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## Special Article

# Potential impact of COVID-19 on colorectal disease management



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### ABSTRACT

The current recommendations for management of colorectal diseases are still evolving, due to the limited experience on this issue. As the new coronavirus can be transmitted through breath droplets, by contact and orofecally, there is no consensus of how this fact may affect the investigation and treatment of anorectal diseases. Thus, high-quality multicenter studies are urgently needed to provide better information to both patients and the multiprofessional team, in order to build an effective pandemic response plan in our specialty. As a greater operative risk for infected patients has already been demonstrated, the next step lies on the identification of new therapeutic strategies that could minimize this effect on an individual basis. There is a present understanding that the COVID-19 pandemic should change some traditional practices. Therefore, the surgical treatment of suspected or known COVID-19 case demands specific insights. This article analyses potential influences regarding the treatment of patients with Colorectal Cancer (CRC) and Inflammatory Bowel Diseases (IBD). At present, elective surgery must be avoided, and the colorectal surgeon must carefully evaluate the risks and benefits of such decision. Within this context, a change toward nonsurgical and less aggressive modalities of CRC treatment may help to postpone definitive treatment. We also discuss the concerns regarding the viral infection among the population, the influence on clinical symptoms and the proposed modifications on therapeutic schemes.

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## Impacto potencial da COVID-19 no manuseio das doenças colorretais

### R E S U M O

#### Palavras-chave:

Coronavírus  
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As recomendações atuais para manuseio das doenças colorretais ainda estão em evolução, devido à limitada experiência nesse tema. Como o novo coronavírus pode ser transmitido em gotículas da respiração, por contato ou por via oro-fecal, ainda não existe consenso de como este fato pode afetar a investigação e o tratamento de doenças anorretais. Assim, são necessários estudos multicêntricos de qualidade para prover melhor informação ao paciente e equipe multiprofissional, possibilitando a formulação de uma resposta efetiva à pandemia em nossa especialidade. Uma vez que o risco operatório de pacientes infectados é maior, o passo subsequente reside em identificar novas estratégias terapêuticas que possam minimizar esse efeito individualmente. Assim, reconhece-se atualmente que a pandemia pelo COVID-19 deve alterar algumas práticas tradicionais. Conseqüentemente, o tratamento cirúrgico de um doente infectado ou suspeito demanda reflexões específicas. Esse artigo analisa influências potenciais relacionadas ao tratamento do Câncer Colorretal (CCR) e Doenças Inflamatórias Intestinais (DII). No atual momento, cirurgias eletivas devem ser postergadas e o cirurgião colorretal deve avaliar cuidadosamente os riscos e benefícios dessa decisão. Nesse contexto, uma mudança na direção de modalidades não-cirúrgicas e menos agressivas do CCR pode favorecer a prorrogação do tratamento definitivo. Aqui também se discutem as preocupações sobre a infecção viral em pacientes com DII, sua influência sobre os sintomas clínicos e as modificações propostas nos esquemas terapêuticos.

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## Introduction

The Coronavirus Disease (COVID-19) has spread globally and quite rapidly since it was reported as a global health emergency and identified as a pandemic. After that, there is an urgent need to assess its impact on diseases and the treatment of colorectal disorders.

This finding brings several challenges to the colorectal surgeon. When treating a patient, this individual might have no infection, have an infection not yet diagnosed or a detected infection. Thus, in addition to care to avoid contamination of the team and the patient, we must take into account the need to change some criteria for surgical indications or even operative procedures. That is because viral infection may require clinical or surgical interventions that are different from the conventional ones, as the infection is associated with additional risks that culminate in a significant increase in morbidity and mortality.

The present review aimed to review the experiences and results published in the literature in relation to the treatment of colorectal tumors and inflammatory bowel diseases, two important conditions of our specialty, of which management will eventually have to incorporate new therapeutic strategies.

