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The COVID - AGICT study: COVID-19 and advanced gastro-intestinal cancer surgical treatment. A multicentric Italian study on the SARS-CoV-2 pandemic impact on gastro-intestinal cancers surgical treatment during the 2020. Analysis of perioperative and short-term oncological outcomes

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Abbreviations: MIS, minimally invasive surgery; NCTs, Neoadjuvant treatments; CCI, Charlson Comorbidity Index.

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ABSTRACT

Background: This Italian multicentric retrospective study aimed to investigate the possible changes in outcomes of patients undergoing surgery for gastrointestinal cancers during the COVID-19 pandemic.

Method: Our primary endpoint was to determine whether the pandemic scenario increased the rate of patients with colorectal, gastroesophageal, and pancreatic cancers resected at an advanced stage in 2020 compared to 2019. Considering different cancer staging systems, we divided tumors into early stages and advanced stages, using pathological outcomes. Furthermore, to assess the impact of the COVID-19 pandemic on surgical outcomes, perioperative data of both 2020 and 2019 were also examined.

Results: Overall, a total of 8250 patients, 4370 (53%) and 3880 (47%) were surgically treated during 2019 and 2020 respectively, in 62 Italian surgical Units. In 2020, the rate of patients treated with an advanced pathological stage was not different compared to 2019 ($P = 0.25$). Nevertheless, the analysis of quarters revealed that in the second half of 2020 the rate of advanced cancer resected, tended to be higher compared with the same months of 2019 ($P = 0.05$). During the pandemic year 'Charlson Comorbidity Index score of cancer patients (5.38 ± 2.08 vs 5.28 ± 2.22 , $P = 0.036$), neoadjuvant treatments (23.9% vs. 19.5%, $P < 0.001$), rate of urgent diagnosis (24.2% vs 20.3%, $P < 0.001$), colorectal cancer urgent resection (9.4% vs. 7.37, $P < 0.001$), and the rate of positive nodes on the total nodes resected per surgery increased significantly (7 vs 9% - 2.02 ± 4.21 vs 2.39 ± 5.23 , $P < 0.001$).

Conclusions: Although the SARS-CoV-2 pandemic did not influence the pathological stage of colorectal, gastroesophageal, and pancreatic cancers at the time of surgery, our study revealed that the pandemic scenario negatively impacted on several perioperative and post-operative outcomes.

1. Introduction

On March the 9th, 2020, the first national lockdown was imposed across Italy by the Prime Minister to flatten the curve of the COVID-19 pandemic and reduce its potential impact on the population. Health resources were mostly dedicated to the care of COVID-19 infected patients.

These measures dramatically impacted cancer screening programs, routine diagnostic examinations, elective oncological treatments, and emergency surgery [1–4]. Preoperative delay of oncological surgery increased [5], and a significant increase in the number of avoidable cancer-related deaths is expected in the near future [1,6].

Italy was one of the first and most affected Countries by the pandemic among Western Countries, and the actual extent of the disruption in the provision of Italian surgical services for oncological patients has only been partially investigated [4,7,8].

This multicentric national study aimed to investigate the possible changes in outcomes of patients undergoing surgery for colorectal, gastroesophageal, and pancreatic cancers in the year before the pandemic outbreak and the year after.

2. Methods

Data were collected from a national multicentric retrospective cohort study including adult patients that underwent surgery for colorectal, gastroesophageal, and pancreatic cancers from January 2019 to December 2020 in 62 Italian surgical divisions. This research was approved by the ethics committee of the coordinating center (reference number 18886) and registered at [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT04686747) (NCT04686747). As of the anonymized nature of patient data and retrospective design of the study, the informed consent was waived.

Local principal investigators were responsible for the acquisition of ethical approval to participate in the study.

All Italian surgical divisions treating colorectal, gastroesophageal, and pancreatic cancers were eligible for participation. Sixty-two Italian surgical divisions were included in this study. Data were collected from a disease-specific database sent to participating hospitals.

All adult patients surgically treated for localized, locally advanced, or metastatic cancers with curative or palliative intent during the study period were included in the study. Exclusion criteria were patients under 18 years of age or with multiple tumors, patients not surgically treated and hospitals that were not able to provide data for both 2019 and 2020.

