



Article title: The impact of COVID-19 pandemic in colorectal cancer screening, a systematic review.

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The impact of COVID-19 pandemic in colorectal cancer screening, a systematic review.

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ABSTRACT

Introduction: COVID-19 pandemic brought a major impact on cancer screening services, among those, colorectal cancer (CRC). This study evaluated the COVID-19 pandemic impact on the quantity of colonoscopies performed at different countries and its consequences. **Method:** Articles from PUB-MED, Scielo and LILACS databases were manually collected between April 25th and June 30th of 2021. Cross-sectional, observational and retrospective studies were selected; 11 articles remained applying the inclusion and exclusion criteria. **Results:** There was significant reduction of colonoscopies performed during the COVID-19 pandemic demonstrated in all of the studies. A 90% reduction was shown in 3 studies, the lesser reduction was demonstrated by Challine et al., (2021), which was 20%. Also was found a reduction on CRC diagnosis during that period, 72% and 22% at UK in Rutter et al. (2021) and Morris et al., (2021), respectively. At Italy the reduction was of 11,9% as Buscarini et al., (2021) shows. Lui et al., (2020) demonstrated a 37% reduction at Hong-Kong. **Conclusion:** The impact of COVID-19 pandemic in CRC screening and diagnostic services was significant, increasing the morbidity and mortality due to late diagnosis. Beyond that it was observed an increase on the diagnosis probability of colonoscopy during that period. More studies are required to fully understand the impact of the screening decreased capacity.

Key-words: Colonoscopy. Cancer. Diagnosis. COVID- 19.

INTRODUCTION

Colorectal cancer (CRC) is the third malignant neoplasm in terms of prevalence worldwide, it is also the second most diagnosed type of cancer [1], and shows high mortality when late diagnosed [2]. The prevalence between genders is similar, likewise the mortality rate caused by the disease; however, there is a long period of development between the initial carcinogenic event and the disease itself. The correct screening of CRC and the early treatment are essential, interfering directly in the prognosis. Thereby, there's possibility of cure in most of the cases with early diagnosis [3].

The worldwide health crisis caused by SARS-CoV pandemic brought, among other consequences, the under-reporting of malignant neoplasms and other chronic pathologies undiagnosed [4], especially because of issues related to variable periods of "lockdown" and also for the impossibility of health services to perform screening tests, making them limited or cancel-

ing [5]. The available resources for CRC screening were redirected for high diagnosis probability situations, like colonoscopy for symptomatic patients and CRC suspicious cases [6]. Besides, the isolation measures adopted around the world have restricted the outpatient routine screening, which was displaced for a secondary position [7].

Furthermore, stands out that, due to the critical period of pandemic, Part of the population has not reached out for diagnostic health services or follow-up procedures, which, consequently, may impact, in the short time, with increased morbidity and mortality due to late diagnosis of CRC [8]. Therefore, this study seeks, through a literature systematic review, to conclude if quantitatively there was a CRC diagnosis test (colonoscopy) reduction during specific pandemic period in several countries and the potential risk of increased morbidity and mortality due to that.

METHODS AND MATERIALS

This study consists of a systematic review of the literature, articles indexed in the electronic databases PUBMED, Scielo and Lilacs were manually collected in period from April 25th to June 30th. Cross-sectional observational retrospective studies were selected, using the following descriptors and keywords: (Colonoscopy OR Endoscopy) AND (Colorectal Neoplasms OR Colorectal Cancer) AND (Diagnosis) AND (COVID-19 OR SARS-CoV-2). The descriptors were obtained according to the Descriptors of Health Sciences (DeCs). Many of the articles bring data collected from surveillance health systems (electronic means of registration) of each country.

The pre-determined criteria for the article selection to compose this systematic review were the following:

1. Discuss the colonoscopies performing in critical periods of the COVID-19 pandemic compared to pre-pandemic periods;

2. Discuss the relation between the number of CCR diagnoses before and during the COVID-19 pandemic;
3. . Discuss the impact of the COVID-19 pandemic on morbidity and mortality due to CCR;
4. Articles with non-speculative data presentation;
5. Availability of the article in free form on the electronic databases;
6. Articles translated to at least one of the following languages: English, Portuguese or Spanish.