## Is it necessary to change surgical procedures?

In case of an infected patient, a recent discussion concerns the decision to avoid performing an anastomosis in high-risk situations (low anastomosis, diabetics, preoperative radiotherapy,

the elderly), in order to reduce complications and hospitalization costs.<sup>1</sup> However, this option must be weighed against the demand for a future hospitalization to reconstruct intestinal transit (in addition to the psychological consequences associated with a stoma). For this reason, this decision must be individualized and shared, based on the team's experience and clinical conditions at the time of surgery.

Another presented proposal concerns the management of cases with intestinal obstruction, a situation in which one proposes evaluating less aggressive alternatives, such as stent placement or intestinal bypass with a stoma, without resection.<sup>2</sup> However, one must remember that the management of an intestinal stoma can increase the risk of infection through the handling of contaminated stool. Digestive transit reconstruction procedures should be postponed, as they do not represent an emergency contingency. Similarly, it is necessary to consider potentially contaminated surgical specimens when they are sent to the pathologist.

In the current situation, the COVID-19 infection should be part of the differential diagnosis when investigating postoperative fever. This is particularly important when low symptomatic or asymptomatic patients infected with SARS-CoV-2 require urgent surgery and cannot be effectively screened.

Patients with fever of unknown etiology or respiratory symptoms should be isolated, submitted to a chest CT scan and laboratory tests. The uncertainty about the etiology of postoperative fever can be reduced by the universal testing of all surgical patients. Even if the patient has been tested negative in the preoperative period, further tests must be performed.

**Table 1 – Treatment priority categories according to tumor types.**

Priority	Tumor types
High	Obstructive, perforated tumors, with repetitive bleeding
Middle	Stages I, II and III colon cancer Stage I rectal cancer or stages II-III after neoadjuvant treatment
Low	Early rectal cancer after complete RT/CT response Prophylactic surgery for hereditary CRC cases

### Initial recommendations for the management of colorectal cancer (CRC)

Overall, cancer patients can be fragile and show different degrees of malnutrition and immunosuppression, due to the neoplasm itself or to antineoplastic therapies. This group is estimated to have a two-fold risk of contracting SARS-CoV-2, when compared to the general population.<sup>2</sup>

The surgical treatment of these patients adds important dilemmas, as the surgery can trigger important complications and its delay can affect prognosis. It is crucial to evaluate the operative risks and the chances of respiratory infection, as COVID+ patients are more prone to infection associated with surgery, adjuvant treatment or immunosuppression. This entire scenario must be explained and discussed with the patient.

The following are considered essential measures in cases of colorectal neoplasms:

- Keeping minimum nutritional conditions;
- Avoid immune system worsening by the implemented treatments;
- Avoid prolonged hospitalization and visits that favor contamination;
- Adopt therapeutic planning that does not require a specific surgical schedule that may not be possible;
- Include the patient in multidisciplinary discussion groups;
- Provide psychological assistance.

Surgery is the therapeutic method with the greatest benefits in terms of survival. However, possible alternative measures to radical surgery should be discussed in early or very advanced stages, and patients should be referred to tertiary hospitals with intensive care.<sup>3</sup> Similarly, it is the only alternative for managing complications caused by the neoplasia.

To make it easier, we can propose the separation of patients according to their treatment priority (Table 1).

In situations where hospital resources are all dedicated to the care of infected patients, operative indications should be restricted to urgent cases only (perforation, local or generalized peritonitis, obstruction, bleeding tumors that require repeated transfusion). In this way, the treatment of malignant polyps, large non-obstructive polyps, prophylactic surgeries in patients with genetic diseases and rarer tumors, such as small-sized neuroendocrine tumors, would be postponed.<sup>4</sup>

Obstructive tumors will eventually require the creation of a stoma and chemotherapy indication. In these cases, special care must be taken during the handling of the stoma in order to reduce infection among the team. The big problem lies in cases where the surgery has a curative intention, only. All situations should be discussed on a case-by-case basis, taking into account the oncological risk, the chance of evolving to an obstructive condition and also of inducing immunosuppression, which could be harmful.<sup>5</sup> In initial lesions with a good prognosis (T1-2, N0), it is possible to delay the surgery, although not for long, aiming to minimize the risk of complications and progression. The administration of neoadjuvant therapy in these cases is not standardized.<sup>6,7</sup>

In intermediate cases, it is difficult to estimate the impact of the delay. When treatment is delayed for more than 90 days since the diagnosis, it can affect survival<sup>8</sup> in comparison to treatment implemented between 3 and 6 weeks.<sup>9</sup> During the pandemic, it is estimated that this period cannot be respected, possibly influencing results in the medium and long terms, since the time between the diagnosis and surgery is considered a measure of treatment quality.

