Impact of the COVID-19 Pandemic on Colorectal Cancer Patients at a Major Brazilian Cancer Center: An Increase in Metastatic Patients upon Presentation?

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Abstract

Introduction The years 2020 and 2021 were peculiar due to the coronavirus disease 2019 (COVID-19) pandemic, which may also have had an impact on people with colorectal cancer (CRC). In the state of Bahia, Brazil, Hospital Aristides Maltez (HAM) is responsible for most of the oncological care, including malignant neoplasms of colon and rectum. Considering that most of metastatic CRC cases are no longer curable, evaluate if there was an increase in the proportion of that stage of disease can serve as a metric of the impact of this epidemic.

Materials and Methods Retrospective analysis of HAM's electronic medical records of patients with CRC that had their first consultation during the first 12 months of COVID-19 epidemic at Bahia, in comparison to those that had their first consultation during the 12 previous months.

Results Main characteristics of both groups were similar. Median age was 63 years old, with near representation of both genders, and predominance of brown skin color and a low level of education. However, in the first year of COVID-19 epidemic, there was a 26.89% increase of subjects with already metastatic CRC in the first medical evaluation at HAM (although without statistical significance).

Discussion We found a numerical increase in metastatic CRC in the COVID period cohort. In consonance with this, another Brazilian study found an increase in the proportion of new cases of advanced CRC, between March and July 2020, in comparison to the same period in 2019. Moreover, in another publication, an increase in colorectal cancer mortality in USA is projected due to delays in screening and diagnosing during the COVID-19 pandemic.

Conclusion These results urge attention to CRC in the following years and in the next pandemic.

Keywords
- colorectal neoplasms
- colonic neoplasms
- rectal neoplasms
- COVID-19
- SARS-CoV-2
- pandemics

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Introduction

Colorectal cancer (CRC) is one of the most prevalent types of cancer worldwide, and one of the major causes of cancer-related deaths[1,2]—and this is not different in Brazil.[3,4] In the state of Bahia, Hospital Aristides Maltez (HAM) is responsible for most of the oncological care.[5] According to the Brazilian National Cancer Institute (INCA), 1,480 new CRC cases were estimated in Bahia in 2020.[3] A report from the Bahia League Against Cancer (LBCC, from the Portuguese Liga Bahiana Contra o Câncer) shows that 538 new cases of CRC were treated at HAM in 2019 (corresponding to 36% of the total estimated for the whole state in 2020), with similar numbers in the 2 previous years.[5]

The years 2020 and 2021 were peculiar due to coronavirus disease 2019 (COVID-19) in several aspects. Tackling the pandemic was prioritized. Therefore, cancer patients, including those with colorectal malignancies, may have been affected by oncological care delays. In an article published in 2020, it was recommended that resection of CRC occurred as soon as possible, depending on the availability of resources and the epidemics situation at the local level, as delaying resection could have a negative impact on survival.[6] Another study, done before the COVID-19 pandemic, demonstrated a negative impact on survival when the time between CRC diagnosis and its resection was increased.[7] In line with this, a systematic review published in 2020, which took into account studies from 2005 to 2020, demonstrated that a delay of 30 to 40 days in primary colon cancer resection was associated with shorter survival.[8] This systematic review also showed that, in rectal cancer cases, a time interval above 7 to 8 weeks between neoadjuvant treatment and surgery resulted in decreased survival.[8]

The main objective of the present research is to evaluate the impact of the COVID-19 pandemic in CRC patients care at HAM. The secondary objective is to describe the characteristics of the patients treated at HAM with this malignancy.

Materials and Methods

Data from electronic medical records of HAM (a reference cancer hospital in Salvador, Bahia, Brazil) were retrospective accessed. A list of adult patients with CRC was generated using the coding system (codes C18, C19, C20) of the International Classification of Diseases, 10th edition[9] (ICD-10). It was restricted to 2 periods of time: first year of COVID-19 epidemic in the state of Bahia (COVID period)[10] and the 12 months prior to the pandemic (pre-COVID period). The COVID period's list had 469 people, and the pre-COVID's one had 443.

Sample sizes were calculated separately using the tool "sample size for % frequency in a population (random samples)," available at the OpenEpi (open source) website.[11] Anticipating a frequency of 20% of metastatic disease[12] and with absolute precision of 5%, the sample size was 162 (COVID period) and 159 (pre-COVID period), with 95% confidence interval.

Sample sizes were also calculated considering both groups in the same analysis, using the tool "Sample Size: Cross-sectional, Cohort and Randomized Clinical Trials," also available on the OpenEpi website.[11] Considering a bilateral confidence level of 95%, power of 80%, with a "non-exposed-to-exposed rate" of 0.94 (443/469), an estimated percentage of metastatic disease in the "non-exposed group" of 20%,[12] and an odds ratio of 2, the results of sample size calculation were 177 people for the COVID group and 166 people for the pre-COVID group.

