

Surgical Treatment and Follow-Up of Colorectal Cancer During COVID-19 Pandemic: The Exception to the Rule?

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Received: November 11, 2020; **Published:** January 19, 2021

Abstract

Background: COVID-19 pandemic has had a major impact in all aspects of health care creating unprecedented challenges for health-care systems. Impact on colorectal cancer (CRC) patients remains undetermined. We aim to compare results between patients operated before and during the COVID-19 pandemic for CRC in a University Hospital.

Methods: A retrospective analysis of a prospectively collected database was made regarding two groups of patients operated for CRC during 2019 (group A) and during the COVID-19 pandemic (group B). A comparison was made considering age, comorbidities, time between first consult to surgical procedure, information about surgical intervention, tumour stage and follow up.

Results: 67 patients were included, 21 in Group B. Overall patient's median age was 66.94 years (SD: 14.93) and no differences were found regarding age and comorbidities between the groups. Delay in medical consultation for associated symptoms was higher in group A, whereas time from first consult to surgery and type of admission were similar in both periods. Laparoscopic approach was lower in Group B (13 patients: 61.90% vs. 40 patients: 86.96%, $p = 0.019$), and 23 (50%) patients of Group A and 8 (38.10%) patients of Group B had early stage tumours ($p = 0.365$). Complications were greater in group A. During the pandemic, 39 (88,64%) patients of group A received adequate oncological follow-up.

Conclusion: Patients with CRC who underwent surgery before and during COVID -19 pandemic weren't different in terms of delay in medical attention, surgical outcomes and tumour stage.

Keywords: COVID-19; Colorectal Cancer; Pandemic; Surgery

Introduction

Since its outbreak in December 2019, Coronavirus Disease 2019 has rapidly spread globally and was declared a pandemic on March 11, 2020 by the World Health Organization [1]. In Argentina the cases have slowly risen since the first one reported in March 3rd, 2020 [2].

At the time we wrote this article in August 2020, there were more than 390.000 infected and more than 8.000 deaths [3]. Argentina being one of the 10 countries with the highest number of infections around the world [4].

This pandemic continues challenging the whole health system, including patients with all kinds of pathologies and its scope and consequences remain uncertain.

The title “The impact of COVID-19 beyond the viral infection” [5] describes the thoughts behind many health care professionals around the world, who wonder how many patients the pandemic would affect beyond the COVID-19 infection itself. Collapsed emergency services, lack of beds in intensive care, reduction of health personnel, are just some of the problems that medical care faces [6-10].

Regarding surgical interventions, elective surgery has been stopped, emergency surgery and cancer related procedures have undergone too many changes in their management, having to design new ways to triage patients for their correct management and follow-up.

Also, surgical staff and the available units have been modified in order to minimize the risk of contagion among health workers with longer shifts that overstress the staff [11].

On the other hand, besides limiting the capacity of medical care, the COVID-19 pandemic has specific impact on oncological care [12]. It is well known how important it is in terms of survival and also on the quality of life to correctly follow up patients with cancer [13]. The pandemic should not be an impediment in this regard, however, access to health systems is hampered, people are afraid of getting infected and scheduled medical care has been greatly reduced [14-16], all this leads to an important decrease and delay in medical appointments [17].

Considering these factors, many questions have been raised regarding the safe way to treat cancer patients, trying to balance the risk of exposure with the risk of postponing treatments that undoubtedly have an impact on survival. This led to the creation of multiple treatment guidelines, most of them based on expert opinions as there is not much strong scientific evidence on cancer treatment during this pandemic [18-20].

The aim of this study is to compare a group of patients operated for CRC during the COVID-19 pandemic to those operated before, in order to determine differences between surgical results, access to medical care and tumour stages (an indirect marker of delay in diagnosis).

