



Impact of the COVID-19 Pandemic on Colorectal Cancer Screening: a Systematic Review

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Abstract

Background After the World Health Organization (WHO) announcing about global pandemic of COVID-19 in March 2020 and relocation of health care resources for controlling this infection, cancer screening programs especially colorectal cancer (CRC) have been suspended in many countries. According to GLOBOCAN 2020 data, CRC is the third prevalent and second deadliest cancer in the world. So, early detection through screening is essential to reduce the mortality associated with this cancer. The present study was designed to investigate the impact of COVID-19 pandemic on colorectal cancer screening.

Methods and Materials A comprehensive search performed on June 2021 in various databases, including Medline, Web of Science, and Scopus. Keywords such as “Early Detection,” “Cancer,” “Cancer Screening,” “Cancer Screening Tests,” “Coronavirus Disease-19,” “COVID 19,” “Coronavirus Disease,” “SARS-CoV-2 Infection,” “SARS-CoV-2,” “2019-nCoV,” “coronavirus, 2019 Novel,” “SARS COV 2 Virus,” “Severe Acute Respiratory Syndrome Coronavirus 2,” “COVID-19,” “COVID-19, Coronavirus Disease 19,” “SARS Coronavirus 2,” “Colorectal neoplasm” and “Colorectal Cancer” were used individually or in combination to search. All articles were entered into Endnote X7 software that remove duplicates. Then, studies were first selected by title and then by abstract and at the end full texts were investigated.

Results Of the 850 identified studies, 25 were identified as eligible. The results of studies show that in general, colorectal cancer screening has decreased from 28 to 100% in different countries and at different times after the onset of the COVID-19 pandemic. During this period, only 2 to 2.5% of hospitals and screening centers with 100% capacity continued to operate, and more than 77% of them limited their activities to less than 10% of their normal capacity. Also, completion of colonoscopies requiring examination showed a decrease of 65.7%, surveillance colonoscopy showed a decrease of 44.6 to 79%, prescription colonoscopy decreased 60 to 81%, and referrals to colonoscopy showed a 43% decline. However, emergency colonoscopy shows a 2 to 9% increase. The use of the Fecal immunochemical test (FIT) test is also generally declining but is increasing in areas used as a colonoscopy alternative.

Conclusions Considering that the reduction in colorectal cancer screening following COVID-19 pandemic is due to the restrictions imposed for the high prevalence of COVID-19 disease and the lack of referrals due to the fear of developing COVID-19 infection; compensating for the decline and preventing the continuation of this decreasing trend requires serious and effective interventions to maintain the capacity of screening services during the COVID-19 crisis, increase the capacity of screening centers during the lifting of restrictions and reduce fear in the public.

Keywords Screening · COVID-19 · Colorectal cancer · Systematic review

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Introduction

Following the diagnosis of an acute respiratory infectious disease called SARS-COV-2 in early November 2019 in Wuhan, China, and the World Health Organization (WHO) announcing a global pandemic in March 2020 [1], the relocation of staff and health care resources for addressing the pandemic has become a necessity; therefore, cancer

screening programs for asymptomatic patients have been suspended in many countries [2]. Thus, preventive care services including colorectal cancer (CRC) screening in health systems have seen a dramatic decline worldwide [3].

Primary prevention is the main strategy to reduce the growing global burden of colon cancer [4]; however, it should be noted that colorectal cancer, with a mortality rate of 9.4%, is the second cause of cancer death in the world after lung cancer and the third leading cause of cancer death in men and women. It is also the third most common cancer among men and the second most common cancer in women [5].

More than 1.9 million new cases and 935,000 deaths from this cancer occurred in 2020 [5]; therefore, early detection through routine screening is also necessary to improve the mortality rate of this cancer. Since the dramatic reduction in cancer screening due to the Covid-19 pandemic has had a significant impact on the diagnosis of cancer, especially colon cancer, diagnosis at advanced stages or later stages, delayed onset of treatment, decreased quality of life, and increased mortality are associated problems of the COVID-19 pandemic [6].

Yong et al. reported that a 6-month delay in the initial screening of colorectal cancers could increase the incidence of this cancer to 2200 and the death rate to 960. Even when screening resumes, longer intervals and reduced screening rates increase more cancer deaths [7]. A study in the UK also showed that the diagnosis of colorectal cancer was significantly reduced (62%) after the onset of the COVID-19 epidemic. It had also the most delay in diagnosis compared to other cancers [8].

Delays in colon cancer surgery have also been shown to be associated with lower survival [9, 10]. Issaka et al. showed that increasing the use of fecal immunochemical test (FIT) from 15 to 22% over a 3-year period to compensate for the decrease in COVID-19 colonoscopy screening was associated with 655,825 more screening and 2715 colon cancer which 72% were diagnosed in the early stages [11]. Therefore, considering the effects of the COVID-19 epidemic on colorectal cancer screening and the importance of knowing about the reduction in the number of screening on predicting the consequences in health planning, The present study was designed to investigate the impact of COVID-19 pandemic on colorectal cancer screening.

Methods and Materials

Search Strategy

This systematic review was conducted in accordance with the Systematic Review Checklist (PRISMA) and by searching for related articles in three databases of PubMed/

MEDLINE, Scopus, and Web of Science, using the following keywords from 2020 to 2021: “Early Detection,” “Cancer,” “Cancer Screening,” “Cancer Screening Tests,” “Coronavirus Disease-19,” “COVID 19,” “Coronavirus Disease,” “SARS-CoV-2 Infection,” “SARS-CoV-2,” “2019-nCoV,” “coronavirus, 2019 Novel,” “SARS COV 2 Virus,” “Severe Acute Respiratory Syndrome Coronavirus 2,” “COVID-19,” “COVID-19, Coronavirus Disease 19,” “SARS Coronavirus 2,” “Colorectal neoplasm” and “Colorectal Cancer” The AND, OR, and Mesh terms operators were also used to improve the search result. Also a manual search was performed in reputable scientific journals to find articles related to the full text.

Inclusion and Exclusion Criteria

All types of observational studies, addressing the impact of COVID-19 pandemic on colorectal cancer screening, published in the English language were included in the review. Studies that did not address the specific effects of coronavirus on cancer screening, or included patients diagnosed with cancer before the epidemic or patients with a symptomatic diagnosis of early cancer, were excluded. Review studies, case reports, letters to editors, commentaries, and reports were also excluded.

