How COVID-19 Outbreak Is Impacting Colorectal Cancer Patients in Italy: A Long Shadow Beyond Infection

Short title: The long shadow of COVID-19

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Sars-CoV-2 (COVID-19) Outbreak in Italy

Since its first outbreak in Wuhan, China, in December 2019, coronavirus disease 2019 (COVID-19) has rapidly spread globally and was declared on March 11th as a pandemic by the World Health Organization.

In Italy, the outbreak is particularly worrisome, with 17,660 confirmed cases and 1268 deaths as of March 14, 2020, representing 12.4% of all cases and 23.5% of all fatalities related to the disease worldwide, and accounting for 52.3% of cases and 85.2% deaths in Europe. Lombardy is the more seriously affected region, accounting for 65.7% of cases and 70.3% of deaths in Italy. Lombardy is regarded to have one of the most advanced health systems nationally, being considered a model to follow for its efficiency and quality of care. Indeed, COVID-19 is seriously challenging authorities’ ability to respond to the current crisis. The rapid evolution of the present situation calls for prompt awareness of the international community, and, in this sense, Italy can serve as an example to plan for adequate measures to be taken.

Impact of Sars-CoV-2 (COVID-19) Beyond the Viral Infection

The actual impact of COVID-19 goes far beyond the viral infection itself and the associated complications; rather, it profoundly affects the entire health system and patients, including those who are not infected. This is much more relevant for patients needing timely treatment as cancer patients are. Liang et al. were the first to assess the impact of COVID-19 on cancer patients in China. They found that 1% of those infected had a personal history of cancer, higher than that of Chinese population (0.29%), lung cancer being the most frequently found; moreover, patients with history of cancer seemed to have higher risk of severe events. Such information should indeed raise concerns, but it only represents one side of the coin for this group of patients. Wang and Zhang did not attribute the increased risk to cancer itself, and they pointed out that other aspects are probably even more relevant in cancer patients, namely the inability to receive the necessary medical and especially surgical care.
Under this light, the burden of the infection starts to show its actual magnitude. The authors of this Viewpoint have expertise in colorectal cancer surgery. In this emergency setting, people are being asked to stay home for longer periods. This carries the potential risk that postponing specialty outpatient visits, screening, oncologic follow-up and advanced diagnostics like endoscopy could result in several months of diagnostic delay. Furthermore, hospitals of affected areas have had to re-allocate resources for the epidemic, and patients with colorectal cancer are being postponed because of the overwhelming number of COVID-19 patients in the intensive care units.

How Sars-CoV-2 (COVID-19) Is Impacting Colorectal Cancer Patients and Quality of Care

In patients with colorectal cancer, 3-10 years survival is lower if treatment is started more than 90 days from diagnosis, and similar data are reported for other cancers. The ideal time of resection of colon cancer specifically has been estimated to be between 3 and 6 weeks from diagnosis, which is unlikely to be achieved during COVID-19 outbreak. The effects of this can only be guessed, but the huge impact on quality of care might result in a deterioration of mid- and long-term results of cancer treatment. Clinical trials are gasping, and the results of ongoing studies are likely to be jeopardized. With mobility restrictions, blood units are lacking, making treatment even more challenging. Of note, a recent analysis from Northern America suggested that increased waiting times to treatment were associated with increased costs of care. Although this might not be perceived as a priority in the current emergency situation, it should indeed be considered as resource reallocation might be necessary after the crisis has been controlled.

Under such circumstances, priorities and indicators of quality standards need to be reset and adapted. Strict social measures were taken in Lombardy and in Italy in order to face the current situation. Regarding cancer care, possible measures to be discussed include alternative treatment to radical surgery in very early-stage cancer or in very advanced disease, and centralization of patients likely to need postoperative stays in intensive care units in few tertiary care hospitals.
What the U.S. and Other Countries Can Expect Based on the Italian Experience

Italy got hit as first among Western countries, and the Italian experience may represent an opportunity for the US and other countries to put in place timely measures to decrease the potentially devastating effect of the healthcare crisis on other groups of patients with time-dependent disease such as cancer.

However, even if numbers from the US may not seem to be worrisome at first, it is likely that the same logarithmic increase in people affected will occur. According to a recent analysis of the Johns Hopkins Institute published in the *Financial Times*, all countries affected so far may fall above a curve of a 33% increase in cases after the 100th case is registered. The change of the increase trend is visually apparent comparing the progression of the infection between the first and the 100th case registered (Figure 1a) versus from the 100th case onward (Figure 1b).

More alarmingly, the actual incidence is difficult to be accurately estimated because the policy of testing varies greatly among international countries. Therefore, the 1678 cases and 41 deaths in US identified at the time when the present piece is being written might have underestimated the actual incidence of the infection in that particular area – despite the status of national emergency that has been declared by the US Government.

But how many patients with colorectal cancer would this affect in US? According to the American Cancer Society, in 2020 there will be an estimated 147,950 new colorectal cancers in the US, with approximately 40% with localized disease. It would mean that around 24,650 patients could be affected in two months of epidemic in the US alone, of whom approximately 9860 have localized disease. These figures warrant a prompt and joint global effort to reduce the potentially catastrophic impact of a COVID-19 pandemic even on cancer patients, for which the Italian experience could be considered.
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Figure Legends

**Figure 1.** **A.** Number of cases detected according to the day of diagnosis of the first case, until the 100th case was diagnosed. **B.** Number of cases detected over the days following the diagnosis of the 100th case. All countries included fell above the 33% daily increase10 (data from World Health Organisation).1
Figure 1