The exclusion criteria were also pre-determined for the search, being excluded:

1. Articles not freely available on the databases;
2. Editorial articles;
3. Articles published in other languages than those mentioned above;
4. Articles that did not comment on the performance of colonoscopies during the pandemic;
5. Articles with speculative data.

Based on the articles searches for the systematic review during the period of 25th of April to June 30: Passo Fundo, 2021, 82 articles on PUBMED platform were found; the same search was conducted on Scielo and Lilacs platforms resulting on 0 articles. Both searches were made using the descriptors and keywords cited. Of the 82 articles found on PUBMED platform, 21 were excluded for not being available for free, 4 articles were excluded for being editorial and 24 articles were excluded after reading the title for not filling the pre-established requirements. 33 articles had their abstract read, 15 of those

were excluded for not filling the eligibility criteria and the other 18 articles were selected as potentially relevant. The articles were read and independently evaluated by two different reviewers, in order to select those who were excluded or included. In case of divergence of opinions between the two reviewers, a third reviewer was consulted. The 18 articles selected were carefully read and analyzed, of those, only 11 fill the pre-established inclusion criteria and compose this systematic review, the other 7 were excluded.

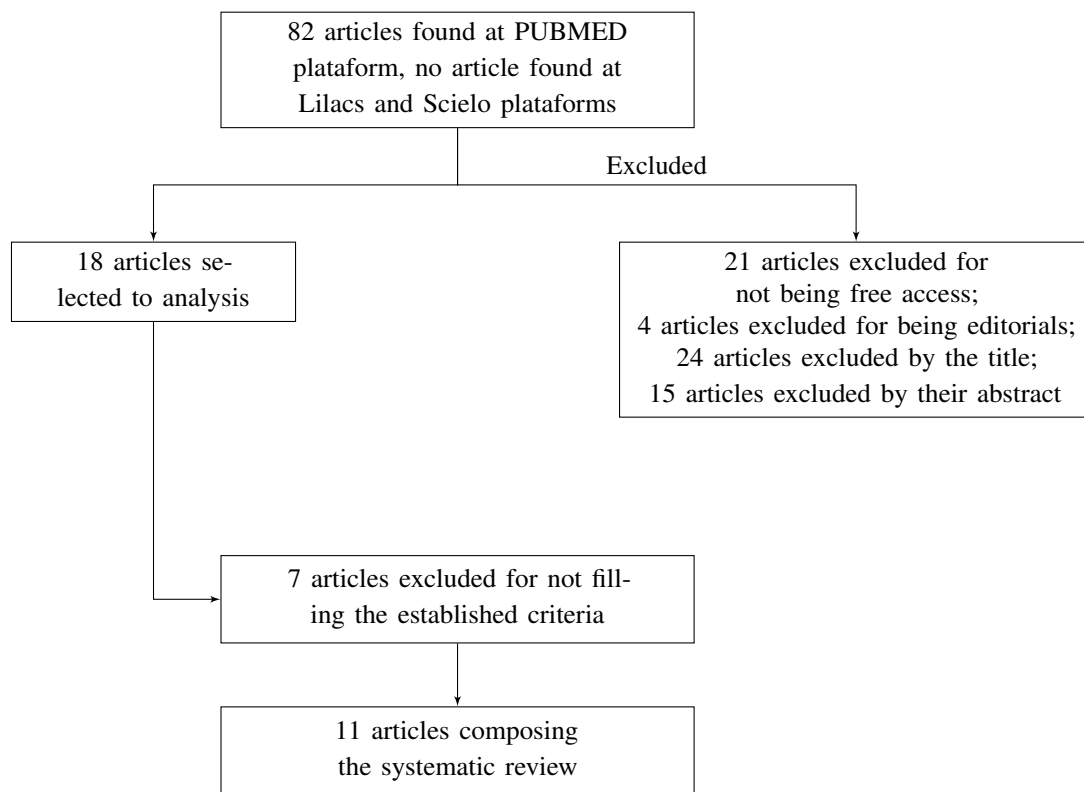


Figure 1 — Flowchart of the articles selection process, by the authors.

