Development of a CFD Procedure for the Axial Thrust Evaluation in Multistage Centrifugal Pumps

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Original Article

Impact of COVID-19 on the oncological outcomes of colorectal cancer surgery in northern Italy in 2019 and 2020: multicentre comparative cohort study

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Members of the COVID-CRC Collaborative Group are listed under the heading Collaborators and in *Appendix S1*.

Abstract

Background: This study compared patients undergoing colorectal cancer surgery in 20 hospitals of northern Italy in 2019 *versus* 2020, in order to evaluate whether COVID-19-related delays of colorectal cancer screening resulted in more advanced cancers at diagnosis and worse clinical outcomes.

Method: This was a retrospective multicentre cohort analysis of patients undergoing colorectal cancer surgery in March to December 2019 *versus* March to December 2020. Independent predictors of disease stage (oncological stage, associated symptoms, clinical T4 stage, metastasis) and outcome (surgical complications, palliative surgery, 30-day death) were evaluated using logistic regression.

Results: The sample consisted of 1755 patients operated in 2019, and 1481 in 2020 (both mean age 69.6 years). The proportion of cancers with symptoms, clinical T4 stage, liver and lung metastases in 2019 and 2020 were respectively: 80.8 *versus* 84.5 per cent; 6.2 *versus* 8.7 per cent; 10.2 *versus* 10.3 per cent; and 3.0 *versus* 4.4 per cent. The proportions of surgical complications, palliative surgery and death in 2019 and 2020 were, respectively: 34.4 *versus* 31.9 per cent; 5.0 *versus* 7.5 per cent; and 1.7 *versus* 2.4 per cent. Cancers in 2020 (*versus* 2019) were more likely to be symptomatic (odds ratio 1.36 (95 per cent c.i. 1.09 to 1.69)), clinical T4 stage (odds ratio 1.38 (95 per cent c.i. 1.03 to 1.85)) and have multiple liver metastases (odds ratio 2.21 (95 per cent c.i. 1.24 to 3.94)), but were not more likely to be associated with surgical complications (odds ratio 0.79 (95 per cent c.i. 0.68 to 0.93)).

Conclusion: Colorectal cancer patients who had surgery between March and December 2020 had an increased risk of advanced disease in terms of associated symptoms, cancer location, clinical T4 stage and number of liver metastases.

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Introduction

Coronavirus disease 19 (COVID-19), which is associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, has spread worldwide since it was first reported in China in December 2019[1,2]. Italy witnessed a rapid and uncontrolled spread of the infection from February 2020, and a number of related deaths, which surpassed those of China by the end of March 2020, especially in the northern regions[3,4]. Due to great pressure on the healthcare system for the diagnosis and treatment of COVID-19 patients, a national lockdown was established on 10 March 2020[5]. As a consequence, elective surgical activities were greatly reduced, and screening programmes were suspended for the greater part of the period between March and May 2020[6]. This included the faecal immunochemical test (FIT), which has been widely adopted in Italy and many European countries for colorectal cancer screening[7]. This has been observed in other countries[8,9] and has raised concerns about delayed diagnosis, later presentation of disease, and the impact on outcomes[10–13]. No evidence has been provided, however, regarding an increase in advanced oncological stage in patients who underwent surgery for colorectal cancer in 2020.

The aim was to analyse the outcomes of patients undergoing surgery for colorectal cancer in northern Italy between March and December 2020, and to compare them to those of patients with the same diagnosis who had had surgery in the same period of 2019.

Methods

Study design and participants

This was a retrospective cohort study enrolling all adult (18 years and older) patients who underwent surgery for a proven or suspected colorectal malignancy, and had been followed for at least 30 days after surgery, from 1 March to 31 December 2019 and from 1 March to 31 December 2020, in 20 referral centres for the treatment of colorectal cancer located in the Italian regions of Lombardy, Piedmont, Emilia-Romagna, Veneto and Friuli-Venezia-Giulia. The details of the centres are listed in *Appendix S2*, while their geographical distribution is shown in *Appendix S3*.

The study was approved by the Ethical Committee of the leading centre (Azienda Ospedaliero Universitaria di Bologna, Alma Mater Studiorum University of Bologna) and subsequently approved by the ethical committees of the participating centres. Informed consent was required from patients participating in the study, according to Italian regulations. The RECORD (REporting of studies Conducted using Observational Routinely-collected Data) Statement check-list was attached as *Appendix S4*. The study was registered on ClinicalTrials.gov (registration number: NCT04712292).

