



## Influence of the COVID-19 Pandemic on the Treatment Patterns and Outcomes of Colorectal Cancer

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**Received** Oct 10, 2023  
**Revised** Oct 27, 2023  
**Accepted** Nov 7, 2023

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### Key Words

COVID-19; Colorectal neoplasms; General surgery; Stage; Complication

Over the past 3 years, the COVID-19 pandemic has posed significant challenges to the healthcare system, leading to delays in the diagnosis and treatment of various diseases due to the need for social distancing measures. Colorectal cancer has not been immune to these disruptions, and research in various countries has explored the impact of COVID-19 on the diagnosis and treatment of colorectal cancer. One notable consequence has been the postponement of colorectal cancer screenings, potentially resulting in disease progression, which can adversely affect surgical and oncological outcomes. Furthermore, the treatment approach for colorectal cancer may vary depending on the extent of disease progression and the healthcare policies implemented in response to the COVID-19 pandemic. In this systematic review, we examine treatment strategies, surgical outcomes, and oncological variables across multiple studies focusing on colorectal cancer treatment during the COVID-19 pandemic. The purpose of this analysis was to assess how medical policies enacted in response to the COVID-19 pandemic have influenced the outcomes of colorectal cancer treatment. We hope that this review will provide valuable insights and serve as a foundational resource for developing guidelines to address potential medical crises in the future.

## Introduction

Colorectal cancer ranks as the second leading cause of cancer-related death worldwide [1]. The crude mortality rate of colorectal cancer was 17.27 per 100,000 in 2020 [2]. Many efforts have been made to enhance the survival rates of colorectal cancer patients, including advancements in surgical procedures, adjuvant or neoadjuvant therapies, and early detection screening methods [3–8].

The World Health Organization declared COVID-19 a pandemic in March 2020 due to its rapid spread and high morbidity and mortality rates [9]. This pandemic has significantly impacted healthcare systems worldwide, presenting challenges across all disease types, including colorectal cancer. It has been reported that the COVID-19 pandemic has indeed affected the treatment patterns, surgical procedures, clinical practices, and oncological outcomes for patients with colorectal cancer [10–14]. A common theme across studies of colorectal cancer treatment during the COVID-19 pandemic has been the question of how to maintain care continuity beyond this pandemic era. In particular, the necessity of continuing appropriate screening is paramount. Research has been conducted to determine whether delays in the diagnosis and treatment of

colorectal cancer impact treatment outcomes, and whether there are viable alternatives when screening is delayed [14,15]. Some studies have reported that treatment delays in colorectal cancer during the COVID-19 pandemic have led to increased mortality rates [16]. In this pandemic era, concerns have also been raised about the timing of surgery and how to manage inevitable surgical delays. There has been a trend towards increased use of preoperative treatment under pandemic conditions, suggested as a safer treatment strategy depending on the stage of the disease [12–14]. These changes in treatment strategies may influence the long-term oncologic outcomes of colorectal cancer. Indeed, there remains a risk of new infectious diseases emerging and impacting colorectal cancer treatment in the future, even if the COVID-19 pandemic stabilizes. Therefore, it is crucial to carefully analyze treatment patterns and surgical and oncological outcomes during the pandemic to prepare for potential future medical crises.

This review aimed to analyze the published data regarding colorectal cancer treatment patterns, as well as surgical and oncological outcomes, during the COVID-19 pandemic. It offers insights into how we can formulate treatment strategies for colorectal cancer in potentially unpredictable situations within the medical community.

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## Methods

A literature search for relevant studies was conducted in August 2023 using the PubMed databases. The search keywords included "COVID," "COVID-19," "colorectal cancer," "colon cancer," "rectal cancer," "colorectal neoplasm," "surgery," "complication," "treatment," "recurrence," and "oncologic outcomes." Publications marked as e-pub ahead of print during the search period were also included. The search was performed using these keywords individually or in combination. The initial search yielded 708 published reports between 2021 and August 2023. From this extensive list of search results, studies that met the following criteria were included in this review: published after 2021, original articles, patient population with colorectal cancer, comparative studies between the COVID-19 period and pre-COVID-19 period, and those reporting at least one of the following results: treatment pattern, stage, operative method, and perioperative outcomes such as complications or mortality. Initially, the type of study was reviewed, followed by a screening of abstracts to identify suitable studies. Ultimately, 22 studies were included in this review and thoroughly evaluated in terms of treatment patterns, surgical procedures, and oncological outcomes (Table 1).