Screening and Selection of Studies

All articles searched in the databases were entered into Endnote X7 software. After removing duplicates, studies were first selected by title and then by abstract according to the relevance of the titles and abstracts with the purpose of the study. Their eligibility was then verified by reviewing the full text. Articles that evaluated every aspect of colorectal cancer screening during the COVID-19 epidemic were included in the analysis.

Data Extraction

To extract the data, the prepared checklist was used and the following information was extracted from each study: surname of the first author, year of publication, country of study, type of study, sample size, age and sex of the target group, period of evaluation, and the main findings.

Quality Assessment

“Adapted Newcastle–Ottawa Quality Assessment Scales” checklist was used to evaluate the quality of the articles in this review. (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp). This tool consists of 3 separate sections: selection, comparison, and conclusion. Studies were scored based on overall scores and divided into 3 categories: good, moderate, and poor.

Result

Selection of Studies

The search result in the databases based on the intended keywords included 850 articles, which after deleting duplicates (403 articles), according to the title and abstract of the remaining articles, 382 articles were deleted. Afterward, a thorough review of the remaining articles was performed; then, 14 other articles were excluded due to publication in a language other than English [4 articles], a letter to the editor [4 articles], etc. Subsequently, the full text of the articles reviewed, 7 articles were deleted due to lack of access to the full text or inconsistency with the objectives of the study, and finally, 25 articles were analyzed in this systematic review (Fig. 1).

Characteristics of Studies and Quality Assessment

The eligible articles that were considered for analysis were divided into the following groups: colonoscopy and sigmoidoscopy screening in general [12–28], surveillance colonoscopy [12, 13, 18], prescribed colonoscopy [12, 13, 18, 24], emergency colonoscopy [12, 14], non-invasive methods [16, 18], referrals to screening colonoscopy [29], completing of screening colonoscopies that needed to be reviewed [12], responding to recalls [12, 24, 30], participating in screening program [31], sales of laboratory materials needed for colonoscopy [32], reducing the capacity of screening centers [33, 34], changing the screening method and admission process in the screening centers [34, 35]. Based on the review using the checklist, 22 articles/studies were of good quality and 3 articles/studies were of medium quality. The results are summarized in Table 1.

Study Results

Colonoscopy and Sigmoidoscopy Screening in General

In a study by Wassie et al. comparing the number of colonoscopies in Australia in two similar time periods (April–June) in 2019 and 2020, they found that during the period in 2020, the total number of completed colonoscopies decreased by 51.1% ($n = 569$) compared to the same months in 2019 ($n = 1164$), with the largest decrease of 88% observed in April 2020, and colonoscopy at the Noarlunga Health Service (NHS) in April 2020 reached to zero [12].

A study by Tinmouth et al. in Canada that compared colonoscopy cases from March to June 2020 with the same

time period in 2019 found that total colonoscopy cases decreased by 60% in 2020 compared to 2019, from 107,034 cases in 2019 to 36,029 cases in 2020 [13].

Shinkwin et al. in their study in the UK showed that the average number of diagnostic endoscopy cases (colonoscopy and flexible sigmoidoscopy) performed per month for 2020 compared to 2018 and 2019 shows a significant decrease so that the total number of diagnostic colonoscopies performed from February 2020 (coinciding with the beginning of the National restrictions) has significant decline observed that reached a peak in April 2020. Despite the gradual increase in diagnostic endoscopy cases, this number has not yet reached the number observed in 2019 and 2018 so that the average number of diagnostic endoscopy cases in April 2020 compared to April 2018 and 2019 decreased by approximately 28% [14].

A study by Rutter et al. in the UK compared the activity of endoscopic centers and the diagnosis of cancer in the three periods, before COVID-19 (6 January 2020 to 15 March), transition period (16–22 March), and the period influenced by COVID-19 (23 March–31 May). They found that, compared to the pre-COVID-19 period, the average number of low colonoscopy cases by 90%, flexible sigmoidoscopy by 91%, and esophagogastroduodenoscopy (OGD) by 86% has decreased per week and the total reduction for all methods was 87.8%. In contrast, this reduction was only 44% for endoscopic retrograde cholangiopancreatography (ERCP) procedures [15].

Myint et al. in a study conducted in the USA, found that in the period before COVID-19 (1/29/2020–3/17/2020), the average screening test was 382.4 ± 54.8 ; colonoscopy ($222.6.0 \pm 33.0$ per week) and FIT (154.0 ± 25.2 per week) were most screening tests performed per week, while during the stop period (3/18/2020–5/4/2020), the total average decreased to 74.3 ± 47.1 per week ($p < 0.01$), as colonoscopy showed the most severe decline (11.4 ± 11.1 ; $p < 0.01$). They also found that in the months following the resumption of elective endoscopy (5/5/2020–10/27/2020), overall use of the screening test increased significantly equal to the pre-epidemic rate ($346.8\% \pm 93.4$; $p = 0.53$). However, it did not correspond to pre-pandemic performance (174.2 ± 47.1 ; $p < 0.02$) [16].

In a study by Longcroft-Wheaton et al. in the UK, after comparing the activity of endoscopic centers in 8 weeks of spring, summer, and autumn in 2019 and the first 6 weeks of the COVID-19 crisis, they found that the average colonoscopy declined from 86 cases per week to 12 cases and the average of flexible sigmoidoscopy decreased from 108 cases per week to 10 cases. Also, the endoscopic procedures required to diagnose colorectal cancer have been reduced from 47 to 12 per week [17].