Inclusion criteria were a preoperative or postoperative histologically confirmed diagnosis of cancer, elective or urgent surgery, palliative or curative surgery, location of the cancer in the colon, the rectum or the anus and any type of surgery, including surgical exploration or palliative procedures.

Exclusion criteria were recurrent colorectal cancer after previous surgery, cancer originating from other organs, lack of significant histological details (except when the cancer was not removed, in palliative procedures, carcinomatosis, etc.) and lack of 30-day follow-up.

All patients were included in the study regardless of the 30-day outcome (discharge, still in the hospital or death) and all data were extracted directly from the charts, validated by trained specialist physicians in the participating centres, and entered in REDCap software (Research Electronic Data Capture)[14]. In order to reduce selection bias, all operative lists and patient charts were checked by study collaborators in each centre. Only the principal investigator had access to the data extraction of the database, which contained anonymized data. The present study included person-level data, and no linkage between more databases was necessary.

The data set included details regarding patient history, comorbidities, preoperative diagnosis (location of the tumour, diagnostic tests, preoperative stage), the use of neoadjuvant therapy, surgical procedures, the onset of 30-day postoperative complications, death and histological examination. The biology of the tumour was considered to have worse prognostic features at histological examination with the presence of signet ring cells, mucinous tumours, tumour budding, lymphovascular invasion, perineural invasion and lymphangitis. Right colon cancers were defined as those in the caecum, ascending and transverse colon proximal to the splenic flexure. Left colon cancers were defined as those located between the splenic flexure and the rectosigmoid junction; and rectum cancers included those located distally to the rectosigmoid junction, including the anus.

The primary outcomes of the study were: advanced TNM stage (cancers with T4N0, any T N1 or N2, any T any N M+ stages, plus all cases without final histology which required palliative surgery); and palliative surgery (defined as any procedure which did not have the aim of radically removing the primary cancer, either planned before surgery in order to reduce the associated symptoms or to confirm the diagnosis, or which became necessary due to unexpected findings during surgery). The presence of distant metastases did not define palliative surgery as long as the surgical procedure was carried out according to the oncological principles of radical surgery.

The study included the following measures of cancer clinical stage or outcome as secondary outcomes: associated symptoms at diagnosis (including bleeding, change in bowel habit, tenesmus, anaemia, abdominal pain, weight loss, bowel obstruction); clinical T4 stage (defined as the presence of cancer-induced spiculations extended over the bowel wall or suspicion of infiltration of the surrounding organs or structures at preoperative radiological imaging); presence of lung metastases; presence of liver metastases (and proportion of patients with oligometastatic disease); surgical complications; emergency surgery (surgery within 48 hours from the admission to hospital); death at 30 days.

Statistical analysis

Continuous variables were expressed as mean(s.d.) and categorical variables were presented as number (per cent).

For each outcome, the differences in the recorded variables between 2020 and 2019 were initially evaluated using the chi-squared test for categorical variables and the *t*-test or Kruskal–Wallis test for normally distributed and non-normally distributed continuous variables respectively (distribution was assessed through the Shapiro–Wilk test). The potential independent predictors of the primary and secondary outcomes were then evaluated using logistic regression. No multivariable analysis was attempted to predict lung metastases and emergency surgery, due to low numbers (3.7 per cent and 9.8 per cent of the sample respectively).

All the models were built adopting a stepwise forward process for co-variable selection, limiting their number to 10 per success to avoid overfitting, and including those resulting in a change in

Table 1 Selected clinical and organizational characteristics of the sample, overall and by year of surgical procedure (2020 *versus* 2019)