Those with advanced colonic tumors may undergo neoadjuvant chemotherapy (5-FU or oxaliplatin) until the peak of the pandemic has occurred, before proposing any radical treatment. Remember that the benefit of tumors with Microsatellite Instability (MSI) is limited or even harmful.<sup>10</sup>

As for precancerous rectal lesions or early tumors, there is the alternative of resection using less invasive endoscopic techniques such as EMR or ESD. In the more advanced cases, the biggest problem will not necessarily be the newly diagnosed patient, but the one who has finished radiotherapy and chemotherapy. After completing the neoadjuvant treatment, patients with stage II-III rectal tumors can be operated, but surgery can also be delayed in cases that responded well or completely. At the oncologist's discretion, adding more cycles of chemotherapy may further extend the interval before surgery. T3-4 or N+ tumors that completed the neoadjuvant treatment without achieving a full tumor response should be operated so as not to miss the chance of having a curative procedure, with a greater chance of cure than the risk of infection.<sup>4,11</sup>

Transanal Total Mesorectum (TaTME) excision procedures require insufflation with a high CO<sub>2</sub> flow, exposing the medical team to aerosolized viral particles. Consequently, it would be prudent to avoid this access route during the pandemic.<sup>12</sup>

Eventually, the adoption of new neoadjuvant treatment protocols will allow the definitive treatment to be delayed for up to 12 weeks, without major consequences.<sup>13</sup> At the Memorial Sloan-Kettering Cancer Center em Nova York, the reassessment of practices in the emergency situation that we are currently experiencing led to the adoption of short-course radiation therapy to the detriment of total neoadjuvant therapy, despite being associated with less tumor mass reduction. The adoption of therapeutic strategies involving short-course radiation therapy has the advantage of reducing the patient's exposure to the hospital environment.<sup>14</sup>

Eventually, a patient with a less advanced tumor develops a complete response, a situation in which a lower chance of new tumor growth is recognized.<sup>15</sup> This situation would be potentially ideal, despite all the controversy that involves a

**Table 2 – Strategies suggested for the treatment of colorectal cancer in its different stages.**

Tumor	Staging	Conduct
Early CRC	T1N0M0	Endoscopic resection, transanal excision or delay surgery
Early CRC	T2N0M0	Delay surgery
Locally advanced colon tumor	T3-4	Chemotherapy?
Locally advanced mid-rectal tumor	T4N0 or T4qN+	Neoadjuvant CRT
	T3N0M0	Neoadjuvant CRT or delay
Locally advanced high rectal tumor	T0N0 complete response	Surgery with/without neoadjuvant CRT or Watch and wait Protocol

conduct that is divergent from the traditional one, allowing the organ to be preserved and the patient not to be exposed to surgical risk, with clear benefits for the elderly.

Table 2 depicts a summary of the strategies suggested for the treatment of colorectal cancer in its different stages.<sup>11</sup>

When considering the risks and benefits of an intervention, one must be carefully assess them on an individual basis. Surgical delay, associated or not with adjuvant treatment, may be possible as long as there is an agreement. Another important measure is to minimize the patient's exposure to other people and the hospital environment.

Due to the limited number of publications with evidence, there are still no international recommendations that indicate the best therapeutic strategy in all situations. Here, we have only outlined the challenges that can be found and listed the practical suggestions proposed so far. But we recognize that only time will bring more appropriate answers to the countless doubts that intrigue us at this moment.