Methods

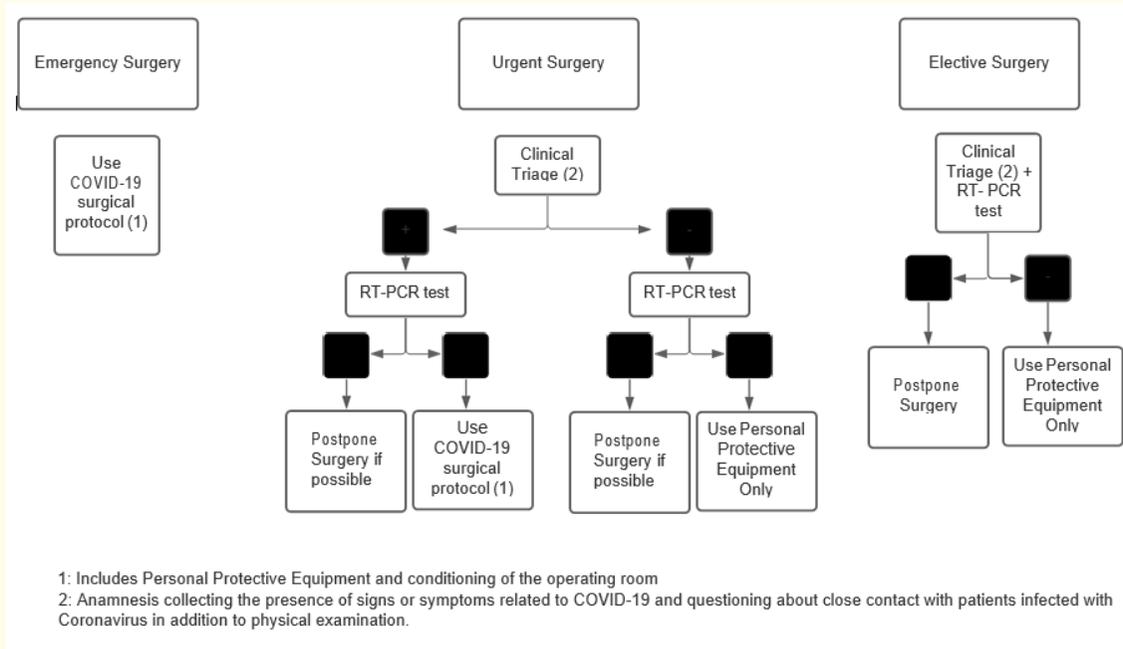
A retrospective review of a prospectively collected database was performed, including patients admitted for scheduled or emergency surgical procedures for colorectal adenocarcinoma in a University Hospital during 2019 and 2020. Patients operated for benign colorectal diseases or for tumours other than adenocarcinoma were excluded from this study. After being identified, the patients were split into two groups: Those who were hospitalized before the pandemic (Group A) and those during the COVID-19 pandemic (Group B). We considered that the pandemic started on March 11th, 2020 [1].

Information about age and comorbidities was assessed in order to detect differences between the groups. Data from the surgical procedures including intention of surgery (curative or palliative), type of admission (scheduled or urgent) and approach (conventional vs laparoscopic), and the results of the surgeries were analysed.

Complications were stratified using the Clavien-Dindo classification [21] and they were discriminated into minor and major complications (grades I and II were considered as minor complications, and grades IIIA to V, as major).

During the first three months there were a lot of changes in hospital protocols as regards ways and needs to determine active COVID-19 infection in surgical patients, similar to what happened around the world. After this period (and till today), clinical triage was performed in all patients in group B to detect Coronavirus Disease and later on a pre-surgical nasopharyngeal swab was implemented. In the case of scheduled surgeries, it was performed within 72 hours before the surgery. Figure 1 shows the algorithm used at our institution regarding surgical procedures and detection of COVID-19 infection.

Those who caught the COVID-19 infection during their hospitalization were identified and their clinical chart was reviewed in order to determine the impact of the infection in their outcome.



Tumour stage was split into two categories: Early tumours (stage I or IIA) and advanced tumours (IIB or more) according to the AJCC classification [22].