Demographic data (Body Mass Index – BMI, age, sex, American Society of Anesthesiologists classification score – ASA, Charlson Comorbidity Index - CCI score) preoperative outcomes (rate of urgent diagnosis secondary to symptomatic cancers, rate of neoadjuvant treatments–NCTs, interval from diagnosis to operation in days),

¹ The members of the COVID-AGICT Collaborative Group are listed in [Appendix 1](#) at the end of the article.

perioperative outcomes (i.e., rate of urgent colorectal cancer resection, rate of unresectable cancer, rate of minimally invasive procedure, length of hospital stay, rate of major postoperative complications) were compared between the two years. Furthermore, in order to collect homogeneous data, early oncological outcomes (i.e., rate of adjuvant therapy, number of lymph nodes retrieved, rate of positive nodes, rate of patients with positive nodes) were evaluated only in patients treated with curative intents. The primary endpoint was to demonstrate whether the COVID-19 pandemic increased the rate of colorectal, gastroesophageal, and pancreatic cancers surgically treated at an advanced stage in 2020. Considering different cancer staging systems (colorectal, gastroesophageal, and pancreatic cancers), we divided tumors into early stages (non-nodal, non-metastatic patients, R0 resection) and advanced stages (nodal, metastatic patients, and R1-R2 resection) according to the *AJCC Cancer Staging Manual*, 8th edition [9]. The secondary endpoint was to study the impact of the COVID-19 pandemic on perioperative and postoperative outcomes.

Urgent diagnosis was defined as diagnosis performed after an admission to the emergency department secondary to symptomatic cancer (e.g. bleeding, bowel perforation, symptoms of acute intestinal obstruction). The interval from diagnosis to surgery was calculated as the interval between the day of diagnosis (i.e., the date of endoscopy, CT scan, and histopathologic diagnosis) and the day of surgery, patients undergoing NCT were excluded. Cancer resectability was specified for each cancer: for example carcinosis peritonei, or not resectable M1 or T4 neoplasm were criteria for colorectal cancers resectability. Further details are provided in the study protocol (Appendix S2).

To better investigate the pandemic's influence on gastrointestinal cancer surgery, we divided the two years in quarters:

- Q1: from January 1 to March 31
- Q2: from April 1 to June 30
- Q3: from July 1 to September 30
- Q4: from October 1 to December 31.

Then we compared the trend of surgical activity, both elective and emergent surgery, the rate of advanced resected cancers, as well as the rate of palliative and emergent surgical procedures performed during the quarters of the two years.

This paper was drafted according to the STrengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist [10].

2.1. Statistical analysis

The quantitative variables included in the study are presented as mean \pm standard deviation at the general level and divided by year. Qualitative (categorical) variables are represented as percentages and absolute values, both at a general level and divided by year. Quantitative variables of interest were compared using two-tailed Student's *t*-test (in case of heteroskedasticity of variances). A comparison between qualitative variables of interest will be carried out to evaluate the association among them through an extension of the chi-square test, suitable for multi-centric studies (the Cochran – Mantel – Haenszel test). This test was used also for distribution comparison among quarters between 2019 and 2020. A *p*-value ≤ 0.05 was considered statistically significant.

Missing data were excluded listwise, which could have affected some numerical discrepancies in the calculation of frequencies. Since the majority of outcomes were provided for about 75–100% of patients, after data aggregation and before the analysis, patients with more than 25% of missing data of a specific outcome were excluded from the analysis of the single outcome. Moreover, we reported the rate of patients with available data for outcomes that was statistically significant.

3. Results

Overall, 62 Italian surgical divisions sent complete data for both



Fig. 1. Geographical distribution of participating centers. Blue: coordinating center.

Table 1

Population study divided by years. CR: Colorectal cancer patients; Pan: pancreatic cancer patients; GE: gastroesophageal cancer patients.

	2019	2020	Tot.	%
Cancer Type				
- CR	3058	2646	5704	69
- Pan	924	892	1816	22
- GE	388	342	730	9
Tot.	4370	3880	8250	

Table 2

Demographic data. BMI: body Mass Index; CCI: Charlson Comorbidity Index; ASA: American Society of Anesthesiologists. *Mean \pm standard deviation.