	Total sample (n = 3236)	March–December 2019 (n = 1755)	March–December 2020 (n = 1481)	P†
Age (years)*	69.6(13.0)	69.6(12.8)	69.6(13.2)	0.898
Male gender	42.9	42.9	42.9	0.987
BMI (kg/m²)*	25.3(4.9)	25.3(4.8)	25.3(5.0)	0.825
Smoking status	(n = 2854)	(n = 1558)	(n = 1296)	
Never	60.7	60.0	61.5	0.641
	(n = 2743)	(n = 1521)	(n = 1222)	
Past	25.6	25.1	26.4	0.721
Current	13.7	14.9	12.1	0.409
Family history of cancer	12.8	13.1	12.5	0.622
Co-morbidities	(n = 2793)	(n = 1508)	(n = 1285)	
Myocardial infarction	54.2	52.1	56.8	0.007
Type II diabetes	15.9	16.6	15.0	0.219
COPD	10.3	10.3	10.4	0.987
Stroke	6.3	5.9	6.9	0.212
Renal disease	5.2	4.7	5.7	0.255
Other malignancies	11.0	10.7	11.3	0.554
Other colorectal cancer	3.2	3.2	3.3	0.895
Primary rectal cancer site	30.8	28.3	33.8	0.001
Neoadjuvant therapy in rectal cancer	52.1	51.9	52.2	0.988
	(n = 1016)	(n = 503)	(n = 513)	
ASA score >2	44.4	42.4	46.7	0.015
Aggressive tumour biology	73.0	71.9	74.4	0.102
Hospital site (region)				
Lombardy	52.8	55.6	49.4	0.011
Emilia-Romagna	15.8	15.2	16.6	0.775
Piedmont	15.2	14.8	15.5	0.918
Veneto	12.4	10.7	14.3	0.323
Friuli-Venezia-Giulia	3.8	3.7	4.2	0.912
Faecal blood test carried out				
Overall	25.5	26.6	24.3	0.131
Among asymptomatic subjects only	12.7	14.4	10.7	0.002

Values are percentages unless indicated otherwise; *values are mean(s.d.). †Chi-squared test for categorical variables; *t*-test and Kruskal-Wallis test for normally distributed (age) and non-normally distributed (BMI) continuous variables, respectively (distribution of the continuous variables assessed through Shapiro-Wilk test). COPD: chronic obstructive pulmonary disease.

the odds ratio of significant predictors greater than 10 per cent[15], with the exception of age, gender, year (2020 *versus* 2019), region (Lombardy *versus* others) and cancer site (rectum *versus* others) which were included *a priori*. Given that clinical T4 stage, advanced cancer and liver metastases were highly collinear, three separate models were fitted for each outcome, each including only one of the three co-variables. The model with the highest pseudo-R^2 was kept as final. In addition, all the models were repeated with the same co-variables, including region as a cluster variable[16], with no substantial changes in the final estimates; they were thus not shown to avoid redundancy.

Standard diagnostic procedures were adopted to check the validity of all the models, performing influential observation analysis (Dbeta, change in Pearson chi-square). Missing data were less than 5 per cent in all the primary analyses therefore no missing imputation technique was adopted. Statistical significance was defined as a two-sided *P*-value < 0.050; all the analyses were carried out using Stata®, version 13.1 (Stata Corp., College Station, Texas, USA).

Results

After the exclusion of 52 patients (35 patients underwent surgery for a tumour recurrence and 17 patients had cancers originating from organs other than the colon or rectum), 3236 cases were analysed. Of these, 1755 (54.2 per cent) had undergone surgery between March and December 2019 and 1481 (45.8 per cent) had undergone surgery between March and December 2020. *Tables 1* and *2* demonstrate the univariable comparison of clinical characteristics and oncological outcomes between the two periods. *Table 3* demonstrates the distribution of the oncological stages according to the American Joint Committee on Cancer in the two periods.

Multivariable analysis of the main outcomes (*Table 4*) showed that undergoing surgery in 2020 was not a significant predictor of advanced oncological stage and palliative surgery. The patients who were treated in Lombardy had a significantly higher risk of being diagnosed with advanced stage (odds ratio 1.22 (95 per cent c.i. 1.03 to 1.45, *P* = 0.019)) and requiring palliative surgery (odds ratio 1.55 (95 per cent c.i. 1.09 to 2.18, *P* = 0.013)).

Patients undergoing surgery in 2020 had a higher rate of symptomatic cancers (odds ratio 1.37 (95 per cent c.i. 1.10 to 1.69, *P* = 0.004)) (*Tables S1 and S2*), a higher proportion of clinical T4 stage tumours (odds ratio 1.40 (95 per cent c.i. 1.04 to 1.87, *P* = 0.024)) and a lower risk of postoperative surgical complications (odds ratio 0.80 (95 per cent c.i. 0.68 to 0.95, *P* = 0.010)). A clinical T4 stage was significantly associated with death at 30 days (odds ratio 5.33 (95 per cent c.i. 2.89 to 9.83, *P* < 0.001)), postoperative complications (odds ratio 1.97 (95 per cent c.i. 1.45 to 2.77, *P* < 0.001)), palliative surgery (odds ratio 7.63 (95 per cent c.i. 5.05 to 11.5, *P* < 0.001)) and liver metastases (odds ratio 2.33 (95 per cent c.i. 1.59 to 3.41, *P* < 0.001)).

