

Impact Of Covid-19 On Colorectal Cancer With Worsening Of Clinical Presentation: Retrospective Study In A Single Center

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Received: 16 Feb 2023

Accepted: 03 Apr 2023

Published: 10 Apr 2023

J Short Name: COO

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Citation:

Gambardella D, Impact Of Covid-19 On Colorectal Cancer With Worsening Of Clinical Presentation: Retrospective Study In A Single Center. Clin Onco. 2023; 6(22): 1-4

1. Abstract

1.1. Aim: The COVID-19 pandemic led to widespread disruption of colorectal cancer services during 2020. Established cancer referral pathways were modified in response to reduced diagnostic availability. The aim of this paper is to assess the impact of COVID-19 on colorectal cancer referral, presentation and stage.

1.2. Methods: This was a single-center retrospective cohort study performed at a secondary referral center. We compared patients diagnosed with colorectal adenocarcinoma between January 2018 and December 2019 with those collected from January 2020 to December 2021 in terms of pathological cancer staging, the prevalence of different localizations of colorectal cancer, type of surgery, TNM, stage of disease, postoperative complications, rehospitalization within 30 days of discharge, percentage of stoma and mortality at 30 days.

1.3. Results: In all, 115 patients were diagnosed with colorectal adenocarcinoma during 2018-2019 (Control Group CG) compared with 137 Patients in 2020-2021 (Study group SG). In SG More patients presented as emergencies ($P = 0.03$) with increased rates of large bowel obstruction in 2020-2021 compared to 2018-2019 ($P = 0.01$). Major differences were found in TNM, with disease stage worsening and malignant disease presentation at stages T4a and T4b compared to 2018-2019 ($P < 0.05$). Other

but not statistically significant differences were found for distant metastasis. We found a reduction of total of laparoscopic surgery in study group.

2. Background

The Covid-19 pandemic in recent months has forced the National Health Service to divert all its energies in the fight against the virus and in assisting Covid-19 patients by suspending diagnostic procedures and non-urgent treatments related to oncological and non-oncological pathology, causing inevitable delays in providing care. Diseases of benign surgical interest have undergone a diagnostic delay and a delay in treatment, manifesting themselves, in the months following the first Lockdown, with a more complicated clinical presentation and difficult surgical management. In fact, in the months of maximum emergency, screening programs were temporarily suspended in Italy, as in many other countries, both because health personnel were diverted to take care of patients with COVID-19 pneumonia and for the need to reduce contagion to a minimum, visits and diagnostic tests were suspended. On the other hand, patients were strongly discouraged from undergoing treatment or diagnostic tests for fear of contagion. 1) During the first phase of the pandemic, with the reduction of diagnostic endoscopies and treatments for early cancer detection, we expect an increase in advanced stage CRC diagnoses in the years to follow with a consequent increase in morbidity and mortality.

We therefore noted that for patients with colorectal cancer (CRC), there was an aggravation of the clinical presentation of this pathology such as to require a higher level of care. We therefore designed a retrospective case-control study in a single center comparing the data collected from January 2018 to December 2019 comparing them with those collected from January 2020 to December 2021 relating to patients undergoing VLS or Open colorectal resection disease to assess whether there was a difference in terms of the difference in the clinical presentation of the pathology, increased number of hospital days, difference in surgical approach, prevalence of stoma, percentages of anastomotic leak and rates of hospital readmission between both groups .

3. Methods

3.1. Study Design

We performed a retrospective case control study in a single center, collecting data on patients who underwent urgent and elective colorectal resection from January 2018 to December 2019, comparing them with the data for January 2020 to December 2021. 115 patients who underwent VLS / open colorectal resection were selected in the CG. In the same observation period, but the previous two years, 137 patients were selected in SG. The surgical interventions were performed by the same equipe and two operators performed laparoscopy.

3.2. Setting

This was a Single Center, retrospective and Case-Control Study.

3.3. Inclusion Criteria for Cases

Including criteria were all patients older than 18 years, both genders, who underwent elective/emergency, that is classical/laparoscopic resection due to CRC. The condition for admission of patients of the SG to the hospital was a negative PCR test for SARS-CoV-2 virus ; Before the surgery we repeat the antigenic Nasal oropharyngeal swab.

3.4. Inclusion Criteria for Control

The criteria for inclusion of the CG are the same without the recognition of the COVID-19 Nasal and oropharyngeal swab.