	2019	2020	<i>P</i>	Rate of patients with available data, %
Age*	69.26 (12.13)	69.1 (12.17)	0.55	100
BMI*	25.18 (4.32)	25.21 (4.22)	0.11	83
CCI*	5.28 (2.22)	5.38 (2.08)	0.04	91
Sex			0.98	78
- Female <i>n</i> ,	1497	1301		
(%)	(43.5)	(43.6)		
- Male <i>n</i> , (%)	1942 (56.5)	1686 (56.4)		
ASA			0.74	93
- 1/2 <i>n</i> , (%)	2247 (55.3)	1986 (54.9)		
- 3/4 <i>n</i> , (%)	1820 (44.7)	1633 (45.1)		

Table 3

Perioperative outcomes. NCTs: Neoadjuvant treatments. *Mean \pm standard deviation.

	2019	2020	P	Rate of patients with available data, %
Preoperative				
Urgent diagnosis n, (%)	857 (20.3)	900 (24.2)	< .001	97
NCTs n, (%)	778 (19.5)	843 (24.1)	< .001	91
Interval of time diagnosis - surgery (days) *	56.8 (8.48)	64.2 (53.03)	< .001	90
Perioperative				
Urgent CRC resection n, (%)	224 (7.3)	248 (9.3)	.005	100
Unresectable n, (%)	244 (5.9)	244 (6.4)	.28	95
Palliative procedure n, (%)	249 (5.7)	256 (6.6)	.11	99
MI procedure n, (%)	2746 (63.4)	2399 (62.1)	.23	99
Conversion rate n, (%)	234 (9.2)	2399 (7.2)	.01	94
MI CRC resection n, (%)	2379 (78.4)	1986 (75.6)	.009	99
Conversion rate of CRC resection n, (%)	191 (8.7)	130 (6.9)	.03	93
Postoperative outcomes				
LOS days *	12.1 (11.4)	11.6 (11)	.04	99
Postoperative Complications III-V n, (%)	583 (13.7)	487 (12.8)	.20	97
30 days re- admission n, (%)	180 (4.4)	189 (5)	.16	95
30 days mortality n, (%)	81 (1.9)	93 (2.5)	.09	96
Short-term oncological outcomes				
Adjuvant treatment n,(%)	1200 (35.9)	1084 (36.2)	.80	77
Number of Lymph nodes Retrieved*	25.4 (15.6)	24.6 (15)	.03	89
Lymph nodes + % - n (*)	7 - 1.96 (4.18)	9 - 2.22 (4.63)	< .001	92
Patients with Lymph nodes + n, (%)	1603 (41.6)	1587 (43.)	.23	92
Resection margin involvement (R1-R2) n, (%)	302 (7.9)	253 (7.4)	.4	91
Lymphovascular and perineural invasion n, (%)	1929 (62.1)	1727 (63.6)	.25	75

years for a total of 8250 patients, 4370 (53%) and 3880 (47%) operated during 2019 and 2020, respectively. Of these, 730 (9%) were patients that underwent surgery for gastroesophageal cancer, 1816 (22%) for pancreatic and 5704 (69%) for colorectal cancer (Fig. 1 - Table 1). More than 50% of centers (37 out of 62) were of North Italy.

3.1. Primary endpoint

The rate of patients operated at an advanced stage during the pandemic year was 51% compared to 49% in the year before. Although in 2020, the rate of patients with an advanced stage tended to be higher, this difference was not statistically significant ($P = 0.25$, 90% of patients with available data). To better investigate this outcome we analyzed the sub group of colorectal cancer patients, as they made the majority of patients included in this study. Although during 2020 the rate of

advanced stage colorectal cancer raised, this difference was not statistically significant (46% vs 44%, $P = 0.23$, 93% of patients with available data).

3.2. Secondary endpoints

3.2.1. Demographic data (Table 2)

The analysis of demographic data showed no differences in terms of mean age, sex, mean BMI, and preoperative ASA score between the two groups. Nevertheless, patients with diagnosis of cancer in 2020 had a higher Charlson Comorbidity Index - (CCI) score (5.38 ± 2.08 vs 5.28 ± 2.22 , $P = 0.04$ –91% of patients with available data).

3.2.2. Pre-operative outcomes

During the pandemic year, 24.2% of patients had a cancer diagnosis consequent to an urgent presentation compared to that of 20.3% in 2019 ($P < 0.001$ –100% patients with available data).