The multivariable analysis including only patients who were diagnosed with liver metastasis (*Table S3*) confirmed that having surgery in 2020 was significantly associated with a higher risk of multiple liver metastases (odds ratio 2.21 (95 per cent c.i. 1.24 to 3.94, *P* = 0.007)).

Table 2 Recorded primary and secondary outcomes, overall and by year of surgical procedure (2020 *versus* 2019)

	Total sample (n = 3236)	March–December 2019 (n = 1755)	March–December 2020 (n = 1481)	P*
Primary outcomes				
Cancer TNM stage				0.614
Early	51.4	51.7	50.9	
Advanced	48.6	48.3	49.1	
Palliative surgery	6.2	5.0	7.5	0.003
Secondary outcomes				
Symptoms at diagnosis	82.5	80.8	84.5	0.006
Clinical T4 stage	7.4	6.2	8.7	0.008
Liver metastasis	10.2 (n = 3101)	10.2 (n = 1642)	10.3 (n = 1459)	0.889
Multiple liver metastases†	76.7 (n = 331)	72.1 (n = 179)	82.2 (n = 152)	0.029
Lung metastasis	3.7	3.0	4.4	0.038
Surgical complications	33.3	34.4	31.9	0.151
Emergency surgery	90.2	91.0	89.2	0.079
30-day death	2.0	1.7	2.4	0.149

Values are percentages. †Including only the 331 patients with liver metastasis. *Chi-squared test.

Discussion

By 31 March 2020, Italy reported the second-highest number of confirmed COVID-19 cases (101 739, after the USA, 140 640 cases) and the highest number of deaths (11 591) in the world. The number of patient deaths in Italy represented almost one third (31.8 per cent) of the total COVID-19-associated deaths worldwide[3]. The huge impact on the healthcare system required reallocation of resources and a national lockdown. Cancer screening activity was discontinued between March and May 2020, and its subsequent reactivation was not immediate or homogeneous across the different regions. The number of FITs in the first 5 months of 2020 was 54.9 per cent less than 2019[6]. A report in December 2020 demonstrated a slight improvement in the situation between October and December 2020 (screening-programme reduction of 23.8 per cent), although at the end of 2020, the number of FITs carried out in Italy was still 45.5 per cent lower than in the previous year[17].

This evidence increased awareness of the potentially detrimental effects of lower screening rates. A study from England estimated an increase in the number of deaths due to colorectal cancer of between 1445 and 1563[12]. It is estimated that delaying presentation by 2 months per patient would result in 3316 to 9948 life-years lost, depending on the delay of referrals in the UK[13]. Screening delays beyond 6 months are associated with an increase in more advanced-stage colorectal cancers while a delay of greater than 12 months would result in a significantly higher cancer mortality rate (+12 per cent)[11].

The present study investigated colorectal cancer outcomes in 20 referral centres located in the regions which were most severely hit during the outbreak of COVID-19 in Italy. No evidence of an increased rate of advanced-stage cancers or palliative surgery was demonstrated, but the analysis found significant discrepancies which were likely to be associated with the reduced screening activity and, more importantly, could have potentially affected oncological outcomes and survival. A significant association was found between undergoing surgery in Lombardy and advanced stage (odds ratio 1.22 (95 per cent c.i. 1.03 to 1.45, $P = 0.019$)) or palliative surgery (odds ratio 1.55 (95 per cent c.i. 1.09 to 2.18, $P = 0.013$)). This could be due to Lombardy being the most severely impacted Italian region during the first wave of COVID-19 pandemic, and witnessing an overall reduction of the screening programme of 73.9 per cent in 2020 (*versus* 2019)[17].

A higher proportion of patients undergoing surgery in 2020 were diagnosed with rectal cancer (33.8 *versus* 28.3 per cent, $P = 0.001$). Symptoms associated with rectal cancer such as rectal bleeding prompt additional diagnostic tests in the population regardless of the screening programmes compared with more proximal cancers[18–21]. Similarly, the relatively higher rate of right-sided colon cancers might be explained by their clinical subtleness, in terms of associated symptoms, which also justifies the risk of worse survival associated with the right-sided colon cancer, which is more often diagnosed at advanced stages.[22,23] The higher rate of rectal cancers requiring surgery in 2020 might reflect the relative decrease in the number of patients without symptoms who would have been diagnosed using the FIT and were not due to discontinuation of screening. This is supported by the lower rate of surgical patients with no cancer-related symptoms in 2020 (15.5 *versus* 19.2 per cent, $P = 0.006$). The proportion of screening participants who are diagnosed with colorectal cancer who lack any symptoms reflects FIT detection of early-stage cancers and improvement in outcomes[24–26].