Lantinga et al. in the Netherlands saw a 45% reduction (from 12,219 to 5609) in colonoscopy cases by comparing

Table 1 The characteristics of articles included in a systematic review of screening delay of colorectal cancer in the COVID-19 pandemic

First author (year)	Place (country)	Sample size	Type of study	Age	Sex	Comparison date	Examined indicators	Result of quality assessment
Wassie et al. (2021) [12]	South Australia	1760: 1164 pre-COVID-19 and 596 after COVID-19	Retrospective analysis	All ages	Both	April–June 2020 vs the same time in 2019	<ul style="list-style-type: none"> - Total number of colonoscopies: 51.1% decrease (596 vs. 1164) - Completed colonoscopies for surveillance: 65.6% decrease (32.0% ($n=182$) vs. 45.5% ($n=530$)) - 3-month delay for surveillance colonoscopies: 68.0% (198/291) vs. 52.9% (162/306); $P<0.001$ - > 6-month delay for surveillance colonoscopies: 46.1% (134/291) vs. 19.3% (59/306); $P<0.001$ - Nonresponses percent to surveillance recall letters in patients ≥ 75 years: 51.6% vs. 25.6%, $P=0.03$ - Proportion of urgent colonoscopies: increase from 71.2% (828/1163) to 78.2% (445/569) - Number of nonurgent colonoscopies: 63.0% reduction, $P=0.002$ (from 335 to 124) - Median time taken to respond to the recall colonoscopy letter: 18 days, IQR 11–41 days vs. 21 days, IQR 12–48 days; $P=0.23$ 	Good
Timmouth et al. (2021) [13]	Canada	143,063: 107,034 before COVID-19 and 36,029 after it	Retrospective cohort	All ages	Both	March–June 2020 vs. the same time in 2019	<ul style="list-style-type: none"> - Decrease by colonoscopy procedures: Surveillance: 182(32.0%) vs. 530(45.5%); $p<0.001$ - Positive FIT: 140 (24.6%) vs. 233 (20.0%); $p=0.03$ - Symptomatic: 204 (35.9%) vs. 349 (30.0%); $p=0.01$ - Abnormal abdominal radiology: 32 (2.8%) vs. 32 (5.6%); $p=0.003$ - gFOBT+/FIT+: 8% increase (4758 vs. 4390) - Symptomatic colonoscopy: 56% decrease (19501 vs. 44651) - Surveillance colonoscopy: 79% decrease (6033 vs. 28,107) - Average-risk screening: 81% decrease (3603 vs. 19,031) - All colonoscopies: 66% decrease (36,029 vs. 107,034) 	Good

Table 1 (continued)

First author (year)	Place (country)	Sample size	Type of study	Age	Sex	Comparison date	Examined indicators	Result of quality assessment
Shinkwin et al. (2021) [14]	UK	811: 272 in 2020; 539 in 2019 and 2018	Retrospective cohort	All ages	Both	March and June 2020 compared with previous years	- Emergency presentation: 36.0% vs. 28.6%; $p = 0.03$	Good
Rutter et al. (2021) [15]	UK	39,790: 4312 COVID impacted and 35,478 pre-COVID	Retrospective cohort	All ages	Both	23 March 2020–31 May 2020 vs. 6 January 2020–15 March 2020	- Average number of all procedures per week: 87.8% reduction (4312 vs. 35,478) - Average number of colonoscopy per week: 89.7% reduction (1300 vs. 12,646) - Average number of flexible sigmoidoscopies per week: 91.4% reduction (632 vs. 7335) - Average number of OGD per week: 86.0% reduction (2091 vs. 14,985) - Average number of ERCP per week: 43.7% reduction (289 vs. 513)	Moderate
Myint et al. (2021) [16]	USA		Cross sectional	All ages	Both	Endoscopy cessation period (3/18/2020–5/4/2020) vs. before the cessation (1/29/2020–3/17/2020)	- Number of total screening tests per week: 74.3 ± 47.1 vs. 382.4 ± 54.8 ; $p < 0.01$ - Number of colonoscopies per week: 11.4 ± 11.1 vs. 223.8 ± 33.3 ; $p < 0.01$ - Number of FIT test per week: 60.6 ± 52.7 vs. 154.0 ± 25.2 ; $p < 0.02$	Good
Morris et al. (2021) [36]	England			All ages	Both	in April, 2020 compared to the monthly average in 2019	- Monthly number of 2-week referrals for suspected cancer: 63% (95% CI 53–71) reduction (from 36,274 to 13,440) - Number of colonoscopies: 92% (95% CI 89–95) reduction (from 46,441 to 3484)	Good
Miller et al. (2021) [29]	UK	422: 202 males and 220 females		Median age 64 years	Both	1 April to 31 May 2020 vs. same times in 2017–2019	- Primary care referrals: 43% reduction (1071 referrals expected reducing to 609) - Median time to first test: 14 days (IQR 10–18 days) - Routine referrals: 64% reduction (from 581 to 211) - Urgent referrals: 79% reduction (from 1071 to 609) - USOC referrals: 40% increase (from 235 to 329)	Good
Meyer et al. (2021) [32]	France	-	-	-	Both	February 17 to September 13, 2020, vs. same time in 2108 and 2019	- Colonoscopy preparations: 68.6% fewer than expected; 83,045 vs 181,826	Good

Table 1 (continued)

First author (year)	Place (country)	Sample size	Type of study	Age	Sex	Comparison date	Examined indicators	Result of quality assessment
Longcroft-Wheaton et al. (2021) [17]	UK	-	Service evaluation	All ages	Both	Over 8-week periods in spring, summer, and autumn 2019 vs. the first 6 weeks COVID-19 crisis	- Number of colonoscopies per week: decrease from 86 to 12 - Number of Flexible sigmoidoscopies per week: decrease from 108 to 10 - Endoscopic procedures/week required to diagnose a CRC cancer: decrease from 47 to 12	Good
Lantinga et al. (2021) [18]	Netherlands	-	Retrospective analysis	-	Both	March 15 to June 25 in 2020 vs same time in 2019	- Number of colonoscopies: 45% decrease (from 12,219 to 5609) - Surveillance colonoscopy: declined from 35.0% (95%CI 33.9–36.1) in 2019 to 19.4% (95%CI 18.1–20.8) in 2020; $P < 0.001$ - Hematochezia indications for colonoscopy: declined from 38.4% (95%CI 36.7–40.1) in 2019 to 26.7% (95%CI 25.7–27.8) in 2020; $P < 0.001$	Good
Lahat et al. (2021) [19]	Israel	-	-	All ages	Both	January–March in 2020 vs. same time in 2019 and 2018	- Colonoscopy and sigmoidoscopy: 52–57% reduction in 2020 (464 vs. 955 and 1058 on 2018 and 2019; $p < 0.0001$)	Good
Koczkodaj et al. (2021) [31]	Poland	-	-	All ages	Both	between January and April 2020 vs. same period in 2019	- Colonoscopy coverage and participation rate (last available month data): 7.09% in 2020 vs. 13.16% in 2019 - Number of oncology diagnosis and treatment cards (ODaTCs): 135 less cards (from 3583 in July 2019 to 3448 in July 2020) - Colonoscopy participation rate in April and May 2020 vs. same time in 2019: 4.93% vs. 17% - Number of patients with referrals to the fast path of oncological diagnosis and treatment: 51% (2161) decrease	Good
Kirac et al. (2021) [20]	Croatia	-	Cross sectional	All ages	Both	From August 1, 2019, until August 31, 2020	- Number of colonoscopies in August 2019 vs. April 2020: 82% decrease (50 vs. 9)	Good
Gurney et al. (2021) [21]	New Zealand	-	-	All ages	Both	2020 vs. 2019	- Gastrointestinal endoscopies: 75% sharp decline during late March and April 2020 (from 5734 to 1426)	Good