In 2020, the number of patients that underwent NCT increased (24.1% vs. 19.5%), and this difference was statistically significant ($P < 0.001$ –91% of patients with available data). To better understand this outcome we analyzed the colorectal cancer sub group, the most frequent tumor in the study. The rate of NCT for rectal cancer increased in the 2020 compared to the 2019 (389 vs 365 patients, $P < 0.001$ –87% of patients with available data).

The mean time from diagnosis to surgery increased significantly during the pandemic year, being 56.8 days in 2019 and 64.2 days in 2020 ($P < 0.001$ –90% of patients with available data).

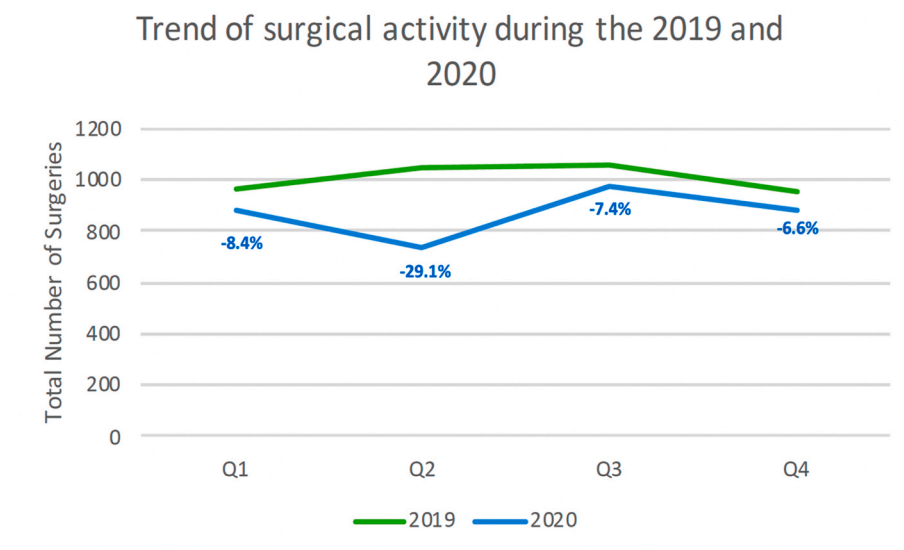
3.2.3. Perioperative outcomes

Overall, in 2020, rather than in 2019, a reduction in surgical activity of 5.2% was registered and this difference was statistically significant ($P < 0.001$ –91% of patients with available data). Quarters analysis showed that surgical volume decreased significantly during Q1 of 2020 ($-8%$, $P = 0.04$), until the beginning of Q2 in 2020 which showed the most important reduction compared to that in the same months of 2019 ($-29%$, $P < 0.001$). (Fig. 2).

During the Q3 and Q4 of 2020, an increased rate of advanced cancers resected was noted, compared with Q3 and Q4 of 2019, and this difference tended to be statistically significant (50% and 49% vs 48% and 45% - $P = 0.05$). Conversely, palliative and urgent surgical procedures increased during the last two quarters of 2020 compared with the same months of 2019, without a statistical significance ($P = 0.6$ and $P = 0.7$, respectively).

In 2020 there was a significant increase in urgent colorectal cancer resection (9.3 vs. 7.4%, $P = 0.005$ –100% of patients with available data). The analysis of data on cancer resectability showed that 5.9% of patients operated in 2019 were unresectable, compared to 6.4% of patients resected in 2020 and this difference was not statistically significant ($P = 0.28$). During both years, there were no differences in terms of minimally invasive surgery (MIS) (63.4% vs. 62.1%, $P = 0.23$). Interestingly, conversion rate during 2020 was lower than that in 2019 (7.2 vs 9.2%), and this difference was statistically significant ($P = 0.01$ –94% of patients with available data). To better assess these findings, we analyzed the subgroup of patients with colorectal cancer since it was the most frequent included in the study. The analysis of data showed that the rate of MIS for colorectal cancer resections decreased significantly in 2020 (78.4 vs 75.6%, $P = 0.009$ –99% of patients with available data). Nevertheless, conversion rate was significantly lower during the pandemic year than in 2019 (6.9 vs 8.7 %, $P = 0.03$ –93% of patients with available data).