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## Changes in Treatment Strategies for Colorectal Cancer during the COVID-19 Pandemic

Screening plays a crucial role in reducing the incidence of colorectal cancer and improving patient survival rates. However, due to the fear of COVID-19, many medical complaints have been delayed, and screenings have been postponed. Indeed, it has been reported that the screening rate for colorectal cancer decreased during the COVID-19 pandemic [17,18]. In the USA, there was an observed 86% decline in colorectal screenings in 2020 [17]. As shown in Fig. 1, the rate of colonoscopies performed in Korea had been increasing by 5% annually until 2019. However, it appears that the outbreak of COVID-19 has reversed this trend, leading to a decrease in initiations (Fig. 1) [18].

The most concerning scenario arises when individuals with cancer miss their screenings, as this can cause a delay in cancer diagnosis and potentially lead to cancer progression. According

**Table 1.** Studies included in this review

| Author                 | Publication year | Country     | Type of study                          | Period                         |  | No. of patients |                   | Comment for inclusion   |
|------------------------|------------------|-------------|--|--------------------------------|--|-----------------|-------------------|---|
|                        |                  |             |  | Pre-COVID-19                   | COVID-19   | Pre-COVID-19    | COVID-19          |   |
| Cano-Valderrama O [34] | 2023             | Spain       | Retrospective Cohort<br>Single center  | 2019.9–2020.1                  | 2020.9–2021.3  | 169             | 220               | Patients who were referred to a multidisciplinary team                              |
| Forse CL [24]          | 2021             | Canada      | Retrospective Cohort<br>Single center  | 2019.8–2020.1                  | 2020.8–2021.1  | 173             | 165               |   |
| Pirozzi BM [33]        | 2023             | Italy       | Retrospective Cohort<br>Single center  | 2018.3–2020.2                  | 2020.3–2022.2  | 147             | 133               |   |
| Miyo M [25]            | 2022             | Japan       | Retrospective Cohort<br>Multicenter    | 2019.3–2020.2                  | 2020.3–2021.2  | 3,569           | 3,198             |   |
| Freund MR [26]         | 2022             | USA         | Retrospective Cohort<br>Single center  | 2016.3–2020.2                  | 2020.3–2021.2  | 180             | 54                |   |
| Eklöv K [21]           | 2022             | Sweden      | NDB                                    | 2019.3–2019.8                  | 2020.3–2020.8  | 590             | 550               |   |
| Eklöv K [22]           | 2022             | Sweden      | NDB                                    | 2019                           | 2020   | 4,016           | 3,964             | Compared with data from 2019  |
| Rottoli M [27]         | 2022             | Italy       | Retrospective Cohort<br>Multicenter    | 2019.3–12                      | 2020.3–12  | 1,755           | 1,481             |   |
| Chen MZ [28]           | 2022             | Australia   | Retrospective Cohort<br>Multicenter    | 2018.7–2019.2                  | 2020.7–2021.6  | 700             | 906               |   |
| Tarta C [29]           | 2022             | Romania     | Retrospective Cohort<br>Single center  | 2019                           | 2020–2021  | 163             | 84                |   |
| Meijer J [20]          | 2022             | Netherlands | NDB                                    | 2020<br>2–8 weeks              | 2020.<br>1) 9–11 weeks<br>2) 12–17 weeks<br>3) 18–26 weeks | 410             | 161<br>231<br>385 | Division of period: according to the proportion of expected colonoscopy performance |
| Ghosh S [30]           | 2022             | USA         | Retrospective Cohort<br>Single surgeon | 2019.4–2020.3                  | 2020.4–2020.9  | 344             | 166               |   |
| Tang G [31]            | 2022             | China       | Retrospective Cohort<br>Single center  | 2019.1–2019.3                  | 2020.1–2020.3  | 136             | 68                |   |
| Uyan M [35]            | 2022             | Turkey      | Retrospective Cohort<br>Single center  | 2019.3–2019.12                 | 2020.3–2020.12   | 56              | 48                |   |
| Kudou M [44]           | 2022             | Japan       | Retrospective Cohort<br>Single center  | 2018–2019                      | 2020–2021  | 91              | 67                | Only included minimally invasive surgery cases – emergency cases were excluded      |
| Kiss BI [36]           | 2022             | Romania     | Retrospective Cohort<br>Single center  | 2019.3–2020.3                  | 2020–2021  | 160             | 142               |   |
| Choi JY [13]           | 2021             | Korea       | Retrospective Cohort<br>Single center  | 2018.3–2018.9<br>2019.3–2019.9 | 2020.3–2020.9  | 1,985           | 916               |   |
| Kuryba A [40]          | 2021             | England     | NDB                                    | 2019.3–20.3.23                 | 2020.3.23–   | 11,703          | 3,227             |   |