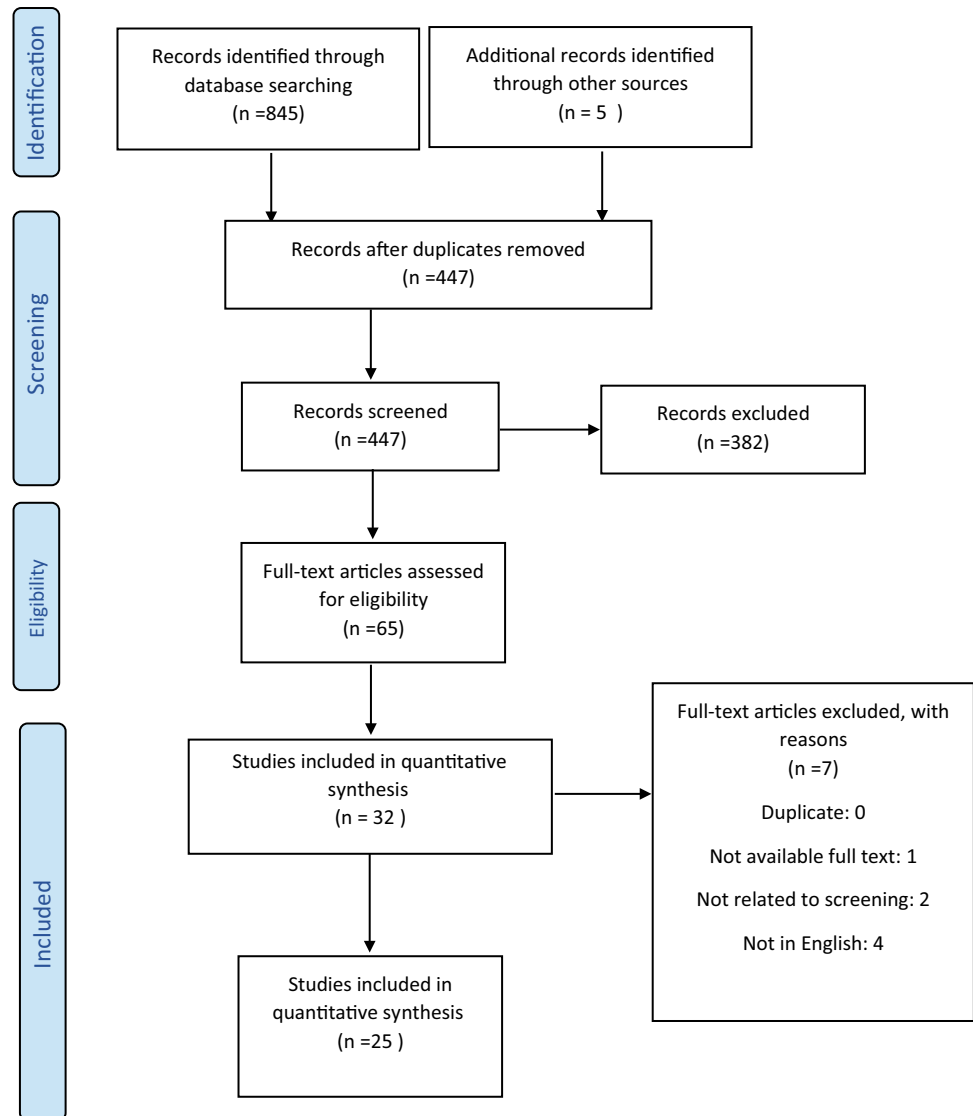
Table 1 (continued)

First author (year)	Place (country)	Sample size	Type of study	Age	Sex	Comparison date	Examined indicators	Result of quality assessment
Gorin et al. (2021) [22]	USA	-	-	All ages	Both	Between March 19 and May 9 in 2017 and 2020	- Colonoscopy screening: decreased from 1291 to 8	Good
Boyle et al. (2021) [33]	England and Wales	-	National survey	All ages	Both	In mid-April 2020	Reduction in diagnostic colonoscopy activity by: - 0–10% of usual capacity: 95 (77%) hospitals; - 11–70% of usual capacity: 26 (21%) hospitals; - 71–100% of usual capacity: 2 (2%) hospitals	Moderate
D'Ovidio et al. (2021) [30]	Italy	Case = 60; control = 238	Retrospective controlled cohort	All ages	Both	9th March–4th May 2020 vs. same time in 2019	- Invited patients underwent endoscopy: 74.8% decrease (from 238 to 60)	Good
Al-Kuwari et al. (2021) [23]	Qatar	-	Retrospective data analysis	All ages	Both	From the 1st of January 2017 to the 31st of July 2020	- Number of missed appointments colorectal cancer screening: 5854 - Dropped in the colorectal cancer screening service utilization by 100% from April to July 2020	Good
Cheng et al. (2020) [24]	Taiwan	-	Prospective observational	Ages 50 to 75	Both	January 21, 2020, to April 2020 vs. same time in 2019, 2018, 2016, 2017	- FIT screening uptake: Q4 2019 to Q1 2020, 88.1% vs. 92.1% Q4 2018 to Q1 2019; 91.2% Q4 2017 to Q1 2018; and 92.7% Q4 2016 to Q1 2017 (<i>P</i> for trend < 0.0001) - Colonoscopy rate: 66.1% in Q1 of 2020 (70.2%, 77.5%, and 75.4% in 2017, 2018, and 2019, <i>P</i> for trend = 0.017) - Diagnostic colonoscopy rescheduling/cancellation rate: 10.9% in Q1 2020 (<i>P</i> for trend = 0.023)	Good
London et al. (2020) [25]	UK	-	-	All ages	Both	January 1, 2019, through April 30, 2020	- Percent change in cancer screenings (2019–2020): 84.5% decrease	Good
Mizuno et al. (2020) [26]	Japan	-	Retrospective cohort	All ages	Both	December 19, 2019, to August 14, 2020 vs. December 18, 2018, to August 14, 2019	- Screening or diagnostic colonoscopies: 14.1% decrease (from 1379 to 1184) - Emergency admission: increase from 18.2 to 38.7%	Good