A higher rate of clinical T4 stage was found in 2020 (odds ratio 1.38 (95 per cent c.i. 1.03 to 1.85, $P = 0.029$)), although the rates of pathological T4 stage were similar between 2019 and 2020 (4.3 *versus* 4.8 per cent, $P = 0.931$). Although the clinical T4 stage was included among the secondary outcomes, since its oncological significance remains unclear, this finding might be of particular

Table 3 Distribution of oncological stages according to the American Joint Committee on Cancer

Cancer stage	March–December 2019 (n = 1755)	March–December 2020 (n = 1481)	P‡
No cancer*	79 (4.5)	81 (5.5)	0.192
Stage 0-I	400 (22.8)	322 (21.7)	0.454
Stage II a	429 (24.4)	351 (23.7)	0.643
Stage II b-c	76 (4.3)	71 (4.8)	0.496
Stage III	511 (29.1)	427 (28.8)	0.851
Stage IV	212 (12.1)	181 (12.2)	0.931
No stage†	48 (2.7)	48 (3.2)	0.401

Values in parentheses are percentages. *'No cancer' includes cases with no residual tumour after endoscopic removal, dysplasia, and pathological complete response after neoadjuvant therapy. †'No stage' includes all palliative procedures in which the tumour was not removed (unless a distant metastasis would define stage IV). ‡Chi-squared test for categorical variables.

Table 4 Multivariable analyses evaluating the association between the recorded clinical and organizational variables and advanced TNM stage and palliative surgery

Variables	Advanced stage ($n = 1574$)			Palliative surgery ($n = 199$)		
	%	Odds ratio	P	%	Odds ratio	P
Year						
2019	48.3	1 (ref. cat.)	–	**5.0**	1 (ref. cat.)	–
2020	49.1	1.01 (0.86, 1.18)	0.918	**7.5**	1.46 (0.92, 1.98)	0.090
Age class (years)						
<60	52.7	1 (ref. cat.)	–	5.8	1 (ref. cat.)	–
60–69.9	48.1	0.92 (0.72, 1.18)	0.488	5.9	1.03 (0.62, 1.83)	0.812
70–79.9	48.2	0.78 (0.62, 0.99)	0.045	5.3	0.74 (0.43, 1.27)	0.362
≥80	46.1	0.59 (0.45, 0.77)	<0.001	7.8	0.88 (0.50, 1.53)	0.619
Age, 10-year increase	–	0.88 (0.82, 0.95)	0.001	–	0.94 (0.80, 1.09)	0.417
Gender						
Female	47.8	1 (ref. cat.)	–	6.2	1 (ref. cat.)	–
Male	49.7	1.02 (0.86, 1.21)	0.611	6.1	0.88 (0.62, 1.27)	0.488
Current smoker						
No	48.2			5.7	–	–
Yes	45.7			5.9	–	–
Family history of cancer						
No	49.2	1 (ref. cat.)	–	6.1	1 (ref. cat.)	–
Yes	42.7	0.75 (0.58, 0.93)	0.013	5.3	1.23 (0.71, 2.11)	0.516
Diabetes						
No	48.8	–	–	6.2	–	–
Yes	47.7	–	–	6.0	–	–
Myocardial infarction						
No	49.4	–	–	5.9	–	–
Yes	48.0	–	–	6.4	–	–
Stroke						
No	49.0	–	–	6.1	–	–
Yes	43.9	–	–	7.3	–	–
Other cancers						
No	49.1	1 (ref. cat.)	–	6.2	1 (ref. cat.)	–
Yes	45.1	0.89 (0.68, 1.16)	0.402	5.9	0.81 (0.44, 1.49)	0.521
Hospital in Lombardy						
No	47.1	1 (ref. cat.)	–	5.4	1 (ref. cat.)	–
Yes	50.0	1.22 (1.03, 1.45)	0.019	6.9	1.55 (1.09, 2.18)	0.013
Faecal blood test						
No	51.3	1 (ref. cat.)	–	**6.8**	1 (ref. cat.)	–
Yes	39.8	0.66 (0.54, 0.79)	<0.001	**3.0**	0.65 (0.40, 0.97)	0.023
Rectum location						
No	50.0	1 (ref. cat.)	–	6.0	1 (ref. cat.)	–
Yes	44.8	0.87 (0.73, 1.05)	0.142	4.8	0.72 (0.47, 1.09)	0.131
ASA score >2						
No	46.7	1 (ref. cat.)	–	**3.8**	1 (ref. cat.)	–
Yes	51.1	1.26 (1.06, 1.50)	0.009	**9.2**	2.40 (1.99, 3.56)	<0.001
Aggressive cancer biology						
No	28.1	1 (ref. cat.)	–	6.3	1 (ref. cat.)	–
Yes	56.2	3.65 (3.01, 4.42)	<0.001	6.1	0.93 (0.60, 1.41)	0.719
Clinical T4 stage*						
No	45.1	1 (ref. cat.)	–	**4.3**	1 (ref. cat.)	–
Yes	87.3	7.41 (4.79, 11.5)	<0.001	**28.0**	7.63 (5.05, 11.5)	<0.001
Advanced stage*						
No	–	–	–	**0.6**	–	–
Yes	–	–	–	**12.0**	–	–
Liver metastasis*						
No	43.3	–	–	**3.4**	–	–
Yes	95.2	–	–	**30.5**	–	–
Surgical complications						
No	46.6	1 (ref. cat.)	–	**5.3**	1 (ref. cat.)	–
Yes	52.7	1.22 (1.03, 1.44)	0.023	**7.9**	1.12 (0.88, 1.42)	0.447