Table 1. Continued

| Author            | Publication year | Country                  | Type of study                         | Period         |                | No. of patients |          | Comment for inclusion |
|-------------------|------------------|--------------------------|---------------------------------------|----------------|----------------|-----------------|----------|-----------------------|
|                   |                  |                          |                                       | Pre-COVID-19   | COVID-19       | Pre-COVID-19    | COVID-19 |                       |
| Williams E [37]   | 2021             | Australia<br>New Zealand | Retrospective Cohort<br>Multicenter   | 2017-2019      | 2020-          | 1,565           |          |                       |
| Radulovic RS [45] | 2021             | Serbia                   | Retrospective Cohort<br>Single center | 2019           | 2020.3-2021.4  | 152             | 49       |                       |
| Lee T [38]        | 2022             | Singapore                | Retrospective Cohort<br>Single center | 2019.10-2020.4 | 2020.4-2020.10 | 41              | 64       |                       |
| Lim JH [39]       | 2021             | Korea                    | Retrospective Cohort<br>Single center | 2017-2019      | 2020           | 2,514           | 715      |                       |

NDB, national database.

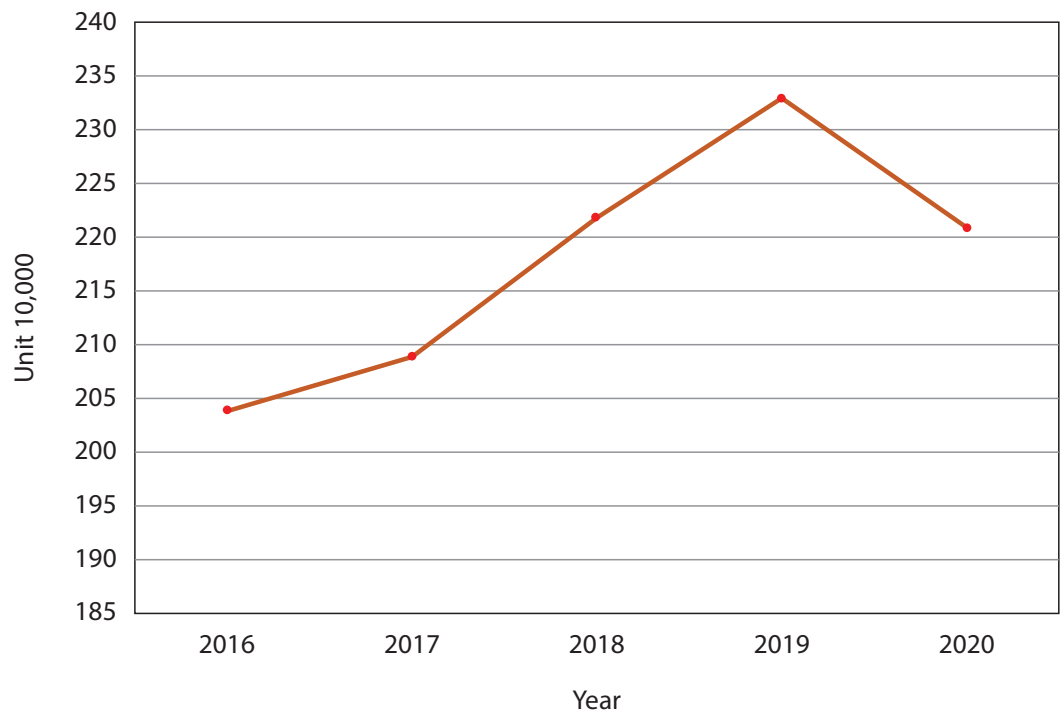


Fig. 1. Number of colonoscopies performed for screening purposes by year in South Korea.