The mean LOS was significantly shorter in 2020 (12.1 ± 11.4 vs 11.6 ± 11 days, $P = 0.04$ –99% of patients with available data). The analysis of major postoperative complications (grade III-V, according to the Clavien–Dindo classification system [11]) demonstrated no difference between the two years (13.7 vs 12.8%, $P = 0.20$). Thirty-day readmission rate occurred more frequently in patients operated in 2020 (5



a.

	2019	2020	Tot	P
Q1 n, (%)	959 (23.4)	878 (25.2)		.04
Q2 n, (%)	1044 (26)	740 (21.2)		< .001
Q3 n, (%)	1056 (26.3)	977 (28)		.08
Q4 n, (%)	948 (23.6)	885 (25.4)		.14
Tot	4007	3480	7487	< .001

b.

Fig. 2. a. Line graph showing the trend of surgical activity during the 2019 and 2020; b. Trend of surgical activity during the 2019 and 2020 analyzed on 7487 patients (91%) with available data. Q1-4: quarters.

vs. 4.4%), without a significant difference ($P = 0.16$). Similarly, the 30-day mortality rate was higher in 2020 than in 2019, but without a significant difference (1.9 vs 2.5, $P = 0.09$).

3.2.4. Early oncological outcomes (Table 3)

These outcomes were evaluated only in patients treated with a curative intent during the two years. The rate of adjuvant treatments of patients with positive lymph nodes, or with R1/R2 resected cancers and of tumors with lymphovascular and perineural invasion were not statistically different between the two years. The mean number of retrieved lymph nodes was higher in 2019 compared to 2020 (25.4 vs 24.6 nodes, $P < 0.05$ –89% of patients with available data). Conversely, the rate of positive nodes on the total nodes resected per surgery was significantly higher in 2020 compared to that in 2019 (9% vs 7% - 2.22 ± 4.63 vs 1.96 ± 4.18 , $P < 0.001$ –92% of patients with available data).

4. Discussion

The results of the COVID-AGICT study revealed that in 2020, the pandemic conditions did not increase the rate of colorectal, gastroesophageal, and pancreatic cancers diagnosed and operated at an advanced stage. However, the analysis of quarters revealed that in the second half of 2020 the rate of advanced cancer resected, tented to be higher compared with the same months of 2019. Nevertheless, our study demonstrated that patients who were diagnosed with cancer in 2020 had more comorbidities. Furthermore, increased preoperative delay and decreased surgical activity were observed during the first half of 2020. Consequently, the diagnosis of cancers after urgent admission and the rate of NCTs, as well as the rate of urgent colorectal resection increased.

Despite this, a reduction in the conversion rate to open surgery and mean LOS was found in 2020. Finally, during the pandemic year, the rate of positive lymph nodes increased significantly without a significant impact on other pathological outcomes. The SARS-CoV-2 pandemic had catastrophic consequences not only for patients infected by COVID-19. Screening systems were damaged and the waiting time to elective surgery increased [5].

Although several studies have shown that short-term oncological outcomes were not compromised by the COVID-19 pandemic, the disruption of standard cancer care will have negative consequences on long-term oncological outcomes [6,12,13].

Pathological findings from our study showed no difference in stages in 2020 compared to 2019, whereas an increased number of positive nodes was found in 2020. Several studies have found no statistically significant difference in the pathological stage between the pandemic period and the previous year [14–16]. A recently published multicentric retrospective study analyzed the impact of the pandemic on patients with colorectal cancer treated in 2019 and 2020 in 20 hospitals of northern Italy. The authors found that patients treated 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, compared with those in the same period in 2019 [16].

Nodal status is an important prognostic factor [18,19]. Patients treated with a curative intent during 2020 were found to have an increased rate of positive lymph nodes. The increased rate of urgent surgery, that usually involves patients with a poor preoperative workup, and the delayed time from diagnosis to surgery shown in our study, could partially explain this result [20,21]. As other pathological outcomes evaluated in COVID-AGICT were not compromised, the increased

of lymph nodes positivity could represent the initial impact on pathological outcomes for patients resected during the COVID-19 pandemic period.