Research subjects' selection was aleatory. The aleatory number generation tool "Gerador de números aleatórios"[13] was used for this purpose.

Data was collected by a team of six people, using the RedCap software (Vanderbilt University)[14,15] authorized to Fiocruz Bahia. Data extraction form is available in the ►**Supplementary Appendix 1** (online only).

Inclusion Criteria

Adults that had their first appointment at HAM specifically due to CRC (either suspected or confirmed), with adenocarcinoma or carcinoma not otherwise specified histological types, at one of the following 2 periods of time: from March 18, 2020, to March 17, 2021,[10] or from March 1, 2019, to February 28, 2020.

Non-inclusion Criteria

Subjects that were misclassified with one of CRC's international codes; subjects that already concluded one step of oncological treatment at another institution, as oncological surgery, radiotherapy or systemic treatment (with the exception of those who previously received just a non-specialized surgical treatment, as for bowel obstruction).

Statistical Analysis

Descriptive analysis methods were used, as absolute numbers, frequencies, proportions, measures of central tendency and dispersion. This part of the statistical analysis was done with the same system used for data collection, the RedCap[14,15] authorized to Fiocruz Bahia. Comparative analysis between the groups was done with the STATA software (StataCorp LLC), version 18.0.[16] For this, the Pearson's Chi-squared test was applied.

Risks of this Research

Subjects' confidential data leakage. Measures to avoid it were taken, such as identification of research subjects with a new coding system, and use of a special data storage system, the RedCap.[14,15] Access to it was protected by an individual password for each member of the research team.

Research protocol was previously submitted to (and approved by) both ethics committees of the main institution, Fiocruz Bahia, and the coparticipant institution, HAM. The Brazilian Certificate of Presentation for Ethical Appreciation (CAAE) number is 66752823.5.0000.0040 (available for consultation at the "Plataforma Brasil" website[17]).

Table 1 Identification and sociodemographic data of the study sample

	Pre-COVID group	COVID group
Number of subjects	152	170
Age (years)		
Median	63	63
Percentile 25–75	54.00–73.25	53.00–75.75
Gender		
Female	78 (51.3%)	93 (54.7%)
Male	74 (48.7%)	77 (45.3%)
Skin color or ethnicity		
Yellow	0	0
White	11 (7.2%)	0
Native American	0	0
Brown	129 (84.9%)	144 (84.7%)
Black	7 (4.6%)	26 (15.3%)
Other	3 (3.3%)	0
Marital status		
Single	80 (52.6%)	63 (37.1%)
Married	53 (34.2%)	74 (43.5%)
Stable union	0	0
Separated	1 (0.7%)	0
Divorced	8 (5.3%)	12 (7.1%)
Widow(er)	11 (7.2%)	21 (12.4%)
No data	0	0
Place of birth		
Brazil – Bahia	139 (92.1%)	158 (92.9%)
Brazil – Other states	11 (7.3%)	12 (7.1%)
Brazil – Not specified	2 (1.4%)	0
Other countries	0	0
Location of residency		
Brazil – Bahia	152 (100%)	170 (100%)
Regional Health Nucleus (Bahia)[19] of residency		
Eastern*	78 (51.31%)	88 (51.76%)
Others	74 (48.68%)	82 (48.23%)
No data	0	0
Education		
Analphabet	8 (5.30%)	10 (5.88%)
Elementary school	85 (55.92%)	92 (54.11%)
High school	51 (33.55%)	59 (34.70%)
Bachelor's degree	6 (3.94%)	9 (5.29%)
Masters or Doctorate degree	0	0
No data	2 (1.31%)	0

Abbreviation: COVID, coronavirus disease 2019.
Notes: Results presented in absolute numbers (with respective percentages in parentheses). *Eastern Regional Health Nucleus (of Bahia), made up of 47 municipalities, including Salvador.[19]

Results

Sociodemographic and health data are shown in ►**Tables 1** and **2**.

As demonstrated in ►**Table 2**, there was an increase of 26.89% of metastatic disease at presentation from pre-COVID to COVID group (from 27.7–35.15%, after excluding subjects that were not possible to determine if metastatic or not at admission). Despite this numerical increase, the Pearson's Chi-squared test result was 2.00, Pr 0.15 (without statistical significance).

Discussion

We found that there was a numerical increase in the percentage of metastatic CRC patients at first presentation, during the first year of the COVID period, in comparison to the 12 previous months (but without statistical significance).