to a meta-analysis of seven studies, it is recommended that elective surgery for colorectal patients not be postponed for more than four weeks. The available evidence suggests that extended delays from diagnosis are associated with poorer outcomes [14]. Neoadjuvant treatment is recommended for advanced disease to increase resectability. Conversely, several countries recommended a modified surgical approach during the initial stage of the 2020 pandemic, with the goal of reducing the workload in intensive care units by avoiding complications [12,19]. Therefore, changes in treatment patterns during the pandemic were not only a result of disease status but also of healthcare strategies.

The proportion of patients who received preoperative treatment during the pandemic,

**Table 2.** Treatment strategies for colorectal cancer during the COVID-19 pandemic compared to the pre-COVID-19 period

| Author          | Publication year | Proportion of patients treated with neoadjuvant treatment |                                  | P-value         | Comment  |
|-----------------|------------------|---|----------------------------------|-----------------|--|
|                 |                  | Pre-COVID-19  | COVID-19                         |                 |  |
| Forse CL [24]   | 2021             | 19%<br>17%  | 11%<br>13%                       | <0.001<br>0.044 | Chemotherapy post-shutdown<br>Chemoradiotherapy post-shutdown        |
| Miyo M [25]     | 2022             | 3.7%  | 3.7%                             | 1               |  |
| Freund MR [26]  | 2022             | 65%<br>TNT 15%  | 76%<br>TNT 52%                   | 0.0001          |  |
| Eklöv K [21,22] | 2022             | 3.5%<br>44%   | 5.1%<br>45%                      | 0.0016<br>NS    | Chemotherapy for colon cancer<br>Chemoradiotherapy for rectal cancer |
| Rottoli M [27]  | 2022             | 51.9%   | 52.2%                            | NS              | Rectal cancer  |
| Chen MZ [28]    | 2022             | 13.7%   | 16.2%                            |                 |  |
| Tarta C [29]    | 2022             | 7.2%  | 6.3% (2020)<br>9.5% (2021)       | NS              |  |
| Meijer J [20]   | 2022             | 37.7%   | 1) 10.3%<br>2) 19.8%<br>3) 34.1% | NS              | Chemoradiotherapy  |
| Ghosh S [30]    | 2022             | 52.9%*  | 40.4%*                           | 0.008           | *Patients who could receive surgery                                  |
| Tang G [31]     | 2022             | 7.4%  | 11.8%                            | NS              |  |
| Kiss BI [36]    | 2022             | 14.8%   | 17.6%                            | NS              |  |
| Choi JY [13]    | 2021             | 36%   | 38.7%                            | 0.039           | All kinds of neoadjuvant therapy                                     |

TNT, total neoadjuvant therapy; NS, non-specific.

compared to the pre-pandemic period, has been reported to vary. Some studies have indicated that a higher proportion of patients received neoadjuvant treatment during the pandemic, while others found no difference between the two periods (Table 2) [12,13,20–31]. According to data from the Netherlands Cancer Registry, there was no difference in the proportion of patients treated with (neo)adjuvant therapy between the two periods [20]. Eklöv et al. documented changes in the treatment patterns of colon cancer between the pre-pandemic and pandemic periods using the Swedish Colorectal Cancer Registry [21,22]. Their reports indicated that a higher percentage of patients received preoperative chemotherapy in 2022 (5.1%) compared to 2019 (3.5%;  $P=0.0016$ ). However, in the case of rectal cancer, there was no significant difference in the number of patients who received neoadjuvant (chemo) radiotherapy between the two periods.

