-0.98, p=0.038)	0.69 (0.48-0.98, p=0.041)
	3-4	18 (16.4)	92 (83.6)	0.28 (0.17-0.51, p<0.001)	0.33 (0.17-0.66, p=0.001)
RCRI grade	1-2	184 (6.6)	2618 (93.4)	-	-
	≥3	16 (6.6)	228 (93.4)	1.00 (0.61-1.76, p=0.995)	1.00 (0.56-1.88, p=0.999)
Stage group	Stage I	24 (2.2)	1061 (97.8)	-	-
	Stage II	21 (3.0)	682 (97.0)	0.73 (0.41-1.34, p=0.308)	0.77 (0.42-1.41, p=0.390)
	Stage III	63 (6.3)	941 (93.7)	0.34 (0.21-0.54, p<0.001)	0.36 (0.22-0.58, p<0.001)
	Stage IV	92 (36.2)	162 (63.8)	0.04 (0.02-0.06, p<0.001)	0.04 (0.03-0.07, p<0.001)

Number in dataframe = 3046, Number in model = 3046, Missing = 0, AIC = 1227.6, C-statistic = 0.784. Delay was defined as a time from decision to treat to surgery of >4 weeks. Data reported as odds ratio (95% confidence interval, P value). OR>1 means higher odds of resectability for delayed patients, OR<1 means lower odds of resectability for delayed patients. ASA=American Society of Anaesthesiologists classification, ECOG=Eastern Cooperative Oncology Group, RCRI=Revised Cardiac Risk Index

Supplementary Table 7: Multivariate logistic regression model exploring the association between delay to surgery and resectability in rectal cancer patients, adjusting for patient and disease factors.

		Non-resectable (n=97)	Resectable (n=823)	OR (univariable)	OR (multivariable)
Delay	Non-delayed	51 (10.5)	434 (89.5)	-	-
	Delayed	46 (10.6)	389 (89.4)	0.99 (0.65-1.52, p=0.977)	0.91 (0.58-1.44, p=0.692)
Age	<70 years	58 (10.9)	475 (89.1)	-	-
	≥70 years	39 (10.1)	348 (89.9)	1.09 (0.71-1.68, p=0.695)	0.96 (0.59-1.56, p=0.857)
Sex	Female	34 (9.4)	328 (90.6)	-	-
	Male	63 (11.3)	495 (88.7)	0.81 (0.52-1.26, p=0.360)	0.80 (0.50-1.27, p=0.356)
ASA grade	1-2	66 (10.0)	595 (90.0)	-	-
	3-5	31 (12.0)	228 (88.0)	0.82 (0.52-1.30, p=0.379)	1.08 (0.62-1.94, p=0.783)
ECOG grade	0	51 (9.7)	474 (90.3)	-	-
	1-2	40 (10.6)	336 (89.4)	0.90 (0.58-1.41, p=0.650)	0.88 (0.53-1.47, p=0.619)
	3-4	6 (31.6)	13 (68.4)	0.23 (0.09-0.69, p=0.005)	0.18 (0.06-0.64, p=0.006)
RCRI grade	1-2	94 (10.9)	769 (89.1)	-	-
	≥3	3 (5.3)	54 (94.7)	2.20 (0.79-9.15, p=0.191)	2.32 (0.74-10.32, p=0.197)
Stage group	Stage I	15 (4.0)	357 (96.0)	-	-
	Stage II	14 (8.2)	156 (91.8)	0.47 (0.22-1.00, p=0.048)	0.47 (0.22-1.01, p=0.049)
	Stage III	39 (12.9)	264 (87.1)	0.28 (0.15-0.52, p<0.001)	0.29 (0.15-0.53, p<0.001)
	Stage IV	29 (38.7)	46 (61.3)	0.07 (0.03-0.13, p<0.001)	0.07 (0.03-0.13, p<0.001)

Number in dataframe = 920, Number in model = 920, Missing = 0, AIC = 567.8, C-statistic = 0.745. Delay was defined as a time from decision to treat to surgery of >4 weeks. Data reported as odds ratio (95% confidence interval, P value). OR>1 means higher odds of resectability for delayed patients, OR<1 means lower odds of resectability for delayed patients. ASA=American Society of Anaesthesiologists classification, ECOG=Eastern Cooperative Oncology Group, RCRI=Revised Cardiac Risk Index

Supplementary Table 8: Multivariate logistic regression model exploring the association between delay to surgery and resectability in patients with early disease, adjusting for patient and disease factors.