RESULTS

Among the 11 analyzed articles, 9 talk about the percentage of colonoscopies performed in relation to the expected amount for the period, composing category 1.1 presented at Table 1. The studies number 1 [5] and 3 [9] [Figure 2] were conducted in United Kingdom

and presented a 90% reduction (march to may of 2020) and 46% (april to october of 2020), respectively. Similarly, article number 2 [10] shows a 45% reduction (march to may of 2020) of the colonoscopies performed in Netherlands. The study number 5 [11] was conducted at Hong-

Kong, and presents a 58,8% reduction (january to march of 2020). Likewise, at United States of America (USA), the article number 7 [1] shows a 85% reduction (january to april of 2020), and in the article 10 [12], 90% (march to may of 2020) [Figure 3]. At France, studies number 8 [13] and

9 [14], [Figure 4], present a 20% (march to october of 2020) and 68,8% reduction (january to october of 2020) respectively. Article number 11 [15] shows a 90% reduction (march to april of 2020) in India.

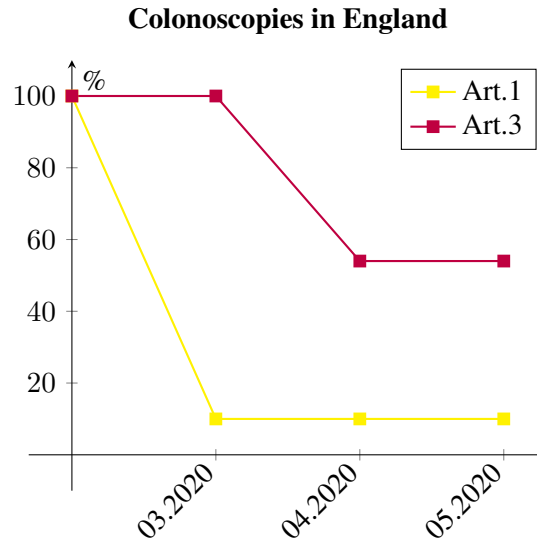


Figure 2 – The "y" line represents the percentage of colonoscopies performed in relation to the expected amount in the months, represented at "x" line, with data collected from the researched articles. [Art.1: RUTTER, Matthew D. *et al.*, 2021; Art.3: MORRIS, Eva J.A. *et al.*, 2021;], by the authors.

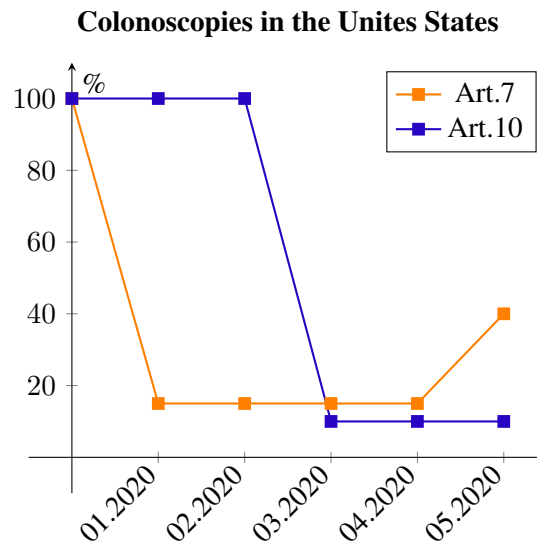


Figure 3 – The "y" line represents the percentage of colonoscopies performed in relation to the expected amount in the months, represented at "x" line, with data collected from the researched articles [Art.7: KADAKUNTLA, Anusri *et al.*, 2021; Art.10: PATEL, Shreya *et al.*, 2021], by the authors.