According to a multicenter study conducted in the UK, 22.3% of colorectal cancer patients experienced a change in the initial outcomes of management via a multidisciplinary team following the national lockdown. The use of short-course chemoradiotherapy increased from 15.4% to 45.2%, while the use of long-course chemoradiotherapy decreased from 56.3% to 14%. The researchers reported that this represented a significant deviation from standard practice in the UK [23].

Single-center cohort studies have reported a range of outcomes regarding neoadjuvant treatment (Table 2). Some studies have reported a significant increase in the use of neoadjuvant treatment, while others have found no difference in the proportion of patients undergoing preoperative treatment.

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## Changes in Surgery for Colorectal Cancer during the COVID-19 Pandemic

Limited data exist concerning the safety of colorectal cancer surgery during the early stages of the COVID-19 pandemic. Initial reports suggested that cancer patients were at an increased risk of contracting COVID-19 and often experienced more severe outcomes. As a result, both surgeons and patients were hesitant to proceed with elective surgeries that could potentially be postponed to a more opportune time [32]. Therefore, the number of operations performed has decreased due to delays during the pandemic period, which also impacted the surgical approach, referral type, and tumor-related complications.

Most studies have reported fewer patients undergoing surgery during the pandemic compared to the pre-pandemic period (Table 1). Aside from a small number of studies, most have described a higher proportion of emergency or urgent operations during the pandemic period (Table 3) [33–39]. However, this was not directly associated with treatment delays from diagnosis to surgery [22,28,31,33]. Studies that showed a higher proportion of emergency operations did not demonstrate a significant delay in treatment [28,33].

During the pandemic, surgeons have expressed significant concern about the transmission of the virus. In the early stages of COVID-19, a study indicated that while there was insufficient evidence to confirm the safety of minimally invasive surgery in terms of transmission, it could still be performed provided that appropriate precautions were taken. Disease progression was a factor that interfered with laparoscopic surgery. The proportion of patients who underwent laparoscopic surgery during the pandemic was comparable to that of the pre-pandemic period, according to most reports (Table 3). However, some studies reported a significant decrease in the use of the laparoscopic approach for elective surgeries during the pandemic [13,40].

The frequency of stoma formation increased notably during the pandemic period. Additionally, there was a rise in the number of palliative resections during the same period [13,20,27,36]. Lim et al. [39] reported a significant decrease in the percentage of patients who were candidates for surgery during the pandemic (73.6%) compared to the pre-pandemic period (82.2%;  $P < 0.001$ ).

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## Surgical Complications after Colorectal Cancer Surgery during the COVID-19 Pandemic

After surgery, a higher disease severity often predicts an increased likelihood of post-surgical complications. However, numerous studies have reported comparable surgical complications between the pandemic and pre-pandemic periods (Table 3). Uyan et al. noted a significant increase in postoperative complications during the pandemic period (20% vs. 42%;  $P = 0.014$ ). Patients in the pandemic period experienced significantly more extraperitoneal complications (18.8%) compared to the 5.4% observed in the pre-pandemic period. Nevertheless, the length of postoperative hospital stay and early postoperative mortality rates did not differ between the two periods [35]. The enhanced recovery program, already adopted by many societies for colorectal cancer management, has been proven to be suitable even for fragile patients [41–43]. This could be one of the reasons why most studies did not show a difference in the length of hospital stay.

Several studies have reported increased mortality rates during the pandemic. Kuryba et al. observed a significant rise in surgical mortality following emergency surgery (5.6% vs. 8.9%,  $P = 0.003$ ), based on a national study in England that used administrative hospital data. Although