A telephone survey was conducted with all the patients included in the study in order to obtain precise information regarding the delay in seeking medical consultation and oncological follow-up during the pandemic. Lastly, the data was analysed taking into account how patients were diagnosed (either by screening studies or by symptoms associated with CRC). For those who had presented with symptoms, time to first consult was assessed in order to see if the COVID-19 pandemic was associated with delayed care. Also, time between diagnosis and surgical treatment was analysed for all patients. On the other hand, for group A, information was gathered about oncologic follow-up in order to detect missed visits during the pandemic.

Statistical analysis

Stata version was used for this purpose (v11.1, Statacorp, College Station, Texas USA). Categorical variables were described as percentages whereas numerical variables were described as median and range. Chi square test was used for the comparison of categorical variables and Student’s t-test for the comparison of numerical variables. All variables with a p value < 0.05 were considered statistically significant.

Results

A total of 67 patients was included, 46 operated during 2019 and 21 operated during the pandemic. Table 1 summarizes patient demographics. No significant differences were shown in terms of gender, age, or comorbidities.

	Group A	Group B	P value
N	46	21	
Age (median-range)	65.4 (37-89)	67.1 (37-89)	0.660
Females (n, %)	28 (60.87)	10 (47.62)	0.310
Previous abdominal surgeries (n, %)	25 (54.35)	8 (38.10)	0.217
Body mass index (median, range)	27.29 (18-40)	26 (16-36)	0.335
Comorbidities (n, %)			
HTA	23 (50)	10 (47.62)	0.856
Diabetes type II	6 (13.04)	5 (23.81)	0.270
Dyslipidemia	20 (43.48)	7 (33.33)	0.432
Smoking	4 (8.70)	3 (14.29)	0.488
Chronic kidney disease	2 (4.35)	1 (4.76)	0.939
Chronic pulmonary disease	3 (6.52)	1 (4.76)	0.939
Purpose of surgery (n, %)			
Curative	41 (89.13)	16 (76.19)	0.168
Palliative	5 (10.87)	5 (23.81)	0.168

Table 1: Patient demographics.

Preoperative data

Table 2 outlines data related to the preoperative assessment of patients.

	Group A	Group B	P value
N	46	21	
Admission (n, %)			
Urgent	8 (17.39)	6 (28.57)	0.296
Scheduled	38 (82.61)	15 (71.43)	0.296
Approach (n, %)			
Laparoscopic	40 (86.96)	13 (61.90)	0.019
Conventional	6 (13.04)	8 (38.10)	0.019
Operative time (minutes, median, range)	153.26 (60-280)	153.57 (85-370)	0.984
Days of hospitalization (median, range)	8.30 (3-30)	8.71 (4-32)	0.836
Complication rate (n, %)	24 (52.17)	8 (38.10)	0.151
Minor complications (n, %)	15 (62.50)	5 (62.50)	1.000
Major complications (n, %)	9 (37.50)	3 (37.50)	1.000
Mortality (n, %)	2 (4.35)	1 (4.76)	0.939
Primary anastomosis (n, %)	42 (91.30)	16 (76.19)	0.092
Anastomotic leak (n, %)	3 (7.14)	1 (6.25)	0.778
Re-operation rate	4 (8.70)	1 (4.76)	0.526
Re-hospitalization rate (n, %)	3 (6.52)	6 (28.57)	0.01
Disease stage (n, %)			
Early stage	23 (50)	8 (38.10)	0.365
Advanced stage	23 (50)	13 (61.90)	0.365

Table 2: Intra operative information and outcomes of surgical treatment.

Regarding the reason for consultation, only six patients (13%) operated during 2019 and two patients (9.5%) ($p = 0.680$) operated during 2020 were referred after a pathological finding in the context of screening.