Preoperative delay was the most important concern of the surgical community for oncological patients during the pandemic period [6,22,34]. We demonstrated that the interval from diagnosis to surgery increased during the entire 2020 from 76.7 days in 2019 to 93.9 days in the pandemic year ($P < 0.001$). The COVIDSurg collaborative group recently published an international prospective cohort study to assess the nonoperation rate (defined as the proportion of patients who did not undergo planned surgery) of patients who were candidates for curative surgery during the COVID-19 pandemic. The authors included 20006 patients from 61 countries and 15 cancer types and demonstrated that one in seven patients who were residing in regions with full lockdowns experienced longer preoperative delays and did not undergo planned surgery [5].

The reduction in surgical activity caused by the outbreak secondary to the COVID-19 pandemic was another important finding of our study. In the first two quarters of 2020, during the first pandemic wave, the surgical activity decreased up to 29%. Recently, an Italian multicentric study investigated the influence of COVID-19 on the diagnostic and therapeutic pathways of surgical pancreatic diseases across 10 Italian referral centers. The authors included 1423 patients: 638, and 785 patients in 2020 and 2019, respectively. This study demonstrated an 18.7% reduction in the surgical activity in the first six months of 2020 ($P < 0.0001$), with the most significant impact during the lockdown period (phase 1: -33.9% ; $P < 0.0001$) and the partial easing of restrictions (phase 2: -23.9% ; $P = 0.01$) compared to that in the same weeks of 2019 [23].

Although the primary endpoint did not show a worsening of stage in 2020, other points of our investigation could show indirectly that as the pandemic spread, the rate of advanced cancers at the diagnosis increased. First, patients with cancers diagnosed during the pandemic year had a higher CCI score (5.38 ± 2.08 vs 5.28 ± 2.22 , $P = 0.036$). A recent multicentric study published by the *Covid ICE International Collaborative Group* compared the outcomes of patients admitted to 45 international emergency surgical units during the months of March and April 2020 (COVID-19 pandemic outbreak) and the same months in 2019 (pre-Covid-19). The authors showed that during the COVID period the rate of patients with ASA>1 patients with frailty score >2 increased from 46% to 53% during the COVID-19 pandemic outbreak [24]. This difference could be a consequence of a higher rate of symptomatic cancers diagnosed in 2020, and patients with more comorbidities were more likely to attend the hospital than the healthier ones.

Indeed, as showed by others studies [16,25,26], during the pandemic year the rate of cancer diagnosis following an emergency admission (24.2% vs. 20.3% , $P < 0.001$) and of urgent colorectal cancer resection (9.4% vs. 7.37% , $P < 0.001$) increased significantly. These findings could reflect that during 2020, the analyzed tumors were more symptomatic, requiring an emergent admission, and could be an indirect sign of a worsened stage.

The COVID-AGICT study showed that during 2020, more neoadjuvant treatments were delivered, increasing from 19.5% to 23.9% ($P < 0.001$). Morris et al. demonstrated a decrease in the number of operations occurring in parallel with an increase of 44% in the use of radiotherapy, predominantly in the form of short-course radiotherapy for rectal cancer in England, between April and August 2020 [26]. Furthermore, Quero et al. showed that patients with pancreatic cancer in 2020 underwent neoadjuvant treatment more frequently than those in 2019 (29.9 vs. 23.7% , $P = 0.009$) [23]. The increase in neoadjuvant treatments in 2020 could reflect an indirect sign of advanced disease during this period. At the same time NCTs could also be implemented for early-stage cancers to avoid disease progression caused by increased preoperative delay. Than NCT may be considered as a “bridge to surgery strategy”, used during the 2020 to minimize the COVID-19 effect on disease progression.

In 2020, particularly during the early phase, the feasibility and safety of minimally invasive surgery were debated and discouraged to minimize the risk of inhalation of the surgical plume [26,28,29]. To date, there is no clear evidence suggesting the transmission of viral particles through surgical smoke [30,31]. We demonstrated that during 2020 in Italy, there was no reduction in MIS and that the conversion rate to open approach was significantly reduced. To better understand these findings, we analyzed the colorectal cancer subgroup, the most frequent tumors included in the study, and cancers that are more suitable for MIS. Indeed, the analysis showed that the rate of MIS for colorectal cancer resection decreased significantly in 2020 (78.4 vs 75.5% , $P < 0.001$). At the same time, conversion rate to open approach reduced significantly in 2020 (9.5 vs 7.41% , $P = 0.03$). The reduction in MIS for colorectal cancer patients could reflect the consequences of restrictions suggested by several guidelines and the significant increase in emergency resection in 2020. The lower conversion rate of the entire cohort of patients and that of the colorectal cancer patient group could be a consequence of better patient selection for MIS in 2020 [24].