Values in parentheses are 95 per cent confidence intervals. In all models, age, gender, year, region (Lombardy versus others) and cancer site (rectum versus other sites) were included *a priori*. *Given the multicollinearity across T4 stage, advanced stage and liver metastases, three separate models were fitted, each including only one of the three co-variables. The model with the highest R^2 was kept as final. All the models were repeated with the same co-variables, including region as a cluster variable, with no substantial changes in the final estimates. They were thus not shown to avoid redundancy. In all the univariable analyses, significant results ($P < 0.050$) are indicated in bold. The P-values shown in the Table are referred to the multivariable models. ref. cat., reference category.

importance. A clinical T4 stage was defined as the presence of cancer-induced spiculations extended over the bowel wall or the suspicion of infiltration of the surrounding structures at pre-operative radiological examination. These signs do not necessarily indicate pathological cancer infiltration as they could reflect perineoplastic inflammation and fibrosis. There is evidence that these radiological characteristics are significantly associated with worse survival, even in patients who were eventually diagnosed with a pathological T3 stage[27], implying a strong effect of the neoplastic environment on the progression and outcomes of colorectal cancer[28].

Although the overall rate of stage IV (12.1 *versus* 12.2 per cent, $P = 0.9$) and the specific incidence of liver metastases (10.2 *versus* 10.3 per cent, $P = 0.9$) were similar in the two study intervals (*Tables 1* and *2*), patients who had surgery in 2020 had a significantly higher risk of being diagnosed with more than one liver metastasis, as shown in *Table S3* (odds ratio 2.21 (95 per cent c.i. 1.24 to 3.94, $P = 0.007$)). The number of liver metastases has widely been recognized as a meaningful prognostic factor in patients affected by colorectal cancer[29,30].

The present study has some limitations. It did not represent the overall population of patients affected by colorectal cancer as it only included 20 hospitals in Northern Italy (representing the major hospitals in the 10 largest provinces—out of 36—in the four regions) and may not represent outcomes of colorectal cancer internationally.

The number of patients with metastatic disease could be underestimated if they were referred to the oncology unit or treated in the community. The retrospective nature of the study did not allow analysis of whether the COVID-19 outbreak impacted on the time between the onset of symptoms and the referral to surgery. The short time frame of the study might have prevented the observation of significantly more advanced cancer.

Despite SARS-CoV-2 vaccine campaigns internationally, no global response has been proposed, and the pandemic is far from being resolved[31]. In particular, the risk of significant new COVID-19 variants cannot be underestimated[32]. Although it is still not conclusive whether the outcome variations which have been identified in the present study will impact the long-term survival of patients, it is clear that large-scale interventions are required in order to alleviate the long-term effects of the COVID-19 pandemic on the diagnostic delay of patients affected by colorectal cancer.

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Data will be made available from the corresponding author upon reasonable request.

Declaration

The authors declare no conflicts of interest.

Supplementary material

Supplementary material is available at BJS Open online.

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