		Non-resectable (n=49)	Resectable (n=2006)	OR (univariable)	OR (multivariable)
Delay	Non-delayed	28 (2.5)	1090 (97.5)	-	-
	Delayed	21 (2.2)	916 (97.8)	1.12 (0.63-2.01, p=0.697)	1.20 (0.67-2.18, p=0.537)
Site	Colon	28 (1.8)	1513 (98.2)	-	-
	Rectum	21 (4.1)	493 (95.9)	0.43 (0.25-0.78, p=0.004)	0.41 (0.23-0.74, p=0.003)
Age	<70 years	22 (2.2)	975 (97.8)	-	-
	≥70 years	27 (2.6)	1031 (97.4)	0.86 (0.48-1.52, p=0.608)	0.93 (0.50-1.71, p=0.805)
Sex	Female	21 (2.4)	837 (97.6)	-	-
	Male	28 (2.3)	1169 (97.7)	1.05 (0.58-1.85, p=0.874)	1.01 (0.56-1.80, p=0.970)
ASA grade	1-2	29 (2.2)	1280 (97.8)	-	-
	3-5	20 (2.7)	726 (97.3)	0.82 (0.46-1.48, p=0.507)	0.86 (0.44-1.70, p=0.651)
ECOG grade	0	21 (1.9)	1058 (98.1)	-	-
	1-2	26 (2.8)	894 (97.2)	0.68 (0.38-1.22, p=0.198)	0.66 (0.34-1.27, p=0.213)
	3-4	2 (3.6)	54 (96.4)	0.54 (0.15-3.40, p=0.407)	0.48 (0.12-3.28, p=0.367)
RCRI grade	1-2	46 (2.5)	1817 (97.5)	-	-
	≥3	3 (1.6)	189 (98.4)	1.59 (0.58-6.61, p=0.437)	1.93 (0.66-8.25, p=0.292)
Stage group	Stage I	30 (2.3)	1286 (97.7)	-	-
	Stage II	19 (2.6)	720 (97.4)	0.88 (0.50-1.61, p=0.678)	0.86 (0.48-1.56, p=0.603)

Number in dataframe = 2055, Number in model = 2055, Missing = 0, AIC = 470.7, C-statistic = 0.634. Delay was defined as a time from decision to treat to surgery of >4 weeks. Advanced disease was defined as T4, N1/2 or M1 disease; early disease was all other stages. Data reported as odds ratio (95% confidence interval, P value). OR>1 means higher odds of resectability for delayed patients, OR<1 means lower odds of resectability for delayed patients. ASA=American Society of Anaesthesiologists classification, ECOG=Eastern Cooperative Oncology Group, RCRI=Revised Cardiac Risk Index

Supplementary Table 9: Multivariate logistic regression model exploring the association between delay to surgery and resectability in patients with advanced disease, adjusting for patient and disease factors.

		Non-resectable (n=239)	Resectable (n=1531)	OR (univariable)	OR (multivariable)
Delay	Non-delayed	158 (13.9)	979 (86.1)	-	-
	Delayed	81 (12.8)	552 (87.2)	1.10 (0.83-1.47, p=0.516)	1.11 (0.81-1.52, p=0.517)
Site	Colon	165 (12.0)	1212 (88.0)	-	-
	Rectum	74 (18.8)	319 (81.2)	0.59 (0.44-0.80, p=0.001)	0.51 (0.37-0.71, p<0.001)
Age	<70 years	131 (13.8)	821 (86.2)	-	-
	≥70 years	108 (13.2)	710 (86.8)	1.05 (0.80-1.38, p=0.732)	1.02 (0.74-1.40, p=0.915)
Sex	Female	104 (12.9)	704 (87.1)	-	-
	Male	135 (14.0)	827 (86.0)	0.90 (0.69-1.19, p=0.476)	0.91 (0.67-1.22, p=0.530)
ASA grade	1-2	154 (12.7)	1056 (87.3)	-	-
	3-5	85 (15.2)	475 (84.8)	0.81 (0.61-1.09, p=0.161)	1.10 (0.77-1.58, p=0.594)
ECOG grade	0	103 (12.1)	749 (87.9)	-	-
	1-2	114 (13.5)	733 (86.5)	0.88 (0.66-1.18, p=0.398)	0.76 (0.55-1.06, p=0.103)
	3-4	22 (31.0)	49 (69.0)	0.31 (0.18-0.54, p<0.001)	0.24 (0.12-0.46, p<0.001)
RCRI grade	1-2	226 (13.5)	1443 (86.5)	-	-
	≥3	13 (12.9)	88 (87.1)	1.06 (0.60-2.02, p=0.848)	1.16 (0.61-2.34, p=0.669)
Stage group	Stage II	16 (11.9)	118 (88.1)	-	-
	Stage III	102 (7.8)	1205 (92.2)	1.60 (0.89-2.73, p=0.099)	1.83 (1.01-3.16, p=0.037)
	Stage IV	121 (36.8)	208 (63.2)	0.23 (0.13-0.40, p<0.001)	0.25 (0.14-0.44, p<0.001)