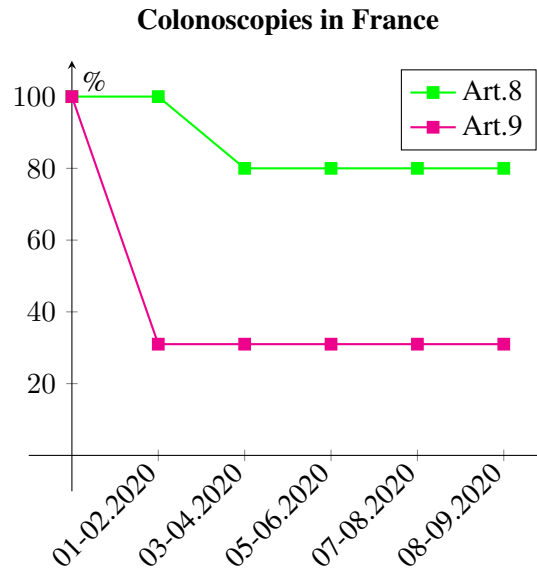


Figure 4 – The "y" line represents the percentage of colonoscopies performed in relation to the expected amount in the months, represented at "x" line, with data collected from the researched articles [Art.8: CHALLINE, Alexandre *et al.*, 2021; Art.9: MEYER, Antoine *et al.*, 2021], by the authors.

Category number 1.2 was contemplated with 10 of the 11 researched articles, it is about the weekly average of colonoscopies reduction, data obtained using the absolute number of non performed colonoscopies in relation to the expected number for the period, divided by the number of whole weeks during the analyzed period. Study number 9 [14] presented 10380,6 colonoscopies non performed per week, and in article number 8 [13], also performed at France, it was found a reduction average of 5612,9. At USA it was obtained the reduction averages of 183,2; 3518,5 and 160 in the studies number 6 [16], 7 [1] and 10 [12], respectively. The articles 1 [5] and 3 [9], performed at United Kingdom, presented 11346 and 4796,9 least colonoscopies per week, respectively. In Netherlands the obtained average was of 734,4; shown in

study number 2 [10]. Article number 5 [11] demonstrated that 699 colonoscopies weren't performed weekly at Hong-Kong. At India the reduction weekly average, retracted by study number 11 [15], was of 41,7.

Another analyzed aspect was the colorectal cancer diagnosis reduction percentage during the researched period [Figure 5], nominated as 2.1 category; presented in 4 articles. In the United Kingdom a 72% (march to may of 2020) and 22% (april to october of 2020) reduction was obtained at studies number 1 [5] and 3 [9], respectively. At Italy 11.9% (january to october of 2020) fewer colorectal cancer diagnosis were made according to study number 4 [17]. In article number 5 [11], made at Hong-Kong, the reduction was of 37% (january to march of 2020).

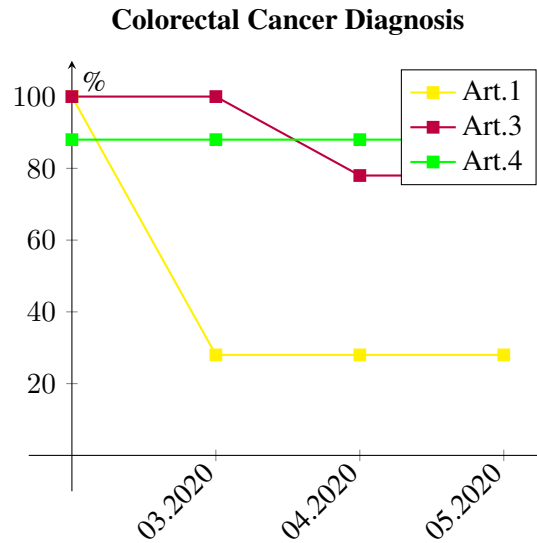


Figure 5 – The "y" line represents the percentage of colorectal cancer diagnosis performed in relation to the expected amount in the months, represented at "x" line, with data collected from the researched articles. [Art.1: RUTTER, Matthew D. *et al.*, 2021; Art.3: MORRIS, Eva J.A. *et al.*, 2021; Art.4: BUSCARINI, Elisabetta *et al.*, 2021.], by the authors.

Three articles bring data of the category 2.2, the monthly reduction average of colorectal cancer diagnosis; obtained from the division of the predicted number of non performed colorectal cancer diagnosis, by the number of whole months of the period. The most expressive number was obtained in study number 6 [16], 4700 non performed colorectal cancer diagnosis monthly in USA. Likewise in Italy, the reduction monthly average was of 57,4 accordingly to study number 4 [17]. In article number 3

[9] it was found a monthly reduction average of 500 colorectal cancer diagnosis in United Kingdom.