Of the patients who presented tumour-related signs and symptoms, 19 (48.72%) in group A and eight (42.11%) ($p = 0.636$) in group B took less than one month to consult. A striking fact is that 12 patients (30.77%) in group A presented a delay of more than five months in consulting, while seven patients (36.84%) of group B took between one to two months.

Time between diagnosis and surgery was significantly lower during the pandemic, with 90.47% of patients in group B operated within one month, compared to 36.96% of patients in group A who had a delay of more than one month.

Seven patients (33.33%) from Group B were swabbed preoperatively, all of them were negative.

Intraoperative data

Table 3 shows the surgical outcomes and tumour stages.

	Group A	Group B	P value
N	46	21	
Diagnosis (n, %)			
Tumour associated symptoms	40 (86.96)	19 (90.48)	0.680
Screening studies	6 (13.04)	2 (9.52)	0.680
Delay between symptoms and first consult (n, %)			
Less than one month	19 (48.72)	8 (42.11)	0.636
1-2 months	6 (13.04)	7 (36.84)	0.034
3-4 months	3 (7.69)	0 (0)	0.214
More than 5 months	12 (30.77)	4 (21.05)	0.437
Delay between diagnosis and surgery (n, %)			
Less than 2 weeks	17 (36.96)	13 (61.90)	0.057
2-4 weeks	12 (26.09)	6 (28.57)	0.831
4-8 weeks	5 (10.87)	2 (9.52)	0.867
8-12 weeks	3 (6.52)	0 (0)	0.231
More than 12 weeks	9 (19.57)	0 (0)	0.029
Oncologic follow up during the pandemic	39 (88.64)		

Table 3: Delay in consult and follow-up information.

The laparoscopic approach was lower during the pandemic months (40 patients: 86.96% in group A vs 13 patients: 61.90% in group B) ($p = 0.019$). Regarding the purpose of surgery, five patients (10.87%) had a palliative procedure in group A and five patients (23.81%) ($p = 0.168$) in group B. The days of hospitalization were similar in both groups.

Postoperative complications were greater in the 2019 group (52.17% vs 38.10%; $p = 0.151$), and of these, nine patients (37.50%) in group A vs 3 patients (37.50%) in group B had major complications ($p = 1.000$).

Related to the aforementioned, the reoperation rate was 8.70% (four patients) in group A vs 4.76% (one patient) in group B ($p = 0.526$). Regarding group A, there were three patients with anastomotic dehiscence, one patient with evisceration, one requiring surgical

drainage of an intra-abdominal collection, one with intestinal sub-occlusion due to an adhesion and a patient with ostomy necrosis. In every case, they were patients over 55 years of age with at least one comorbidity. In group B, one patient presented anastomotic dehiscence (the only death described below) and another patient presented a blocked femoral hernia, in both cases they were patients older than 80 years of age with multiple comorbidities.

The percentage of readmission was higher in group B (28.57% vs 6.52%; $p = 0.01$): in 2019 two patients had to be rehospitalized because of complications related to the surgical procedure (dehiscence of the anastomosis and intestinal sub-occlusion due to an adhesion) and the rest of the patients presented clinical conditions unrelated to the surgery. In 2020, two female patients aged 40 and 56, without comorbidities, presented fever secondary to a collection. Both were tested for COVID 19 with a negative result.

During the postoperative period in group B, five patients (23.81%) were swabbed for presenting symptoms consistent with Coronavirus disease. A chest CT was also performed, causing one of them, who presented a pulmonary infiltrate to remain isolated as a probable case and to be re - swabbed.

The only patient who needed a reoperation because of an anastomotic leak during the pandemic required admission in the ICU during the postoperative period, where he finally tested positive and died on the same day. We believe he was already infected with Coronavirus during the reoperation.

This was the only patient who died during hospitalization in group B. The mortality rates in the groups are similar (4.35% group A vs 4.76% group B; $p = 0.939$). In 2019, two patients died while they were hospitalized, both were older than 75, with a history of cardiovascular disease who had undergone scheduled surgery. The causes of death were acute myocardial infarction and cardiac arrhythmia.