**Table 3.** Surgery patterns and complications after colorectal cancer surgery

| Author                 | Publication year | Emergency surgery        |  | Laparoscopic surgery |                            | Surgical complications   |                          | Stoma formation |          |
|------------------------|------------------|--------------------------|--|----------------------|----------------------------|--------------------------|--------------------------|-----------------|----------|
|                        |                  | Pre-COVID-19             | COVID-19   | Pre-COVID-19         | COVID                      | Pre-COVID-19             | COVID-19                 | Pre-COVID-19    | COVID-19 |
| Cano-Valderrama O [34] | 2023             | 9.5%                     | 15.5%  |                      |                            | -                        | -                        | -               |          |
| Pirozzi BM [33]        | 2023             | 49%*                     | 67%*   | 63%                  | 68%                        | 8.8%                     | 15.7%                    |                 |          |
| Miyo M [25]            | 2022             | 3.8%                     | 4.1%   | 78.5%<br>Ro 8.9%     | 75.6%<br>Ro 13%            | -                        | -                        |                 |          |
| Freund MR [26]         | 2022             | -                        | -  | 8%                   | 83%                        | -                        | -                        |                 |          |
| Eklöv K [21]           | 2022             | 10%                      | 13%  |                      |                            | 14%*<br>20% <sup>‡</sup> | 11%*<br>13% <sup>‡</sup> | -               |          |
| Eklöv K [22]           | 2022             | 14%                      | 14%  | 54%*                 | 58%*                       | 12%                      | 11%                      | -               |          |
| Rottoli M [27]         | 2022             | 91%                      | 89.2%  | 51.9% <sup>‡</sup>   | 52.2% <sup>‡</sup>         | 34.3%                    | 31.9%                    |                 |          |
| Chen MZ [28]           | 2022             | 19.8*                    | 28.1%*   | 70.1%                | 73%                        | 19.5%                    | 16.3%                    |                 |          |
| Tarta C [29]           | 2022             | 68.7%* <sup>¶</sup>      | 50% (2020)* <sup>¶</sup><br>42.9% (2021)* <sup>¶</sup> | 31.3%                | 23.8% (2020)<br>19% (2021) | 163                      | 84                       |                 |          |
| Meijer J [20]          | 2022             | 5.3%*<br>1% <sup>‡</sup> | 7.7%*<br>1.3% <sup>‡</sup>                             | -                    | -                          | -                        | -                        | 12.2%*          | 18.7%*   |
| Ghosh S [30]           | 2022             | 12.7%                    | 20.6%  | 59.5%                | 61.8%                      | Leakage<br>6.4%          | 5.9%                     |                 |          |
| Tang G [31]            | 2022             | 7.4%                     | 8.8%   | 89%                  | 88.2%                      | 26.5%                    | 30.9%                    |                 |          |
| Uyan M [35]            | 2022             | 23%*                     | 52%*   | 29%                  | 19%                        | 20%*                     | 42%*                     |                 |          |
| Kiss BI [36]           | 2022             | 27.5%*                   | 40.8%*   | 8.8%                 | 5.3%                       | -                        | -                        | 31.9%*          | 43.7%*   |
| Choi JY [13]           | 2021             | -                        | -  | 88%                  | 81.2%                      | -                        | -                        | 1.8%*           | 4.1%*    |
| Kuryba A [40]          | 2021             | -                        | -  | 62.5%*               | 35.9%*                     | -                        | -                        |                 |          |
| Williams E [37]        | 2021             | 15.1%*                   | 29.6%*   | -                    | -                          | -                        | -                        |                 |          |
| Radulovic RS [45]      | 2021             | -                        | -  | 23.7%                | 26.5%                      | -                        | -                        | 21.7%           | 26.5%    |
| Lee T [38]             | 2022             | 11.7%                    | 17.1%  | 60.5%                | 71.7%                      | 10.5%                    | 3.8%                     |                 |          |
| Lim JH [39]            | 2021             | 0.3%                     | 0.2%   | -                    | -                          | -                        | -                        |                 |          |

Ro, robotic surgery.

\*Statistically significant.

\*Colon cancer.

†Rectal cancer.

¶Elective surgery.

there was a minor increase in mortality after elective surgery (0.9% vs. 1.2%,  $P=0.06$ ), it was not as noteworthy [40]. Intriguingly, Chen et al. reported a significantly lower in-hospital mortality rate during the pandemic period (2.7% vs. 0.5%;  $P=0.003$ ). They proposed that the allocation of additional resources and a higher staff-to-patient ratio during the pandemic may have contributed to the decrease in inpatient mortality, even during the pandemic period.

In general, surgical complications following colorectal cancer surgery did not significantly increase during the pandemic period.