Table 1 (continued)

First author (year)	Place (country)	Sample size	Type of study	Age	Sex	Comparison date	Examined indicators	Result of quality assessment
Maida et al. (2020) [34]	Italy	-	National survey	All ages	Both	After the COVID-19 pandemic	<p>GI divisions activity compared to before the pandemic:</p> <ul style="list-style-type: none"> - Without change: 3/121 (2.5%) - Undergone a clinical rearrangement: 118/121 (86.8%) - Converted to COVID Units: 13/121 (10.7%) - Sharp slowdown in admissions and consultations: 103/121 (85.1%) - Completely suspended: 18/121 (14.9%) - Activating the remote consultancy and follow-up service: 83/121 (68.6%); (63.9% by phone, 31.3% by email, 4.8% by video) 	Good
Maclean et al. (2020) [35]	UK	381	Observational cohort	All ages	Both	26 March to 2 July 2020 vs. 1 October to 31 December 2019	<ul style="list-style-type: none"> - Time waiting for consultation: increase from 0 day to 2 weeks - Referral for colonoscopy: reduced from 62 to 34%; $P < 0.001$ - Telephone consultations: decrease from 590 to 381 with below outcomes: - Colonoscopy \pm OGD \pm CT abdomen/pelvis screening: decrease from 365 (62%) to 129 (34%); $p < 0.001$ - CT abdomen/pelvis screening: increase from 40 (6.8%) to 46 (12%); $p = 0.005$ - Discharged from screening: decrease from 31 (5.3%) to 82 (22%); $p < 0.001$ 	Good
Lui et al. (2020) [27]	China	-	-	All ages	Both	Jan 21–27 2020 vs. Jan 21–27 2019	<ul style="list-style-type: none"> - Average number of lower endoscopies per week: 58.8% decrease (from 1190 to 491); $p < 0.001$ 	Good
Carethers et al. (2020) [28]	USA	-	Commentary	All ages	Both	April 2020 vs. 2019	<ul style="list-style-type: none"> - Colorectal cancer screening: 84.5% decrease 	Moderate

Fig. 1 Flow of information through the various phases of the systematic review



the two time periods before and after the constraints in 2019 and 2020 [18].

In a study by Lahat et al. in Israel, which compared endoscopy from January to March 2020 with the same period in 2019 and 2018, colonoscopy and sigmoidoscopy decreased by 52–57% in 2020 (464 in 2020 compared to 955 and 1058 in 2018 and 2019) ($p < 0.0001$) [19].

A study by Kirac et al. in Croatia from August 1, 2019, to August 31, 2020, showed that the number of colonoscopy cases decreased from 50 in August 2019 to less than 9 in April 2020, but 3 months later return to normal condition [20].

Gurney et al. in their study found that New Zealand experienced a sharp decline in the number of gastrointestinal endoscopies during the National Corona Restriction Period (late March and April 2020); as the number of gastroscopic and colonoscopic cases in April 2019 decreased

from approximately 5734 cases to less than 1426 cases in April 2020, and then, with a gradual increase until August 2020, it returned to the same number of before March [21].

In a study in the USA, Gorin et al. compared cancer screening between March 19 and May 9 in 2017, 2018, 2019, and 2020. They concluded that the number of colonoscopy cases has decreased from 1291 to 8 cases [22].

Al-Kuwari et al. conducted a study in Qatar, during the period of March to July 2019, and reported 5854 missing colonoscopies, and from April to July 2020, colorectal cancer screening services have decreased by 100% [23].

A study by Cheng et al. in Taiwan found that the screening uptake rate from winter 2019 to spring 2020 was 88.1%, which was significantly lower than the previous 3 years (92.1% from winter 2018 to Spring 2019, 91.2% from winter 2017 to spring 2018, and 92.7% from winter 2016 to spring 2017) (P for trend < 0.0001) [24].

London et al. in a UK study found that from January to April 2020, colorectal cancer screening decreased by 84.5% compared to the same period in 2019 [25].

A study by Mizuno et al. in Japan showed that with the release of COVID-19 in March 2020 in Kyoto, the number of outpatients and screening or diagnostic colonoscopy decreased (14.1%) and continued for some time. After the cancelation of the emergency on May 21, 2020, the number increased again [26].

In a study by Lui et al. in Hong Kong, it was found that on January 21–27, 2020 (after the diagnosis of the first case of the coronary artery), compared to the same period in 2019, the average of lower endoscopy decreased by 58.8% and reached from 1190 cases per week to 491 cases ($p < 0.001$) [27].

Carethers, J.M. et al. in the USA, by comparing screening tests for colon cancer in April 2020 and 2019, found that it had decreased by 84.5% in 2020 [28].

Surveillance Colonoscopy

A study by Wassie et al. comparing the number of colonoscopies in Australia in two similar timeframes (April–June) in 2019 and 2020 found that during the study period in 2020, the proportion of surveillance colonoscopy decreased. There were 597 cases of surveillance colonoscopy evaluated during the period, including 22.6% that recalled after 3-year care interval ($n = 135$) and 36.5% that recalled after a 5-year interval ($n = 218$) [12].