## Inflammatory bowel disease management during the pandemic

### Introduction

On March 11, 2020, the World Health Organization declared that Coronavirus-19 Disease (COVID-19) was a pandemic. Three weeks later there were already 1,000,000 affected individuals and more than 46,000 deaths worldwide. This disease affects people in all age groups, being more prevalent in males and has a more unfavorable evolution in people with chronic comorbidities such as diabetes, respiratory diseases, obesity and hypertension.<sup>16</sup>

The main clinical manifestations of COVID-19 are fever and respiratory symptoms; however, we know that a significant part of affected patients will experience symptoms related to the digestive tract. These symptoms seem to be related to the swallowing of the virus and the expression of the Angiotensin-2 Converting Enzyme in intestinal cells. Recent studies have demonstrated the presence of the virus in the stool, even after the disappearance of respiratory symptoms and even the absence of the virus in the oropharynx.<sup>17</sup>

Since this disease presents itself as a pandemic, it is natural for patients with Inflammatory Bowel Disease (IBD) to express a special concern regarding their situation. We must remember that the drug control of IBDs fundamentally involves the continued and chronic use of immunosuppressive medications. In this article, we will attempt to clarify some doubts pertaining to the inherent risk of contamination of these patients, those with active disease and the ones in remission,

the need to change the prescription of their medications to prevent contagion and how to manage those with IBD who may be affected by COVID-19.<sup>18</sup>

### IBD and risk of contracting COVID-19

Inflammatory bowel diseases, more specifically ulcerative colitis and Crohn's disease, are characterized by chronic gastrointestinal inflammation, which affect millions of people worldwide. Most of these individuals require the use of immunosuppressive medications that increase the risk of several infections. Corticosteroids, immunomodulators, biological agents and several other commonly used medications are associated with higher rates of viral, bacterial and fungal infections. Therefore, it is logical to assume that SARS-CoV-2 infection and the development of COVID-19 is greater among individuals with IBD. Despite the potential risk for the development of COVID-19 in these patients, this fact has not yet been observed. Patients with IBD do not seem to have an increased risk of acquiring SARS-CoV-2 infection or developing COVID-19.<sup>19</sup>

The fact that the individual has an active IBD or is in remission also does not seem to make any difference in relation to the risk of developing COVID-19. However, it seems logical that a great effort should be made to keep these patients in remission; thus avoiding the increase in medications, the need for exams, hospitalizations and, eventually, more invasive procedures.

Patients with IBD who do not have SARS-CoV-2 infection should not have their medications suspended. There is no evidence of prophylactic benefit for this conduct.<sup>17</sup>

### Evolution of IBD in patients with COVID-19

The evolution of IBD does not seem to be altered in patients with COVID-19. To date, no worsening in the inflammatory activity in individuals with Crohn's disease or ulcerative colitis that have been contaminated by SARS-CoV-2 has been observed. The patient's overall evolution will depend fundamentally on the severity of the two diseases separately.<sup>20</sup>

### Drug management of IBD during the pandemic

One of the important questions raised by patients with IBD and also by their medical teams is what to do and how to manage drug therapy during the pandemic. We still do not have enough data to be able to support a conduct unequivocally; however, one thing is very clear: the management will depend fundamentally on the clinical presentation of IBD and

the form of SARS-CoV-2 infection. Therefore, we divided drug management into different situations:

**Patient with IBD without SARS-CoV-2 infection:** IBD patients are not at increased risk of developing COVID. Thus, it is strongly suggested that they maintain their medication without changing doses or intervals. It is essential at this point that they maintain the clinical and endoscopic remission of the disease.

