



The impact of COVID-19 pandemic in the colorectal cancer prevention

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Abstract

Background The coronavirus disease 2019 (COVID-19) has led to a policy of severe restrictions in almost all countries strongly involved by the pandemic. National Health System is among activities suffering from the COVID-19 and the lockdown.

Aim To evaluate the impact of COVID-19 in colorectal cancer (CRC) prevention.

Methods We report the change in the hospital organization to meet the growing healthcare needs determined by COVID-19. The limitations of CRC prevention secondary to COVID-19 and their effects on the healthcare are analyzed considering the features of the CRC screening programs in the average-risk population and endoscopic surveillance in patients with inflammatory bowel diseases (IBD).

Results The interruption of CRC prevention may lead to a delayed diagnosis of CRC, possibly in a more advanced stage. The economic burden and the impact on workload for gastroenterologists, surgeons, and oncologists will be greater as long as the CRC prevention remains suspended. To respond to the increased demand for colonoscopy once COVID-19 will be under control, we should optimize the resources. It will be necessary to stratify the CRC risk and reach an order of priority. It should be implemented the number of health workers, equipment, and spaces dedicated to performing colonoscopy for screening purpose and in subjects with alarm symptoms in the shortest time. To this aim, the funds earmarked for healthcare should be increased.

Conclusion The economic impact will be dramatic, but COVID-19 is the demonstration that healthcare has to be the primary goal of humans.

Keywords Colonoscopy · Colorectal cancer · Colorectal cancer screening · COVID-19 · Fecal occult blood test

Introduction: the coronavirus disease 2019 outbreak and restrictions involving the National Health System

The coronavirus disease 2019 (COVID-19) outbreak in Italy has led to a policy of restrictions by the Italian Council of Ministers. Since February 23, 2020, a series of decrees limited progressively traveling and working activities. Restrictions

peaked on March 23 when a complete lockdown involved all Italian regions. The National Health System is among the working activities suffering from the COVID-19 and the lockdown. The Italian Ministry of Health and the governors of regions have established a progressive increase in the number of hospitalizations to be dedicated to patients potentially affected by COVID-19. This led to the opening of new wards and the change of destination of a large part of those existing and of the health personnel who worked in them. Hospital activities reserved for outpatients were limited to urgent cases, while all scheduled activities were interrupted until April 3. Since the Council of Ministers has ordered the continuation of the lockdown after April 3, it is foreseeable that the current health restrictions will also be maintained until an indefinite date. Among clinical activities limited by the current healthcare restrictions are all screening tests including the procedures for colorectal cancer (CRC) prevention.

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Colorectal cancer and screening programs in the average-risk population

CRC represents the third cancer in men (14%) and second in women (12%). The possibility of developing CRC over the life is 1/13 in men and 1/21 in women in Italy. In Italy, there are about 481,000 people with a previous diagnosis of colorectal cancer (16% in men and 12% in women) (https://www.aiom.it/wp-content/uploads/2019/09/2019_Numeri_Cancro-operatori-web.pdf). Since the early 2000s, organized CRC screening has been progressively activated in Italy, and 112 CRC screening programs are active by the end of 2012 [1]. Most of CRC screening programs are sequential. Men and women aged 50–69 years are invited to undergo every 2 years to a first-level test consisting in the fecal occult blood test (FOBT). If FOBT is positive, the screened subject is contacted by phone to arrange an appointment for a colonoscopy as a second-level investigation. According to colonoscopy findings, individuals are referred for surgery, post-colonoscopy surveillance, or further rounds of FOBT. All tests and treatments are free of charge. Effectiveness of CRC screening has been well-demonstrated, the most substantial CRC mortality reductions occurring in countries with the highest uptake of screening [2]. Indeed, as a two-stage screening strategy, the effectiveness of FOBT depends on receiving an adequate follow-up colonoscopy. Recommendations for the appropriate time interval to follow-up colonoscopy are conflicting. Colonoscopy in FOBT-positive subjects should be scheduled within 31 days according to the European guidelines [3], within 2 months in Canada [4], while US guidelines did not define a specific interval [5]. Indeed, it is reasonable to argue that increasing time to colonoscopy following a positive FOBT plays a negative role in terms of CRC prevention. It has been observed that every month, more until colonoscopy is associated with an increased risk of a CRC in an advanced stage and mortality risk in subjects with a positive FOBT [6, 7]. In addition, a recent simulation model study [8] estimated that a delay of up to 12 months might reduce the total years of life gained from screening up to nearly 10% when colonoscopy is delivered within 2 weeks after a positive FOBT. Thus, it has been proposed that colonoscopy should be delivered as soon as possible in patients with a likelihood of CRC and within 1 month in subjects with positive FOBT [9].