According to the fact that previous dates are based on the results of previous colonoscopy pathology for up to 5 years, the total number of such colonoscopies in 2019 ($n = 306$) was similar to 2020 ($n = 291$). Of these, the number of care colonoscopies that were not completed 3 months later that time increased from 52.9 (162/306) in 2019 to 68.0% (198/291) in 2020 ($P < 0.001$). The number of surveillance colonoscopies that were not completed within 6 months of the deadline increased from 19.3 (59/306) in 2019 to 46.1% (134/291) in 2020 ($P < 0.001$). During the COVID-19 pandemic, the percentage of care colonoscopies with a delay of 3 months was higher in April compared to May and June. The majority of the delay in colposcopies was observed in patients with an interval of 3- and 5-year follow-up reminder during and before the COVID-19 pandemic [12].

A letter has been sent to consider another colonoscopy for patients over the age of 75. In 2020, the number of non-response cases was significantly higher (16/31, 51.6%) than that observed in 2019 (10/39, 25.6%) ($P = 0.03$). However, for respondents, there is no difference in the reservation request ratio (62.1% in 2019 and 73.3% in 2020, $P = 0.46$) and the patient less involved to perform the colonoscopy with the physician; therefore, during the period of

COVID-19, they were excluded from the Southern Cooperative Program for the Prevention of Colorectal Cancer (SCOOP) [12].

A study by Timmouth et al. in Canada that compared colonoscopy cases from March to June 2020 with the same time period in 2019 found that reduction in surveillance screening in patients who required surveillance colonoscopy due to a previous polypectomy or colorectal cancer or a previous adenoma (low-risk or high-risk adenoma) was 79% [13].

Lantinga et al. who compared the two time periods before and after the constraints in 2019 and 2020 in the Netherlands, found that surveillance colonoscopy which was the most important cause of colonoscopy in 2019 (35.0% (95% CI: 33.9–36.1)) was decreased to 19.4% (95% CI: 33.9–36.1) in 2020 ($P < 0.001$) [18].

Prescribed Colonoscopy

A study by Wassie et al. which compared the number of colonoscopies in Australia in two similar time periods (April–June) in 2019 and 2020 found that performed colonoscopies due to abnormal abdominal radiology increased in April 2020 ($P < 0.05$). There was no difference in the colonoscopies rate performed before and after the epidemic due to a IBD or FIT positive test result or suspicious symptoms ($P > 0.05$), except for a slight increase in the number of positive FIT tests in May during the pandemic period ($P = 0.003$) [12].

A study conducted by Timmouth et al. in Canada and has compared the colonoscopy performing from March to June 2020 with the same period in 2019 found that screening reduction was 80% in patients who have been screened for a family history of colorectal cancer; in patients screened for moderate risk of colorectal cancer, was 81%; and in those who had screening because of suspicious symptoms, was 56%. However, the colonoscopy number due to the positive results of the fecal immunochemical test (FIT) and guaiac fecal occult blood test (gFOBT), increase 8% and reached from 4390 cases in 2019 to 4758 cases in 2020 during the period of study [13].

A study by Cheng et al. which was conducted in Taiwan was reported that the colonoscopy rate in people with positive FIT test and colonoscopy prescribed for them was 66.1% in the spring of 2020, which was significantly lower than the same period in the last 3 years (70.2% in 2017, 77.5% in 2018, and 75.4% in 2019) (P for trend = 0.017) [24].

Emergency Colonoscopy

In a study by Wassie et al. that compared the number of colonoscopy cases in Australia in two similar time periods

(April–June) in 2019 and 2020, they found that the emergency colonoscopy rate increased from 71.2 (828/1163) in 2019 to 78.2% (445/569) in 2020, which was accompanied by a significant decrease in the number of unusual colonoscopies from 335 to 124 (63.0% decrease, $P=0.002$). Although the total number of unusual incomplete colonoscopies decreased significantly during the pandemic, it increased from 4 cases in April to 35 cases in May and reached 73% ($n=85$) of the average capacity in 2019 by June [12].

Shinkwin et al. in their study in the UK showed that emergency colonoscopies increased from 28.6 in 2018 and 2019 to 36.0% in 2020 ($p=0.03$) [14].

Non-invasive Methods

A study by Myint et al. that was conducted in the USA found that in the period before COVID-19 (1/29/2020 to 3/17/2020), performing the FIT test (154.0 ± 25.2 Per week) that was the most screening tests after a colonoscopy during the cessation period significantly decreased to 60.6 ± 52.7 ($p < 0.02$) but several weeks later the cessation period began to increase [16].

They also found that in the months following the restarting of screening, although the use of several non-invasive screening methods including FIT (154 ± 25.2 to 162 ± 55.2 ; $p=0.54$) and fecal DNA (0 to 6.0 ± 3.2 per week; $p < 0.01$) is equal to or even greater than the pre-pandemic, the use of FS and CTC remained low during the study period [16].

Referrals to Screening Colonoscopy

The study by Miller et al., which examined the effects of COVID-19 on the diagnosis of colorectal cancer and compared it from the period of April 1 to May 31 in 2020 with the same period from 2017 to 2019 in the UK, showed that overall colonoscopy referrals decreased by 43%, from an average of 1071 in previous years to 609 in 2020; this reduction includes a 79% (324 to 69) reduction in emergency referrals and a 64% (581 to 211) reduction in routine referrals. Referrals from urgent suspicion of cancer (USOC) showed a 40% (235 to 329) increase [29].

Completion of Screenings that Needed to Be Reviewed

A study by Wassie et al. in Australia compared the number of colonoscopies in two similar time frames (April–June) in 2019 and 2020 which revealed that in 2019, 45.5% ($n=1164.530$) of the colonoscopies needed further examination, which decreased to 32.0% ($n=1869/569$) in 2020, and

as a result, the overall number of colonoscopies which need further examination decreased by 65.7% ($P < 0.001$) [12].

Responding to Recalls

A study by Wassie et al. in Australia by comparing the number of colonoscopies in two similar timeframes (April–June) in 2019 and 2020 found that the average time spent for responding to a colonoscopy call letter has been comparable in 2019 (21 days, IQR 12–48 days) and 2020 (18 days, IQR 11–41 days) ($p=0.23$). In addition, compared to the same period in 2019 (18/102, 17.6%), no significant difference was observed in the number of cases of non-response in the COVID-19 period (34/162, 21.0%) ($p=0.44$) [12].