Number in dataframe = 1770, Number in model = 1770, Missing = 0, AIC = 1236.1, C-statistic = 0.743. Delay was defined as a time from decision to treat to surgery of >4 weeks. Advanced disease was defined as T4, N1/2 or M1 disease. Data reported as odds ratio (95% confidence interval, P value). OR>1 means higher odds of resectability for delayed patients, OR<1 means lower odds of resectability for delayed patients. ASA=American Society of Anaesthesiologists classification, ECOG=Eastern Cooperative Oncology Group, RCRI=Revised Cardiac Risk Index

Supplementary Table 10: Demographic features of patients stratified by length of delay.

		0-4 weeks (n=2559)	5-8 weeks (n=1089)	9-12 weeks (n=384)	>12 weeks (n=271)	P value
Site	Colon	2028 (79.2)	798 (73.3)	289 (75.3)	187 (69.0)	<0.001
	Rectum	531 (20.8)	291 (26.7)	95 (24.7)	84 (31.0)	
Age	<70 years	1374 (53.7)	532 (48.9)	167 (43.5)	120 (44.3)	<0.001
	≥70 years	1185 (46.3)	557 (51.1)	217 (56.5)	151 (55.7)	
Sex	Female	1162 (45.4)	468 (43.0)	150 (39.1)	102 (37.6)	0.014
	Male	1397 (54.6)	621 (57.0)	234 (60.9)	169 (62.4)	
ASA grade	1-2	1764 (69.1)	696 (64.0)	222 (58.0)	166 (61.5)	<0.001
	3-5	789 (30.9)	392 (36.0)	161 (42.0)	104 (38.5)	
	Missing	6	1	1	1	
ECOG Score	0	1343 (53.1)	528 (49.3)	150 (39.6)	117 (44.7)	<0.001
	1-2	1101 (43.5)	511 (47.7)	216 (57.0)	140 (53.4)	
	3-4	85 (3.4)	32 (3.0)	13 (3.4)	5 (1.9)	
	Missing	30	18	5	9	
RCRI	1-2	2382 (93.1)	1010 (92.7)	351 (91.4)	237 (87.5)	0.008
	≥3	177 (6.9)	79 (7.3)	33 (8.6)	34 (12.5)	
BMI	Underweight	92 (3.7)	28 (2.6)	8 (2.1)	9 (3.5)	<0.001
	Normal	1121 (44.7)	414 (38.5)	134 (35.7)	86 (33.1)	
	Overweight	858 (34.2)	390 (36.3)	150 (40.0)	106 (40.8)	
	Obese	437 (17.4)	243 (22.6)	83 (22.1)	59 (22.7)	
	Missing	51	14	9	11	
Stage group	Stage I	806 (32.8)	431 (40.8)	170 (45.5)	108 (41.1)	<0.001
	Stage II	560 (22.8)	241 (22.8)	78 (20.9)	46 (17.5)	
	Stage III	863 (35.1)	312 (29.5)	104 (27.8)	87 (33.1)	
	Stage IV	230 (9.4)	72 (6.8)	22 (5.9)	22 (8.4)	
	Missing	100	33	10	8	
Country Income	High income	2143 (83.7)	987 (90.6)	350 (91.1)	234 (86.3)	<0.001
	Upper middle income	259 (10.1)	67 (6.2)	22 (5.7)	27 (10.0)	
	Low/lower-middle income	157 (6.1)	35 (3.2)	12 (3.1)	10 (3.7)	
Approach	Open	1203 (47.1)	501 (46.0)	161 (42.0)	138 (51.1)	0.299
	Minimally invasive	1216 (47.6)	535 (49.1)	196 (51.2)	119 (44.1)	
	Converted to open	137 (5.4)	53 (4.9)	26 (6.8)	13 (4.8)	
	Missing	3	0	1	1	
Anastomosis	Yes (with defunctioning stoma)	330 (13.1)	116 (10.8)	43 (11.4)	40 (14.9)	0.1
	Yes (without defunctioning stoma)	1716 (68.3)	756 (70.5)	265 (70.5)	166 (61.7)	
	No	467 (18.6)	200 (18.7)	68 (18.1)	63 (23.4)	
	Missing	46	17	8	2	
Anastomotic method	Stapled	1646 (80.5)	714 (82.0)	244 (79.2)	167 (81.1)	0.711
	Handsewn	398 (19.5)	157 (18.0)	64 (20.8)	39 (18.9)	
	Missing	515	218	76	65	