3.5. Outcomes

The aim of the study was to evaluate whether there were statistically significant differences between the two groups regarding the clinical presentation of the pathology, difference in surgical approach, prevalence of stoma, rates of hospital readmission between both groups , postoperative complications such as anastomotic leak ,30-day mortality.

3.6. Ethical Statement

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki.

3.7. Statistical Analysis

Patient characteristics were compared using the χ^2 test and Chi-clinicsofoncology.com

squared test with Yates correction Differences were considered statistically significant at $P < 0,05$. All statistical analyses were performed using BellCurve 3.20 (Social Survey Research Information) for Excel 2016 (Microsoft Corp).

4. Results

A total of 252 patients with a mean age of 68,2 years were included in this study. The CG operated in the period between January 2018 and December 2019 included 115 consecutive patients, most of whom were men ($n=83$, 72%); this was matched to a 2020-2021 SG of patients operated in the period between January 2020 and December 2021, also comprising mostly men ($n=86$, 63%), ; The mean age of the patients in the CG was 67.11 ± 11.621 , while in the SG it was 67.41 ± 10.378 .

4.1. Tumor Sites

The most common tumor localizations in both groups were rectum (in the CG 26.95%, in the SG 22.6%) and sigmoid colon (in the CG 21.7%, while in the SG it is 21,2%). The rarest localization of cancer was the appendix with 4 cases in the SG (3,2 %). Anterior resection of rectum (RAR) was the most common operation performed in both groups of patients, in the CG 47 patients underwent RAR, which accounts for 41% of all types of operations, while in the SG, 53 patients underwent RAR, which represents 37% of all operations.

4.2. Type of Surgery

In CG 72 (62,6 %) patients underwent colorectal elective surgery for malignant disease with 28 (24,3 %) Videolaparoscopic colorectal resection ; 43 (37,4 %) patients afferent from the emergency room underwent colorectal resection with symptoms of obstruction or perforation with 8 Videolaparoscopic colorectal resection in the emergency setting ; Regarding the operative approach in the CG a total of 36 laparoscopic colorectal resections were performed (31 %).

In 2019-2020 study group 78 (57%) patients underwent colorectal elective surgery for malignant disease with 25 (18 %) Videolaparoscopic colorectal resection ; 59 (43 %) patients afferent from the emergency room underwent colorectal resection with symptoms of obstruction or perforation with 3 Videolaparoscopic colorectal resection in the emergency setting ; Regarding the operative approach in the SG a total of 28 laparoscopic colorectal resections were performed (20 %).

Using a Chi-squared test with Yates correction ($p=0.0675$), no statistically significant difference was observed between these two groups.

4.3. Surgery with Stoma

In the SG, in 19% of patients, the operation was completed by creating a terminal stoma, while in the CG that percentage was 14%. Using a Chi-squared test with Yates correction ($p=0.47$), no statistically significant difference was observed between these two groups.

4.4. Hospital Stay, Anastomotik Leak And Readmission To Hospital

The mean postoperative hospital stay in the study group was 9.58 ± 3.64 days, while in the control group it was 10.77 ± 6.09 days. Regarding postoperative complications as anastomotik leakage, there was no statistically significant difference between the control and study group of patients. with 5 patients with radiological or clinical anastomotik leak (3,6 %) in SG, while in the CG was 1,7 %. There was no a statistical significance in readmission hospital rates in the interval of 30 days from discharge (2,2% in the study group, 3% in the control group, $p=0.81$).

4.5. Staging

We analyzed and compared the proportions of different T stages in both groups and we used using Fisher's test to notify statistically significant difference between two groups. T1 stage was represented by 3 patients (2,6 %) in the study group, while in the control group it was represented by 11 patients (9,6%), there wasn't a statistically significant difference in percentage of T1 stage between the study and control group ($p=0.11$), but T1 Stage is higher in control group -T2 stage accounted for 32 patients (10.2%) in the study group, while in the control group it accounted for 32 patients (27,8%), we didn't find statistically significant difference in distribution of T2 stage between analyses groups but we notified higher percentage of T2 Stage patients in control group. In both groups, the most common was the T3 stage (38 % in the study group, while 38,3 % in the control group with $p=0.12$). T4a stage was represented in the study group of patients with 25,5 %, while the control group was represented with 13 %, there was a statistically significant difference between the study and control group of patients in distribution of T4a stage ($p=0,016$). The incidence of T4b stage tumors in the control group was 24 %, while in the study group it was 11 % and using a Chi-squared test with Yates correction ($p=0.02$), statistically significant difference was observed between these two groups also for T4b stage.