Table 2 Health data of the study sample

	Pre-COVID group	COVID group
Primary tumor site		
Cecum	6 (3.9%)	9 (5.3%)
Appendix	0	0
Ascending colon	9 (5.9%)	16 (9.4%)
Hepatic angle	4 (2.6%)	4 (2.4%)
Transverse colon	7 (4.6%)	11 (6.5%
Splenic angle	6 (3.9%)	1 (0.6%)
Descending colon	2 (1.3%)	3 (1.8%)
Sigmoid colon	17 (11.2%)	25 (14.7%)
Colon, with invasive lesion	3 (2.0%)	4 (2.4%)
Colon, unspecified	14 (9.2%)	13 (7.6%)
Rectosigmoid junction	18 (11.8%)	24 (14.1%)
Rectum	77 (50.7%)	71 (41.8%)
Colorectal, not specified	2 (1.3%)	0
Histological type		
Adenocarcinoma	149 (98.0%)	166 (97.6%)
Carcinoma, not specified	3 (2.0%)	4 (2.4%)
Cancer stage		
Metastatic	41 (27.0%)	58 (34.1%)
Non-metastatic	107 (70.4%)	107 (62.9%)
No data	4 (2.6%)	5 (2.9%)
Cancer stage		
Metastatic	41 (**27.7**%)	58 (**35.15**%)
Non-metastatic	107 (72.3%)	107 (64.85%)
Note: "No data" excluded		
Metastatic, but curable		
Yes	7 (17.1%)	4 (6.9%)
No	24 (58.5%)	43 (74.1%)
No data	10 (24.4%)	11 (19%)
Stage, if non-metastatic		
I	7 (6.5%)	3 (2.8%)
II	47 (43.9%)	40 (37.4%)
III	40 (37.4%)	37 (34.6%)
No data	13 (12.1%)	27 (25.2%)
Cancer treatment before HAM		
No	113 (74.3%)	131 (77.1%)
Yes, surgery	40 (26.3%)	39 (22.9%)
Life status in the last record		
Alive	122 (80.3%)	137 (80.6%)
Deceased	30 (19.7%)	33 (19.4%)

Abbreviations: COVID, coronavirus disease 2019; HAM, Hospital Aristides Maltez.
Note: Results presented in absolute numbers (with respective percentages in parentheses).

The pre-COVID group's characteristics represent the usual CRC population that seeks cancer care at HAM. In this group, genders were well balanced, with a median age of 63 years old, which is in line with international data.[18] There was a predominance of brown skin color and low level of education. Although the Hospital is located at the main city of the state, in the far east, there was a similar representation of patients that came from its Regional Health Nucleus (Eastern) and others. This demonstrates the scope of the hospital, which serves people from all parts of Bahia (which is divided in 9 regional health nuclei).[19] The high percentage of people with rectal cancer (half of the sample) calls for attention. This may be due to the fact that radiotherapy, which is frequently used during the treatment of this part of the bowel,[20] is available at HAM, but not at other health centers across the state. Representation of metastatic CRC in the pre-COVID group was higher than international data—27% in this versus 20% in USA data.[12] This may represent a lost opportunity to offer curative treatment, as, in most cases, CRCs are no longer curable when metastatic.[20]

The group of patients who came to HAM and had anatomopathological diagnosis established during the first

year of the COVID-19 epidemic in Bahia (COVID group)[10] presented similar epidemiological data in relation to the previous one. Nonetheless, there was an increase of 26.89% of people presenting at the metastatic stage (from 27.7% in the pre-COVID to 35.15% in the COVID group)—although the Pearson's Chi-squared test did not show statistical significance for this percentage increment. There are some hypotheses that may explain this finding. The sample size was inferior to the one that was calculated, when taking in consideration both groups together, which may have underpowered the study for this evaluation (of the difference of percentages between groups). Another important point is that the representation of metastatic patients since the beginning, in the control group (pre-COVID), was higher than expected (27.7%, instead of 20% according to international data[12]). This might have influenced the results too. If this higher percentage was used to calculate the sample size, it would be larger. That said, there is still the possibility that the current result (without statistical significance) reflects the reality.

A similar study done at another Brazilian hospital, which is a reference center in cancer treatment in the state of São Paulo, found an increase in the proportion of new cases of advanced CRC, between March and July 2020, compared with the same period in 2019.[21] This result reached statistical significance.

According to another study, that evaluated CRC screening programs in 29 countries, there was a decrease of CRC screening during the COVID-19 pandemic.[22] Moreover, this research states that, if measures to correct this problem are not implemented, this could lead to an increase in cases of CRC, as well as greater mortality from this malignancy.

The results of those two other studies[21,22] are in line with the findings of this present research, which highlights the importance of cancer care during special periods, such as the COVID-19 pandemic, as well as in the subsequent years.

Authors' Contributions

JPVMS: conceptualization, data curation, formal analysis, investigation, methodology, project administration, softwares, validation, visualization, writing, review and editing; MGR: conceptualization, methodology, project administration, supervision, validation, writing, review and editing; CTFA: investigation, view and editing; DRR: investigation, view and editing; DMA: investigation, view and editing; DSN: investigation, view and editing; MFPRR: investigation, view and editing;

Conflict of Interests

The authors have no conflict of interests to declare.

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