IBD recurrence is extremely dangerous at this time, as it may lead the patient to require the use of corticosteroids, hospitalizations and even possible invasive procedures, which are situations that should be avoided at this point. Moreover, patients must maintain strict social isolation and adequate hygiene measures. Patients using Infliximab should not switch to Adalimumab, aiming to avoid going to the infusion centers, as it is known that the risk of IBD recurrence during the exchange exceeds the risk of contagion during these displacements.<sup>21</sup>

Patients with IBD who test positive for SARS-CoV-2 but remain asymptomatic of viral infection: In this situation, there is a real possibility of the development of COVID-19. Therefore, some measures must be taken. Patients should decrease prednisone dose to less than 20 mg/day and, if possible, switch to budesonide. Thiopurines, methotrexate and tofacitinib can be temporarily suspended. Anti-TNF, Ustekinumab and vedolizumab should have their doses delayed for 2 weeks. During this period, the viral infection evolution is possible, and the application should be restarted after this period in patients who did not develop COVID-19. We must keep in mind that the virus remains present in the stool even after its disappearance from the nasopharynx, but the clinical relevance of this fact is not yet clear.<sup>21</sup>

Patients with IBD who develop COVID-19: In this situation, the use of aminosalicylates (oral or topical), dietary management and antibiotics can be safely used. Oral budesonide seems to be safe as well and can be maintained if it is really necessary and shows benefit in controlling IBD. Systemic corticosteroids should be stopped rapidly, taking into account the risk of adrenal failure. Thiopurines, methotrexate and tofacitinib should be suspended. Anti-tnf, anti-interleukin and anti-integrins have an acceptable safety profile but must be suspended in the presence of COVID-19.<sup>22</sup>

### **Colonoscopy: strategy in IBD patients during the pandemic**

Routine endoscopic procedures for IBD monitoring, as well as for detecting dysplasia and early colorectal cancer diagnosis should be delayed at this time. The main indications for endoscopic procedures in patients with IBD during the pandemic would be: (a) Suspected infection by clostridium or cytomegalovirus; (b) Radiological suspicion of colorectal neoplasia due to morphological alteration of the mucosa.<sup>23–25</sup>

### **Surgical procedures in patients with COVID-19**

The surgical treatment of IBD during a pandemic exposes the patient and the surgical team to a high risk of contamination. Patients should be advised and encouraged to remain in social isolation and to avoid hospital environments whenever possible. Additionally, elective surgeries occupy hospital beds

in wards and ICUs that could be very necessary for infected patients.<sup>26</sup>

Unfortunately, emergencies will continue to occur in patients with IBD and many of them will have to be treated surgically. Therefore, patients with perianal abscesses, intestinal obstruction, perforation with peritonitis, severe intestinal hemorrhage, fulminant colitis and toxic megacolon, might need urgent surgical treatment. Some patients diagnosed with colorectal cancer may also need urgent surgical intervention.<sup>27,28</sup>

Some conducts are useful and necessary when it comes to surgical treatment. The number of people in the operating room should be limited to the minimum necessary. There is no absolute contraindication to the use of minimally-invasive techniques; however, there seems to be a decrease in the tolerance to conversion to open surgery.<sup>28</sup> Preferably, the surgery should be performed by an experienced surgeon rather than more inexperienced and resident surgeons. Finally, special care must be taken during patient intubation, peritoneal insufflation, excessive use of electrocautery, aerosolization, aspiration and transoperative endoscopy when necessary.<sup>28,29</sup>

To date, the postoperative mortality in patients who tested positive for SARS-CoV-2 is much higher than that observed for other patients. A retrospective study of 34 IBD patients submitted to surgery showed a 20% mortality in elective surgeries. Obviously, a very large number of variables must be taken into account, but until we have a more concrete idea about these morbidities and mortality, it seems reasonable to postpone, whenever possible, elective surgeries in patients with IBD during the pandemic.<sup>29,30</sup>

## **Conclusion**

Many of the data presented herein are debatable and subject to change once the pandemic enters its final phase and changes in conduct are better appreciated, with a higher number of cases. It is up to the specialist to recognize the need to keep up to date and develop activities with a coordinated multidisciplinary group that can make the best decisions taking into account the short and long-term impact of the viral disease. It is also necessary to perform specific research on the topic to establish norms and recommendations with a higher level of evidence.

## **Conflicts of interest**

The authors declare no conflicts of interest.

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