Surveillance in inflammatory bowel diseases

Patients affected by inflammatory bowel diseases (IBD), ulcerative colitis (UC) and Crohn's disease, have an increased risk to develop CRC. This risk mainly affects UC patients [10, 11]. The risk of developing CRC in UC patients is increased according to the duration, extension, and severity of the disease. It has been reported that CRC cumulative incidence is 1% at 10 years, 3% at 20 years, and 7% at 30 years [12].

Recent epidemiologic studies suggest a lower incidence of IBD-related CRC than historically reported [13]. This may reflect the positive effect of increased implementation of surveillance programs and changing approaches to treatment and surgery [14]. The European Crohn's and Colitis Organization (ECCO) recommends starting the screening 8 years after the onset of symptoms, with subsequent surveillance intervals ranging from 1 to 5 years depending on the individual risk stratification [15]. In presence of high-risk factors of CRC (namely, concomitant primary sclerosing cholangitis, detection of stricture or dysplasia within the past 5 years, extensive colitis with severe active inflammation), patients should have a surveillance colonoscopy every year [14]. Patients with intermediate risk factors (namely, extensive colitis with mild to moderate active inflammation, post-inflammatory polyp, a family history of CRC in a first-degree relative diagnosed at 50 years of age) should have a screening colonoscopy every 2–3 years. Finally, patients at low risk of CRC should undergo screening colonoscopy every 5 years [15].

The limitations of CRC prevention secondary to COVID-19

Due to the current health restrictions related to COVID-19, almost all Italian districts have suspended the first-level screening tests, including FOBT. Governors of some regions with fewer cases of COVID-19-infected patients decreed to continue the second-level tests for CRC screening in subjects having a positive FOBT (<https://www.osservatorionazionalecreening.it/content/screening-e-covid-19-il-quadro-regionale>). Restriction of mobility, patients' fear of becoming infected, and the safety procedures to be followed for avoiding a possible contagion may result in a limitation to perform a colonoscopy. Another obstacle to the delivery of colonoscopy is that part of the healthcare staff, gastroenterologists included, has undergone a change of role to be employed in the new wards dedicated to COVID-19. Other districts have interrupted the CRC screening at any level, leaving unmodified surgery in subjects who completed the diagnostic process. In this period of COVID-19 pandemic, all surveillance colonoscopy in IBD patients have been stopped and the risk of CRC in this group of patients might become high over time.

In keeping with the Italian position about CRC screening, on March 22, the British Society of Gastroenterology released a decision-making on endoscopy activity establishing that colonoscopy should be paused immediately in FOBT-positive subjects as well as the surveillance for polyp and IBD until further notice (unless felt to be clinically high-risk neoplasia still present) (<https://www.bsg.org.uk/wp-content/uploads/2020/03/Advice-for-Endoscopy-Teams-during-COVID-ver-2-4-published-22032020FINAL-1.pdf?x19508>). Other countries strongly involved by COVID-19 pandemic, like Spain, Scotland,

Ireland, and Wales, paused screening procedures or, like the USA, recommend rescheduling non-urgent endoscopy procedures (<https://www.gov.scot/news/health-screening-programmes-paused/>, <https://www.screeningservice.ie/>, <http://www.bowelscreening.wales.nhs.uk/home>, <https://www.cesm-cv.org/wp-content/uploads/2020/03/Instruccio%C3%ACn-2020-03-17.pdf.pdf>, <https://www.asge.org/home/joint-gi-society-message-covid-19>).