4.6. Lymph Node Involvement

The average number of isolated lymph nodes in the study group of patients was 18.32 ± 9.23 , while in the control group it was 17.93 ± 10.16 . We analyzed the percentage of different N stages in the control and study group. In both groups of patients, the most common was the N2 stage.

4.7. Metastatic disease

Patients with metastatic disease in the CG were 3 (2,3 %), instead in the GS were 9 (6,6%) . There are no significant differences between the two groups but we did notice an increase in metastatic disease in SG.

5. Discussion

The Covid-19 pandemic in recent months has forced the National Health Service to divert all its energies to fighting the virus and assisting Covid-19 patients by suspending diagnostic procedures and

non-urgent treatments related to oncological and non-oncological pathologies, causing inevitable delays in the provision of care. [1] In response to the coronavirus disease 2019 (COVID-19) pandemic, all hospitals and outpatient care centers have delayed medical procedures and non-emergency surgeries. This recommendation also led to the suspension of colonoscopies for colorectal cancer screening and surveillance. [2] Screenings are essential in cancer prevention as they allow for the removal of pre-cancerous lesions, preventing the lesion from progressing to the early stages of cancer. Without these early detection and screening methods, the consequences could be fatal. [3] There has been a dramatic reduction in CRC screening during the pandemic. The reduction in screening and colonoscopies delays has led to an increase in CRC diagnoses especially in the late stage as the medical community has already predicted that this delay will lead to more CRC cases and deaths in the future. [4] In our study we have highlighted an overall increase in colorectal cancer cases, an increase in patients undergoing emergency surgery for intestinal obstruction, a worsening of the presentation of the disease in the more advanced stages with a statistically significant difference for T4A and T4B in the group study. Furthermore, more patients were treated in the stage of metastatic disease in SG. [5] A stoma could be created especially in case of emergency resections for bowel obstruction where it is not possible to perform anastomosis in one step, ileostomy to protect a very low anastomosis, or in case of abdominoperineal excision. [5] Despite more cases of resections performed urgently, the increase in the percentage of placement of stoma did not occur in the SG.

6. Conclusion

Continuous CRC screening efforts, from population-wide stool-based testing to diagnostic endoscopies and treatments, have elicited early cancer detection, and improved the devastating statistics regarding the CRC diagnosis outcome. The COVID-19 pandemic caused the world to pause, and instituted lockdowns, notably interrupting CRC screening programs. The reasons for the halt were the allocation of limited hospital resources towards the fight against COVID-19, the ongoing fear of nosocomial SARS-CoV-2 infection, and the overall overwhelming burden that the pandemic placed onto the healthcare system. For CRC screening programs, this included a drop in referrals from a general practitioner, patients' unwillingness to partake in stool-based testing, canceling or rescheduling colonoscopy appointments by patients out of fear or by institutions because they worked in limited capacities, and changing treatment plans to comply with the pandemic-elicited regulations. Although our Surgical department remained fully functional also during the first period of pandemic a substantial number of CRC patients went undiagnosed, which, in the short term, resulted in an increase of obstructive CRC, and the presence of high-risk adenomas. The long-term effects of the diagnosis backlog could result in a devastating rise of late-stage CRC cases, and the overall loss of life years due to the lack of appropriate

treatments for these patients. A late stage CRS cases has changed our surgical approach with more patients treated with open surgery, and more patients treated urgently; These prognostics, however, can be mitigated if proper catch-up screenings are provided. These lessons can also serve as a teaching moment for healthcare leadership, and can provide guidelines for minimizing and altogether avoiding the interruption of cancer screening programs if novel pandemic-causing infectious agents appear [4].

7. Compliance with Ethical Standards

7.1. Funding: This research received no specific grant from any funding agency in the public, commercial, or not-profit sectors.

7.2. Conflict of Interest: The authors have no conflict of interest to disclose, and no other funding or financial relationship with the surgical industry

7.3. Ethical Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

7.4. Informed Consent: Patients signed an informed consent before surgery for dataset use.

Authors' Contributions: All Authors equally contributed to conception, design, manuscript writing and final approval of manuscript.

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