The COVID-AGICT study showed that during 2020, the LOS was shorter than that in 2019 (12.1 vs 11.6 days, $P = 0.037$). An Italian retrospective study by Spinelli et al. investigated the impact of a pandemic scenario on the quality of a long-established enhanced recovery protocol colorectal surgery program. The study revealed that in 2020, the LOS was globally shorter than that in the same period in 2019 (4.3 vs 6.2 d) [14]. These findings could reflect the change in the mindset that the pandemic was induced not only by clinicians, but also by patient behaviors. In our case, we were anxious to release our patients as soon as the discharge criteria were met, to reduce the in-hospital risk of coronavirus infection and, at the same time, to furnish more resources possible for oncological and emergency patients. During the COVID period, patients' awareness increased regarding the risks of COVID-19 infection secondary to prolonged contact with health care workers [32] and a higher presence of family caregivers, as the lockdown forced people to stay home, resulting in a higher motivation for patients to leave the hospital as soon as possible.

The findings of this study should be interpreted with caution because of its limitations that should be acknowledged. First, it was retrospective in nature. Second, the COVID-AGICT study did not considered the patients who did not undergo surgery during the 2020 for the same cancers (i.e. for advanced malignancy, severe comorbidities). This may influenced the understanding on any epidemiology modification during this period: at the same time our study investigated a specific population of oncological patients. Third, some data were not detailed and could have influenced the final outcomes. Fourth, the COVID-AGICT study included five types of gastrointestinal cancers: perioperative and postoperative outcomes could be influenced by the intrinsic biological difference of these cancers. It could jeopardize the strength of COVID AGICT study findings and their generatability. For example neoadjuvant therapy, that has different effects and indications for these five cancer, as well as for the rate of postoperative complications that are influenced by the type of the surgical procedure. Fifth, it must be considered that the time period of our study may be too short to see any difference in pathological outcomes, and others studies analyzing also the year 2021 could show interesting results. Finally, 69% of patients included in our cohort had a colorectal cancer, which could have influenced the final outcomes.

Although the included centers and the number of patients (more than 60 centers and 8000 patients) might not represents the real influence of pandemic on the Italian gastro-intestinal surgery, to the best of our knowledge, the COVID-AGICT study is the first study to assess the impact of the pandemic on the diagnosis and surgical treatment of gastroesophageal, pancreatic, and colorectal cancers across Italy, analyzing several preoperative and postoperative outcomes in detail during the first waves of COVID-19.

5. Conclusion

Although the pandemic scenario did not influence the stage of gastroesophageal, pancreatic, and colorectal cancers, the COVID-AGICT study revealed that during 2020, the CCI score of cancer patients, neo-adjuvant treatments, rate of urgent diagnosis, colorectal cancer urgency resection, and number of positive lymph nodes increased, significantly.

To date we are in a different era with vaccines. Nevertheless, new SARS-CoV-2 variants could lead in the future to new pandemic scenario [33]. Our findings should serve as a lesson to guide specific assessment of the clinical impact of the pandemic on gastrointestinal cancer patients in the future. In the future, specific pathways for diagnosis and treatment of GI cancers should be preserved to offer the same standard of treatment also in these difficult moments [2,5].

Conflict of interest disclosures

The authors have no conflicts of interest or financial ties to disclose related to the research presented.

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The study was preregistered without an analysis plan

This paper reports the results of NCT04686747 preregistered studies, which can be accessed at <https://clinicaltrials.gov/ct2/show/NCT04686747>.

Whether the paper has been presented in part elsewhere

Not applicable.

The COVID – AGICT

study group is an Italian collaboration, hosted centrally from the Misericordia Hospital, Grosseto. In [appendix 1](#) is provided a complete list of the group.

Data access, responsibility, and analysis

Giuliani Giuseppe had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Data will be made available upon reasonable request.

Appendix 1. COVID-AGICT Collaborative Group

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Appendix A. Supplementary data

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