## Changes in Tumor Stage and Oncological Variables of Colorectal Cancer during the COVID-19 Pandemic

Potential delays in the diagnosis of colorectal cancer could lead to disease progression and a higher proportion of advanced disease, which may be associated with worsening oncologic outcomes. Reports on stage migration during the pandemic period have been inconsistent. Many studies have reported an upshift in staging during the pandemic period, demonstrating a decrease in early-stage disease and an increase in metastatic disease (Table 4). In a study comparing patients who underwent minimally invasive surgery for colorectal cancer before and during the COVID-19 pandemic, Kuodo et al. [44] found a significantly higher number of cases with advanced tumor stage (pT4) in the COVID-19 group compared to the pre-COVID-19 group (P=0.026). Furthermore, the proportion of cases requiring combined resection of adjacent organs due to advanced T4 colorectal cancer was significantly greater in the COVID-19 group (16.4% vs. 4.4%, P=0.010). Kiss et al. [36] also reported an increased proportion of pT4b disease during the pandemic period, as well as a different stage distribution between the pandemic and pre-pandemic periods. Radulovic et al. [45] did not find differences in the proportion of emergency operations, surgical approaches, and stoma formation rates between the two periods. However, they reported a significantly increased incidence of T4b disease (3.3 % vs. 20.2%, P<0.01) during the COVID-19 pandemic and a decreased incidence of stage IIA disease

**Table 4.** Time to the initiation of treatment and stage distribution of colorectal cancer

| Author                 | Publication year | Time to treatment start, days |          | P-value | Comparison                | Stage (%)           |                     | P-value        |
|------------------------|------------------|-------------------------------|----------|---------|---------------------------|---------------------|---------------------|----------------|
|                        |                  | Pre-COVID-19                  | COVID-19 |         |                           | Pre-COVID-19        | COVID-19            |                |
| Cano-Valderrama O [34] | 2023             | 4.8                           | 6.4      | <0.001  | Stage I/II/III/IV         | 36.7/24.3/22.5/16.6 | 23.6/22.7/30.0/23.6 | 0.019          |
| Pirozzi BM [33]        | 2023             | 14                            | 15       | NS      | Stage I/II/III/IV         | 15/31.6/38.1/15.6   | 18/36.1/34.6/3.6    | NS             |
| Miyo M [25]            | 2022             |                               |          |         | Stage I/≥II               | 26.9/73.1           | 24.2/75.8           | 0.0011         |
| Freund MR [26]         | 2022             | 8.7                           | 11.1     | 0.0068  | Metastasis                | 3                   | 9                   | 0.05           |
| Rottoli M [27]         | 2022             | -                             | -        |         | Multiple liver metastasis | 72.1                | 82.2                | 0.09           |
| Chen MZ [28]           | 2022             | 54.9                          | 54.3     | NS      | -                         | -                   | -                   |                |
| Tarta C [29]           | 2022             | -                             | -        |         | Stage IV                  | 12                  | 12 (2020) 20 (2021) |                |
| Meijer J [20]          | 2022             | -                             | -        |         | Stage I/II/III/IV         | 29.8/26.6/22.2/19   | 20/25.5/26.8/26.2-  | <0.01          |
| Ghosh S [30]           | 2022             | -                             | -        |         | Stage I/II/III/IV         | 32.3/28.4/28.9/6    | 22.2/33.3/31.9/8.3  | NS             |
| Tang G [31]            | 2022             | 6.46                          | 5.18     | 0.0016  |                           | -                   | -                   |                |
| Kudou M [44]           | 2022             | -                             | -        |         | T4b                       | 4.4                 | 16.4                | 0.01           |
| Uyan M [35]            | 2022             | -                             | -        |         | Stage I/II/III/IV         | 16/52/23/9          | 10/23/44/23         | 0.005          |
| Kiss BI [36]           | 2022             | -                             | -        |         | T4b                       | 12.4                | 18.9                | 0.026          |
| Choi JY [13]           | 2021             | -                             | -        |         | Stage 0/I/II/III          | 3.1/25.1/34.2/37.7  | 4.3/26.7/31.2/37.8  | NS             |
| Kuryba A [40]          | 2021             | -                             | -        |         | Stage IV                  | 37.8                | 24.9                |                |
| Radulovic RS [45]      | 2021             | -                             | -        |         | T4b<br>Stage IIA          | 3.3<br>27.6         | 20.2<br>12.2        | <0.01<br>0.033 |

NS, non-specific.