Finally, the oncological follow-up rate during the pandemic months of the patients operated during 2019 was 88.64% (39 patients) and of them, 62.5% used teleconsultation, alone or in combination with face-to-face consultation. Most patients stated that they didn't have any problems to arrive to the health centre despite the restrictions imposed in our country due to the quarantine, only one of them, who also had two hospitalizations in another institution for reasons not related to the CRC, was infected with Coronavirus. Regarding patients operated on in 2020 who had been discharged, they all had access to postsurgical follow up, none have presented Coronavirus infection to this date.

Discussion

If collateral damage of the COVID- 19 pandemic wants to be assessed, we cannot avoid paying attention to cancer patients due to the fact that they regularly attend health centres, they are mostly immunocompromised, are at a higher risk of suffering severe coronavirus infection [23-24] and last but not least, any modification in their follow-up or delay in treatment can directly affect their survival.

Based on this premise, every year in our country 125.000 new cases of cancer are diagnosed, CRC being one of the most prevalent tumours [25].

The concern of cancer patient management during the pandemic has widely been described in the international literature. Guidelines have been drawn up for their management [18-20] and multiple surveys have been conducted on this topic.

In these patients, time is of the essence: From early diagnosis based on screening methods, quick access to surgery and an adequate follow-up. All of these instances have been severely hit by Coronavirus forcing health personnel and patients to look for new ways to move ahead in pursuit of health.

The Official Journal of the National Comprehensive Cancer Network [26] published a guideline for the management of cancer patients. It emphasizes how difficult it is to decide when and how to provide treatment during a pandemic for an oncological disease but continues

to affirm that the challenges that they face as an institution must still align with their overarching goal, which remains to provide cancer treatment to patients in need, as safely and as justly as possible.

On the other hand, taking into account the patients view, The European Journal of Cancer published an original article [27] that describes the impact of the Coronavirus disease pandemic on cancer treatment under a patient's perspective. They were based on an online survey developed by the Dutch Federation of Cancer Patients Organizations conducted on 5 300 patients with cancer in the Netherlands. 55% of the patients had a delay in medical appointments and 63% discontinue their treatments and showed concern about consequences of the COVID-19 pandemic on their health.

However, our experience shows encouraging results. The number of patients surgically intervened during the months of March - August 2020 (n = 21) is similar to the same months in 2019 (n = 24). The reasons for requiring medical care (screening vs signs and symptoms related to the tumour), the delay in reaching a health centre, the time between consultation and surgery, intraoperative findings and operative time, the days of hospitalization and the postoperative follow-up did not show significant differences between both groups.

Reviewing the measures adopted in our hospital, all patients who underwent surgical procedures during the pandemic underwent a pre-surgical clinical triage. Given the increase in cases that occurred in our city, the pre-surgical swab was systematically established later. The Personal Protective Equipment was used during all surgeries and the operating room was conditioned according to institutional recommendations.

According to current recommendations the laparoscopic approach decreased during the first months of the pandemic. Initial documents seemed to conditionally advise against use of laparoscopy [28]. However, later it was describe that with an adequate technique there is no need to suspend this type of approach, since there is no scientific evidence to date about the COVID-19 transmission by laparoscopic surgery [29]. On the other hand, many studies have shown that laparoscopic colorectal surgery is associated with lots of benefits, including less postoperative pain, earlier recovery of bowel transit and shorter hospital stay and well-designed prospective randomized multicentre trials have demonstrated that oncological outcomes of laparoscopy and open surgery are similar when they are performed by a trained surgeon [30].

A decentralization of medical clinics was carried out in order to reduce the flow of patients in inpatient hospitals and there were enabling teleconsultations for the first time. It should be mentioned that to date no surgeon or resident physician from the surgical team presented with COVID-19.