Category number 3 reflects the colorectal cancer patients morbidity/mortality increase percentage, which was addressed only in study number 7 [1], performed in USA, showing a 16,6% increase between january and april of 2020.

All categories analyzed had their data exposed and compiled at Table 1.

Author	Year	Country	ID	1.1	1.2	2.1	2.2	3
RUTTER, Matthew D. <i>et al</i>	2021	UK	1	90%	11346	72%	-	-
LANTINGA, Marten A. <i>et al.</i>	2020	NL	2	45%	734,4	-	-	-
MORRIS, Eva J.A. <i>et al.</i>	2021	UK	3	46%	4796,9	22%	500	-
BUSCARINI, Elisabetta <i>et al.</i>	2021	IT	4	-	-	11,9%	57,4	-
LUI, Thomas K.L. <i>et al.</i>	2020	HK	5	58,8%	699	37%	-	-
GORIN, Sherri N.Sheinfeld <i>et al.</i>	2021	US	6	-	183,2	-	4700	-
KADAKUNTALA, Anusri <i>et al.</i>	2021	US	7	85%	3518,5	-	-	16,6%
CHALLINE, Alexandre <i>et al.</i>	2020	FR	8	20%	5612,9	-	-	-
MEYER, Antoine <i>et al.</i>	2021	FR	9	68,6%	10380,6	-	-	-
PATEL, Shreya <i>et al.</i>	2020	US	10	90%	160	-	-	-
RAJ KUMAR, Barath <i>et al.</i>	2020	IN	11	90%	41,7	-	-	-

Table 1 — Results table, exposing data of the categories 1.1: percentage of colonoscopy reduction, 1.2: weekly average of colonoscopy reduction, 2.1: percentage of colorectal cancer diagnosis reduction, 2.2: monthly average of colorectal cancer diagnosis reduction, 3: increase in mortality or morbidity [ID: identification number, UK: United Kingdom, NL: Netherlands, IT: Italy, HK: Hong-Kong, US: United States, FR: France, IN: India], by the authors.

DISCUSSION

The new coronavirus, later called Covid-19, had its first reports of human infection disclosed in December 2019 in Wuhan, Hubei Province, China [18]. From this moment on, health authorities around the world and even the World Health Organization (WHO) monitored the infection spread [19]. In March 2020, however, the spread of the virus to different regions of the planet, its rapid transmissibility and potential for morbidity and mortality led to the sanitary emergency decree and the SARS-CoV-2 infection was considered a pandemic on March 11, 2021 [19]. This way, it became a major obstacle for health services worldwide. Due to that, many elective procedures and screening exams were limited, postponed or even canceled, including colonoscopies, with great impact on CCR screening [5]. Thus, this review aims to analyze the impacts of the Covid-19 pandemic on colonoscopies, diagnosis, mortality and morbidity of CCR, by reviewing articles available in databases, composing a systematic review.

Analyzing data from colonoscopies per-

formed during the pandemic, according to Rutter et al., (2021)[5], Patel et al., (2021)[12] and Raj Kumar et al., (2020)[15], there was a 90% reduction in the peak of the pandemic, occurring respectively in the United Kingdom, the USA and India, and the most significant restriction occurred in the United Kingdom, with a reduction of 11.346 weekly colonoscopies compared to January and March 2020. On the other hand, Challine et al., (2021)[13] reported an average decrease of 20% in the Netherlands, but still with a significant number of 5.612,9 fewer weekly colonoscopies and a peak reduction of 85% in April, at the critical period pandemic. In addition, in France, according to Meyer et al. (2021)[14], there was a reduction of approximately 10.380,6 weekly colonoscopies, adding up to 250.000 fewer colonoscopies in a period of 6 months, representing a decrease of 68.6%. Consequently, although disparities in numerical variables about the decrease in colonoscopies, all studies agree on the categorical variables shown in the table of results demonstrating there is a sig-

nificant decrease in the number of colonoscopies performed, reported in all studies analyzed in the systematic review.