In a study conducted by D'Ovidio et al. in Italy, they compared colonoscopy data for the period of March 9 to May 4, 2020, with the same time period in 2019 and concluded that in the period of limitations, 60 out of 137 invited patients underwent endoscopy, while at the same time, in 2019, 238 cases (3.9 times higher) underwent colonoscopy [30].

A study by Cheng et al. conducted in Taiwan found that in 2020, there is a reprogramming rate (change of schedule time for colonoscopy) of 7.8% due to change in schedule time and 3.1% due to colonoscopy cancellation in the COVID-19 epidemic. The overall rate of rescheduling or cancellation was 10.9%, which was significantly higher than that in the previous 3 years (P for trend = 0.023). They also found that in the spring of 2020, 50% of people refused to have a diagnostic colonoscopy for fear of developing COVID-19, which had never happened in previous years [24].

Participating in Screening Program

Koczkodaj et al. in their study in Poland found that screening coverage and participation rate in colorectal cancer colonoscopy screening decreased to 7.09% in July 2020, although this rate was 13.16% in 2019 [31].

Sales of Laboratory Materials Needed for Colonoscopy

Meyer et al. in a study in France concluded that following the reduction in colonoscopy cases during the COVID-19 pandemic period, during the 8-week period of restrictions, the distribution of colonoscopy drugs between March 30 and April 12 decreased by 85.6% compared to the expected number. Overall, only 83,045 colonoscopy drugs were distributed during the restrictions, which is 181,826 (68.6%) less than expected [32].

Four months after the removal of the restrictions, the number of colonoscopy preparations remained lower than expected, but gradually returned to the expected level, but finally was the 73,761 (13.9%) lower than expected distributions. In general, during the 6-month period after the outbreak of the pandemic, 25,558 cases of colonoscopy preparations were distributed less than expected [32].

Reducing the Capacity of Screening Centers

Boyle et al. in their study in England and Wales found that according to the COVID-19 incidence rate, 77% of hospitals reduced their diagnostic colonoscopy activities to 0–10% of their normal capacity; 21% of hospitals continued with 11 to 70% of their normal capacity; and only 2% of hospitals with 71 to 100% of their normal capacity continued to perform diagnostic colonoscopy [33].

A study by Maida et al. in Italy, after examining the activity of the gastroenterology divisions in hospitals, found that only 2.5% of the hospitals continued to operate as before and 86.8% changed the way they provide their services; as a result, outpatient admissions and counseling fell sharply by 85.1%, and 14.9% of hospitals suspended operations [34].

Changing the Screening Method and Admission Process in the Screening Centers

Maclean et al. after changing strategies in a regional referral center to manage the crisis of COVID-19 (using the FIT test instead of colonoscopy and telephone counseling instead of face-to-face counseling for patient triage) by evaluating data from patients with colorectal cancer for two periods of March 26 to July 2 in 2020 and October 1 to December 31 in 2019 in the UK, found that the waiting time for counseling has increased from 0 days to 2 weeks; subsequent referrals for colonoscopy decreased from 62 to 34% ($P < 0.001$). Following reducing telephone counseling from 590 to 381 cases, the counseling results also showed changes as colonoscopy \pm OGD \pm CT abdomen/pelvis decreased from 365 (62%) cases in 2019 to 129 (34%) in 2020 (P -value < 0.001); CT abdomen/pelvis increased from 40 (6.8%) cases in 2019 to 46 (12%) cases in 2020 (P -value < 0.005) and the number of discharges increased from 31 (5.3%) cases in 2019 to 82 (22%) in 2020 (P -value < 0.001) [35].

A study conducted by Maida et al. in Italy assessed the activity of the gastrointestinal department in hospitals and found that 68.6% of hospitals to compensate for this decrease due to the crisis of COVID-19 established consulting services and remote monitoring (63.9% launched telephone counseling, 31.3% email, and 4.8% video counseling) [34].

Discussion

This study investigated the effect of the COVID-19 disease pandemic on colorectal cancer screening by systematic review and the final analysis was performed based on 25 articles related to the purpose of the study.

Despite the recommendation to performing CRC screening in many countries of the world [37] and after approving and starting the mass screening programs for colorectal cancer such as breast and cervical cancer in many countries [38], due to the COVID-19 pandemic in many countries, cancer screening programs have been discontinued since March 2020 and screening disrupted for an unknown period of time [2].

Colorectal cancer screening by invasive methods (colonoscopy, flexible sigmoidoscopy, and CT colonography (virtual colonoscopy)) and non-invasive methods (fecal immunochemical test (FIT)), guaiac-based fecal occult blood test (gFOBT), multi-targeted stool DNA mt-s DNA, and CT colonography (virtual colonoscopy) is performed [39]. However, it is used differently depending on the degree of accuracy, sensitivity, and level of access in each community [4], but the most common method is colonoscopy.

The impact of the COVID-19 crisis on different colorectal cancer screening methods varies according to the applied guidelines and restrictions. Most studies have reported a decrease in colonoscopy screening [12–35] so that in some cases, the number of colonoscopies has reached zero [12, 33]; however, in some studies, this reduction was temporary and returned to normal sometime after the cessation of limitations [16, 20, 21, 26], while in some others this reduction continued throughout the post-COVID-19 pandemic period [13, 14].

One study prescript colonoscopy, which is requested due to history and probability of infection, suspicious symptoms, or a positive screening test result other than colonoscopy, is also increased [12], however, decreased in other studies [13, 14, 24].

The use of emergency colonoscopy due to the patient's emergency (rupture or obstruction of the large intestine) has been shown to increase in several studies [12, 14]; however, in a study by Miller et al. in the UK, findings showed 79% decline (from 324 to 69) in emergency referrals [29].

Surveillance colonoscopy that is performed periodically for people at high risk for colorectal cancer due to age or previous screening results also shows a significant reduction compared to the pre-period of COVID-19 [12, 13, 18]. Furthermore, cancelation of appointments [24] or non-response to calls was increased [30].

One study that compared colonoscopy referrals before and after the crisis found that both emergency and routine

referrals decreased, while referred cases to emergency diagnostics centers by general practitioners increased by 40% [29].