Delay was measured from decision to treat to surgery. The total of patients reported in the table is 4303 (missing data for length of delay n=1). Data reported as n (%). Percentages expressed of column total. P values calculated using Chi-square test. ASA=American Society of Anaesthesiologists classification, ECOG=Eastern Cooperative Oncology Group, RCRI=Revised Cardiac Risk Index.

Supplementary Table 11: Unadjusted outcomes compared by length of delay to surgery.

		0-4 weeks (n=2559)	5-8 weeks (n=1089)	9-12 weeks (n=384)	>12 weeks (n=271)	P value
Resectability	Complete resection	2261 (91.9)	993 (93.7)	352 (94.9)	238 (92.2)	0.094
	Incomplete resection	199 (8.1)	67 (6.3)	19 (5.1)	20 (7.8)	
	Missing	99	29	13	13	
Resection margins	Positive	107 (4.4)	48 (4.6)	12 (3.3)	14 (5.5)	0.58
	Negative	2310 (95.6)	1004 (95.4)	356 (96.7)	239 (94.5)	
	Missing	142	37	16	18	
Progression to unresectable disease	Yes	127 (5.0)	24 (2.2)	8 (2.1)	8 (3.0)	<0.001
	No	2432 (95.0)	1064 (97.8)	376 (97.9)	263 (97.0)	
	Missing	0	1	0	0	
Stage change (from baseline to pathology)	Downstaged	393 (18.1)	200 (20.9)	82 (23.9)	53 (23.3)	0.007
	No change	1236 (56.9)	501 (52.4)	166 (48.4)	108 (47.6)	
	Upstaged	543 (25.0)	255 (26.7)	95 (27.7)	66 (29.1)	
	Missing	387	133	41	44	
New metastatic disease	Yes	229 (10.1)	63 (6.4)	18 (5.1)	17 (7.2)	<0.001
	No	2036 (89.9)	919 (93.6)	334 (94.9)	219 (92.8)	
	Missing	294	107	32	35	
30-day mortality	Died	56 (2.2)	17 (1.6)	3 (0.8)	6 (2.2)	0.21
	Alive	2502 (97.8)	1072 (98.4)	381 (99.2)	265 (97.8)	
	Missing	1	0	0	0	
30-day major postoperative complications	Yes	251 (9.8)	100 (9.2)	33 (8.6)	30 (11.1)	0.69
	No	2307 (90.2)	989 (90.8)	351 (91.4)	241 (88.9)	
	Missing	1	0	0	0	
Urgency	Emergency	585 (22.9)	53 (4.9)	14 (3.7)	11 (4.1)	<0.001
	Elective	1973 (77.1)	1035 (95.1)	368 (96.3)	260 (95.9)	
	Missing	1	1	2	0	

Delay was measured from decision to treat to surgery. The total of patients reported in the table is 4303 (missing data for length of delay n=1). Data reported as n (%). Percentages expressed of column total. P values calculated using Chi-square test.

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