In support of these outcomes, a letter to the editor [31] published in The British Journal of Surgery describes the experience in a university hospital located in the Lombardy region, epicentre of the SARS-CoV-2 outbreak in Italy. There were 31 patients operated with a diagnosis of CRC during the pandemic (group A) and their results were compared with patients operated in the same period of 2019 (Group B). Baseline characteristics among the two groups were comparable, there were almost no differences between the approaches, post-operative complications occurred in 22.5% in group A and 32.2% post-operative complications occurred in group B. There was no perioperative mortality. No SARS-Cov-2 infections occurred in group A. The median length of stay was three days for group A vs four days for group B. They conclude that with preoperative screening and COVID-free pathways it is possible to maintain cancer surgery while ensuring patient safety.

Achieving timely treatment in a patient with CRC has been shown to have implications on survival length. This is how Roder [32] describes it in an article published in the British Medical Journal: In patients with colorectal cancer, three to ten year survival is lower if treatment is started beyond 90 days from diagnosis. On the other hand, Kucejko [33] states that the ideal time for resection of colon cancer has been estimated to be between three and six weeks from diagnosis. In our series, none of the patients diagnosed during pandemic had a delay exceeding two months between diagnosis and surgery.

Regarding long-term follow-up, most of the patients operated during 2019 attended their postoperative visits on time. This is important since 80% of the recurrences occurred in the first three years after surgical resection of the primary tumour and a recent study found that 95% of recurrences occurred within the first five years [34].

The postoperative controls have been carried out personally or through teleconsultation, a new tool that we believe is here to stay. Telemedicine may reduce the need for physical attendance in an outpatient clinic, minimizing exposure where possible. It has many advantages including a better environmental profile and lower costs [35]. From our experience this tool has facilitated the monitoring of patients, preserving them and health personnel from Coronavirus infection.

To conclude, even though the COVID-19 pandemic brought us countless challenges that go beyond the coronavirus infection itself as regards patient's care, it seems the impact was not extensive to CRC patients, who exhibit similar results of surgical treatment, tumour stage and timing for consultation, and have also managed to achieve a high rate of oncologic follow-up using old and new resources. As this publication includes a small number of individuals, results need to be compared with those of other hospitals with higher number of patients.

Authors Declare No Conflict of Interest

This paper has been approved by the institutional bioethics committee.

Bibliography

1. World Health Organization (WHO). WHO Director-General's opening remarks at the media briefing on COVID-19 (2020).
2. Argentine Health Ministry. Salud confirma el primer caso de coronavirus en el país (2020).
3. World Health Organization (WHO). Coronavirus disease (COVID-19) Weekly Epidemiological (2020).
4. Business Insider. "These are the 10 most-affected countries with the highest number of COVID-19 cases (2020).
5. Pellino G and Spinelli A. "How Coronavirus Disease 2019 Outbreak Is Impacting Colorectal Cancer Patients in Italy: A Long Shadow Beyond Infection". *Diseases of the Colon and Rectum* 63.6 (2020):720-722.
6. Buenos Aires Times. Virus surge pushes Jujuy's health system to brink of collapse (2020).
7. Mediciens sans frontières. "COVID-19 has made the health system's collapse complete" in Yemen (2020).
8. Mediciens sans frontières. "People are dying at home amid collapsing health system in El Salvador (2020).
9. De Oliveira Andrade R. "COVID-19 is causing the collapse of Brazil's national health service". *British Medical Journal* 370 (2020): m3032.
10. The New York Times. Italy's Health Care System Groans Under Coronavirus - a Warning to the World (2020).
11. Spinelli A and Pellino G. "COVID-19 pandemic: perspectives on an unfolding crisis". *British Journal of Surgery* 107 (2020): 785-787.
12. Indini A., et al. "Reorganisation of medical oncology departments during the novel coronavirus disease-19 pandemic: a nationwide Italian survey". *European Journal of Cancer* 132 (2020): 17-23.
13. Tørring ML., et al. "Advanced-stage cancer and time to diagnosis: An International Cancer Benchmarking Partnership (ICBP) cross-sectional study". *European Journal of Cancer Care* 28 (2019): e13100.