It is important to emphasize that all the authors of the articles included demonstrated a reduction in the number of colonoscopies in the period of the Covid-19 pandemic compared to the previous period, varying only in the percentage and period of greatest impact. Certainly, the lack of uniformity in the data is due to the time difference between the peak of the pandemic in each location. It is also worth pointing that SARS-Cov-2 had repercussions of different magnitudes in different regions, resulting in an unequal impact on CCR screening services, contributing to the heterogeneity of the data.

In addition, a large impact on the number of CCR diagnoses performed was also demonstrated; according to Morris et al., (2021)[9] there was a reduction of about 3,500 diagnoses between April and October 2020 in England, representing a monthly reduction of 500 diagnoses, 22% less than in the previous year. Similar to this, Buscarini et al. (2021)[17] described a 11.9% reduction, about 57.4 least monthly diagnoses, totaling 574 unfinished diagnoses in Italy in the period from January to October 2020, while Gorin et al., (2021)[16] in the USA, presume a loss of 4,700 monthly diagnoses, totaling 18,800 undone diagnoses from March to June 2020. In the same way, in Hong Kong, Lui et al., (2020)[11] estimated a 37% reduction in the diagnosis of CCR, on the other hand, Rutter et al., (2021)[5] estimated a more expressive rate of decrease in diagnoses, reaching 72% due to the impact of Covid-19 on colonoscopy services. Consequently, a significant number of diagnoses have been compromised by the interruption of CCR screening services.

Given the scenario of the reduction in the number of colonoscopy exams, there was

also an increase considered likely in the morbidity and mortality of patients with CRC. Gorin (2021)[16] observed more advanced stages of this pathology at the time of diagnosis, caused by the delay in performing colonoscopies. In the same way, Kadakuntla et al., (2021)[1], in the USA, estimates a 16.6% increase in mortality over the next 5 years, with a significant increase in the diagnosis of advanced-stage cancer. Thus, Challine et al. (2021)[13] expose that, due to the reduction in the number of surgical procedures for the treatment of CRC, an interruption of interventions for just 3 months would lead to an increase of about 5,000 deaths in the United Kingdom.

Besides, according to Rutter et al., (2021)[5], Latinga et al., (2021)[10] and Lui et al., (2020)[11] there was also an increase in the rate of detection of cancer by diagnosis, due to the reduction in the performance of colonoscopies, the exams carried out are now more selectively aimed at people at higher risk of malignancy. Thereby, according to the authors, the probability of diagnosis of CCR by colonoscopy increased by 4.7%, 0.8%, and 4.26%, respectively, compared to previous years.

Given the exposed, and despite the expressive data found, in agreement, in the studies analyzed, there is no consensus on the exact dimension of the impact of the Covid-19 pandemic on CCR. So, what emerges from the present review are variable data that corroborate the reduction in the number of colonoscopies due to the repercussion of the pandemic in health services worldwide. Therefore, this limitation in the performance of colonoscopies tends to have a great impact on the diagnosis, mortality and morbidity of CRC, also evidenced by the review of the studies. Thus, only with more time and the maturity of the data, it will be possible to have the real proportion of the effect of Sars-Cov-2 on morbidity and mortality due to CCR.

CONCLUSION

There was a data concordance between all studies included on the systematic review, all the articles found there was a significant reduction in CRC diagnosis during critical periods of COVID-19 pandemic in many countries.

This fact, as observed, resulted in least colonoscopies during the studied periods. The impact of the reduction of CRC diagnoses during the pandemic cannot be measured yet, but it is presumably that there will be later diagnoses, especially for asymptomatic patients, reducing their chances of treatment and, therefore, cure, after this change in the pattern of screening for

this neoplasm, a fact that was addressed in this review.

More research is required for full understanding and dimension of the transpandemic phenomenon impact of reduce CRC screening capacity.

Furthermore, one of the facts that was observed in this study, was that symptomatic patients kept performing tests for the diagnosis of CRC increasing the probability of diagnosis (CRC diagnosis positive predictive value when performing colonoscopy during the pandemic. This is a fact to be explored in further studies.

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