What the National Health Systems can expect

According to most forecasts, the return to “normal” will not happen before a year or more. Thus, CRC screening and any other procedure for CRC prevention probably will be re-started even later. The interruption of CRC screening programs means that a proportion of subjects who will not be screened this year will receive a delayed diagnosis of CRC. This will have several effects. First, the benefit deriving from FOBT will be reduced, if not lost. In a recent study evaluating the impact of FOBT-based screening programs on CRC at diagnosis between 2002 and 2008, it has been shown that CRC in non-invited subjects was in more advanced stages than CRC in subjects invited to screening [16]. Thus, it is possible that the stopping of screening will lead to CRCs in a more advanced stage at diagnosis compared with what they could have been if the screening test was available. This, in turn, could affect the effectiveness of screening on CRC mortality, estimated at a reduction of up to 20% [17]. In terms of the healthcare economy, the interruption of screening means higher costs due to the management of patients with CRC in a more advanced stage [18, 19], and to the partial loss of the cost-saving effect of CRC prevention [17]. We cannot exactly quantify the economic burden of a delayed diagnosis of CRC on the public health economy. The impact will be greater as long as the screening remains suspended, and it will be related to the number of new diagnoses expected per year. The Italian Association of Medical Oncology estimated more than 49,000 (27,000 in men and 22,000 in women) new colorectal cancer (CRC) diagnoses for 2019 (https://www.aiom.it/wp-content/uploads/2019/09/2019_Numeri_Cancro-operatori-web.pdf). Applying this estimate for the current year, we can expect around 4,000 new CRC cases for each month of the epidemic in Italy. This could have an impact in the colonoscopy demand we should have to satisfy within a short period. In addition to the new diagnoses, we have to include patients already operated on for CRC who are at risk to develop a relapse, up to 30–40% at 5 years after surgery [20]. When the COVID-19 outbreak will be under control, CRC screening procedures and surveillance for IBD patients will be reactivated, although it is not possible to determine how long it will take to return to the level before the pandemic. As a final consequence of this scenario, we must expect a general heavy increase in the healthcare workload for gastroenterologists but also for other specialties, like surgeons

and oncologists, both during the gradual reduction of restrictions but even more later.

CRC prevention post-COVID-19

Some practical considerations can be made to give an adequate answer to the needs that may emerge in a not so far future. First, the colonoscopy demand should be distributed over time by stratifying the candidates according to the individual CRC risk. One way of doing this could be to involve the general practitioner (GP) in the CRC screening in the population at average risk more than what has been done in the past. As an example, the European Society of Gastrointestinal Endoscopy (ESGE), in agreement with the institutions of the National Health Systems, could promote among GPs a questionnaire for the risk stratification of the CRC. The GP could submit his patients to the questionnaire asking several questions, including if there are and how many are first-degree relatives with CRC, if a colonoscopy has been performed even for non-screening purposes in the last 5–10 years and with what result. Based on this questionnaire, the GP could prioritize colonoscopy in subjects at high risk or with alarm symptoms and postpone the investigation in those who are asymptomatic and have already had a negative colonoscopy. To optimize the resources according to growing colonoscopy demand, the knowledge of the guidelines regarding post-surgical, and post-polypectomy endoscopic surveillance should be increased. The deviation from guidelines, reported up to 67% [21], is one of the reasons for colonoscopy over-prescription, often unnecessary. To this aim, one strategy to be implemented is the use of webinars widely diffused in the last 2 months by different scientific societies, including ESGE. As far as IBD patients, endoscopic surveillance will face the long waiting lists generated by the cancellation of endoscopic procedures during the pandemic. Even in these subjects, it will be necessary to stratify the CRC risk and reach an order of priority taking into account the risk factors indicated above. The slots to be used for endoscopic surveillance will be shared with those to be reserved for patients having a flare-up of UC or Crohn’s disease. To do this, it will be necessary to anticipate endoscopies that cannot be deferred any further and to postpone others, following precise indications [22]. Priority should be given to patients with a diagnosis of low-grade dysplasia, high-grade dysplasia, and who are waiting for endoscopic removal or have already had endoscopic removal and who should have the site of the resection checked. Second, it should be implemented the number of health workers, equipment, and spaces dedicated to performing colonoscopies for screening purposes and in subjects with alarm symptoms in the shortest time. To this aim, the funds earmarked for healthcare should be increased, unlike what has been done in the last few decades, not only in Italy. The

economic impact will be dramatic, but COVID-19 is the demonstration that healthcare assistance has to be the primary goal of humans.

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