14. Masroor S. "Collateral damage of COVID-19 pandemic: Delayed medical care". *Journal of Cardiac Surgery* 35 (2020): 1345-1347.
15. Shifat Ahmed SAK, et al. "Impact of the societal response to COVID-19 on access to healthcare for non-COVID-19 health issues in slum communities of Bangladesh, Kenya, Nigeria and Pakistan: results of pre-COVID and COVID-19 lockdown stakeholder engagements". *British Medical Journal Global Health* 5 (2020): e003042.
16. Joode K., et al. "Impact of the coronavirus disease 2019 pandemic on cancer treatment: the patients' perspective". *European Journal of Cancer* 136 (2020): 132-139.
17. The Lancet Oncology. "COVID-19: global consequences for oncology". *The Lancet Oncology* 21 (2020): 467.
18. Asociación Argentina de Cirugía. Guía en Argentina para cirugías oncológicas durante la pandemia.
19. Fligor SC., et al. "Gastrointestinal Malignancies and the COVID-19 Pandemic: Evidence-Based Triage to Surgery". *The Journal of Gastrointestinal Surgery* 30 (2020): 1-17.
20. Curigliano G., et al. "Managing cancer patients during the COVID-19 pandemic: An ESMO Interdisciplinary Expert Consensus". *Annals of Oncology* (2020).
21. Dindo D., et al. "Classification of surgical complications. A new proposal with evaluation in a cohort of 6336 patients and results of a survey". *Annals of Surgery* 240 (2004): 205-213.
22. Weiser MR. "AJCC 8th Edition: Colorectal Cancer". *Annals of Surgical Oncology* 25 (2018): 1454-1455.
23. Centers for Disease Control and Prevention Information for healthcare professionals: COVID-19 and underlying conditions (2020).
24. Liang W., et al. "Cancer patients in SARS-CoV-2 infection: a nation-wide analysis in China". *The Lancet Oncology* 21 (2020): 335-337.
25. Argentine Health Ministry. National Cancer Institute. Estadísticas – Incidencia (2020).
26. Targeted Oncology. "The NCCN Shares Recommendations for the Safety of Cancer Patients During the COVID-19 Pandemic (2020).
27. Joode K., et al. "Impact of the coronavirus disease 2019 pandemic on cancer treatment: the patients' perspective". *European Journal of Cancer* 136 (2020): 132-139.
28. Zheng MH., et al. "Minimally Invasive Surgery and the Novel Coronavirus Outbreak: Lessons Learned in China and Italy". *Annals of Surgery* 272 (2020): e5-e6.
29. Boghdady ME and Ewalds-Kvist BM. "Laparoscopic Surgery and the debate on its safety during COVID-19 pandemic: A systematic review of recommendations". *Surgeon* (2020).
30. Pascual M., et al. "Laparoscopic colorectal surgery: Current status and implementation of the latest technological innovations". *World Journal of Gastroenterology* 22 (2016): 704-717.
31. Carrano FM., et al. "With adequate precautions colorectal cancer surgery can be safely continued during COVID-19 pandemic". *British Journal of Surgery* 107 (2020): e41.
32. Roder D., et al. "Time from diagnosis to treatment of colorectal cancer in a South Australian clinical registry cohort: how it varies and relates to survival". *BMJ Open* 9 (2019): e031421.
33. Kucejko RJ., et al. "How soon should patients with colon cancer undergo definitive resection?" *Diseases of the Colon and Rectum* 63 (2020): 172-182.

34. National Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology Colon Cancer (2020).
35. Nikolian VC., *et al.* "Pilot study to evaluate the safety, feasibility, and financial implications of a postoperative telemedicine program". *Annals of Surgery* 268 (2018): 700-707.

Volume 8 Issue 2 February 2021

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