Patients who did not complete a colonoscopy also increased [12]. The use of flexible sigmoidoscopy has also been significantly reduced during this period [15, 17, 19].

The use of non-invasive methods shows less reduction than invasive methods. The main non-invasive screening method used to screen colorectal cancer is the FIT test, which in a study in the USA temporarily showed a significant reduction [16] but after the resumption of activities showed an increase [16]. However, where it is used as an alternative to colonoscopy [35], its number has increased so that its positive result has become one of the main reasons for colonoscopy [13, 18]. Other methods had not changed significantly [16].

It is generally estimated that due to the decline in care services between 2020 and 2023 in the crisis of COVID-19, approximately 1,179,642 to 2,014,164 cases of colorectal cancer screening, 8346 to 12,894 cases of colorectal cancer diagnosis, and 6113 to 9301 cases of early-stage diagnoses for this cancer will be missed [11].

Given that these screening programs are performed with the aim of identifying precancerous lesions and cancers in the early stages in order to remove the lesions before they progress to tumors and treat the cancers in the early stages [38], it is expected that delays in diagnosis due to COVID-19 epidemic cause a significant increase in the number of preventable cancer deaths [40, 41]. A study in the UK has predicted that according to the 5-year survival of patients, there were 1445 (1392–1591) to 1563 (1534–1592) additional deaths for colon cancer due to the COVID-19 crisis, equal to from 15.3 to 16.6% increase [40].

In addition, another study predicts that if the COVID-19 pandemic disrupts colon cancer screening services, its long-term effects could lead to thousands of deaths from colorectal cancer; if this disruption lasts up to 12 months, it would lead to the deaths of more than 3968 people in Australia, 2366 in Canada, and 1360–1762 in the Netherlands [41].

Therefore, some countries have considered compensatory measures to reduce the damage caused by this disease on screening and early diagnosis of colorectal cancer; these include setting up “cold sites” (non-COVID-19 treatment center) [33], using the FIT test instead of colonoscopy and telephone counseling instead of face-to-face counseling for patient triage [35]; in a modeling study, increasing the use of FIT from 15 to 22% over a 3-year period to compensate for the decline in colonoscopy screening due to the COVID-19 crisis could lead to 655,825 screening cases and 2715 diagnosis of colon cancer, 72% of which will be diagnosed in the early stages [11].

It was also shown that in the short term, the increase in the use of fecal immunochemical tests was associated with

approximately 588,844 additional colorectal cancer screening cases and 2836 colorectal cancer diagnoses, of which 1953 (68.9%) were early-stage diagnoses [11]. In general, the time required to compensate for damage caused by the COVID-19 pandemic varies depending on the proportion of people who redirecting from low-yield colonoscopies to fecal immunochemical test [13]. A study which was conducted in Canada found that without any changes in workflow, the time required to make up for the backlog caused by the COVID-19 crisis was estimated as 41 months; while, by directing 25%, 50%, and 75% of the colonoscopy to the FIT, the compensation time is reduced to 28, 22, and 19 months, respectively. If the direction is not changed to FIT, hospitals will need to increase their colonoscopy capacity to 124%, 134%, and 145% at 28, 22, and 19 months, respectively, to compensate for the delay [13].

Overall, the results of several studies revealed that increased use of fecal immunochemistry (FIT) during COVID-19 epidemic disease is associated with increased participation in colorectal cancer screening and further detection of early colorectal cancer [11]. It is also estimated that follow-up of canceled or delayed screening appointments as soon as possible can reduce the additional colorectal cancer deaths caused by the COVID-19 epidemic to 0.2% [41].

Conclusion

The results of studies show that the reduction of colorectal cancer screening due to the COVID-19 pandemic is completely influenced by the restrictions that have been implemented in different periods of time following the high prevalence of corona disease in different populations. This zigzag effect is visible in populations where the corona outbreak has intensified and the restrictions have been applied more than once.

Following a decrease in the number of screening cases, emergency colonoscopies have increased, followed by a significant decrease in the number of screening methods required to diagnose a case of cancer (17). Therefore, in order to compensate for the decline and prevent the continuation of this trend in colorectal cancer screening, the following suggestions are recommended to governments and government agencies and the public.

Governments and government agencies should consider implementing the following:

- Increasing public awareness by broadcasting educational and practical programs in mass media (radio and television) about the risk of colorectal cancer, the consequences and outcomes of delaying referral to diagnostic centers if there are suspicious symptoms, and the benefits

of timely referral as well as encourage participation in screening programs.

- Providing short and useful educational media content regarding the items considered, by experts and their widespread dissemination through cyberspace in order to increase awareness, change attitudes, and reduce the fear of getting COVID-19 infection.
- Reassure people about the low risk of COVID-19 infection when visiting diagnostic centers through the practical application of preventive health protocols.
- Creating campaigns to support colorectal cancer to increase public knowledge and awareness using existing capacities, including health workers, university students, NGOs, and volunteer groups.
- Replacing non-invasive methods such as FIT testing instead of invasive methods in colorectal cancer screening programs.
- Practical training the FIT test sampling at home to the general public by educational and laboratory specialists.
- Increase the capacity of screening centers at the time of removal of restrictions in order to compensate for the reduction during the time of restrictions.
- Setting up and strengthening not in-person queuing systems (telephone and internet) in order to reduce congestion in diagnostic centers.
- Establish or strengthen telemedicine to reduce the number of face-to-face visits for diagnostic centers and to assist patients who do not have the ability or access to diagnostic centers
- Implementation of free or low-cost screening programs (due to the adverse effects of Covid-19 disease on the economic situation of the people)
- Prompt recall of people who have canceled or delayed their previous appointments for fear of developing COVID-19 infection.
- Provide the necessary forces for screening centers or return the relocated staff to their place of work during the cessation of the COVID-19 epidemic, in order to maintain the capacity of screening centers.

Things that people should keep in mind are:

- Considering the symptoms of colorectal cancer seriously and refer to diagnostic centers in a timely manner.
- Strict observance of health instructions for the prevention of COVID-19 when referring to diagnostic centers.
- Participating in screening programs with the encouragement of family, friends, and acquaintances.
- Participating and launching non-governmental campaigns in order to inform about colorectal cancer to other human beings.

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