(27.6% vs. 12.2%;  $P=0.033$ ).

Even during the COVID-19 pandemic, the distribution of disease stages could be altered due to lockdown policies. Williams et al. [37] examined the trends in diagnosis and treatment of colorectal cancer during the pandemic, using data from the binational Colorectal Cancer Audit registry of Australia and New Zealand. They segmented the year 2020 based on the restrictions implemented across both countries. No difference in disease stage was observed during the period of bidirectional restrictions compared to the previous 3 years. However, fewer cases of stage I disease and more cases of stage II or III disease were identified in the last 3 months of 2020.

Some reports did not find any stage migration during pandemic periods [13,24,33,38,39]. However, other risk factors, previously reported as contributors to recurrence, were observed at higher rates during the pandemic. Choi et al. [13] found no difference in stage distribution, but there was a significant increase in lymphovascular invasion during the pandemic (37.3% vs. 45.2%,  $P=0.001$ ). Pirozzi et al. [33] compared histopathological results during the pandemic, taking into account the strictness of lockdown measures. They found no differences in stage, nodal distribution, extra-mesorectal venous invasion, and tumor grading between two periods (peak-COVID-19 vs. post-peak-COVID-19) within the pandemic.

To date, no studies have reported on the recurrence or disease-free survival of colorectal cancer patients who received treatment during the COVID-19 pandemic. This may be due to the insufficient time that has elapsed since the onset of the pandemic to observe these long-term outcomes. It is crucial that we meticulously examine whether variations in pathological factors during the pandemic correlate with long-term cancer outcomes. This is a topic we hope to delve into in future studies.

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## Discussion

The COVID-19 pandemic has significantly impacted all aspects of our lives, including the healthcare system. COVID-19 has led to a decrease in cancer screenings, with colonoscopic screenings being particularly affected due to the necessity of visiting medical facilities. A decline in colorectal cancer screenings has been confirmed in many countries [17,18,28,33], and there is concern that this could impact the clinical, surgical, and oncologic outcomes of colorectal cancer [12,39]. The treatment patterns for colorectal cancer during the COVID-19 pandemic may vary greatly, depending on national and institutional policies and the healthcare system. Consequently, reports on disease progression, surgical outcomes, and oncologic variables have been quite diverse, even though most indicate a decrease in surgical volume during the pandemic period.

It is surprising that many studies have reported an increase in stoma formation, given that advancements in surgical techniques should enable sphincter preservation even in cases of very low rectal cancer [46–49]. Therefore, the higher rate of stoma formation during the pandemic period likely reflects disease progression rather than technical limitations. Neoadjuvant treatment, which can facilitate sphincter preservation, was even more commonly administered during the pandemic. It can be assumed that the proportion of laparoscopic procedures did not decrease, as suggested by many reports [26, 28–31]. Surgical complications typically remain stable in elective surgery. However, during the pandemic, there was a higher incidence of surgical complications, particularly in emergency cases, which are more prone to post-surgical complications [35–40]. This suggests that the overall increase in surgical complications during

the pandemic could be attributed to the higher proportion of emergency surgeries conducted within a specific medical community or facility.

The reporting of stage upshifting has been inconsistent. Some reports have indicated a higher proportion of advanced diseases, or conversely, a lower proportion of early-stage diseases. To determine whether the COVID-19 pandemic has compromised the long-term oncologic outcomes of colorectal cancer, we must await their long-term reports. Other factors, such as the number of harvested lymph nodes, lymphatic invasion, vascular invasion, perineural invasion, and preoperative obstruction, may also be associated with oncologic outcomes [13,39,50] in addition to the pathologic stage. However, many studies have not reported these variables. Furthermore, surgical difficulty, represented by operation time or the need for adjacent organ resection, may also be related to oncologic outcomes. Therefore, we must also carefully analyze these results in upcoming studies.

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## Conclusion

The COVID-19 pandemic has had various impacts on colorectal cancer treatment, affecting treatment patterns, surgical outcomes, and oncological factors. To formulate effective healthcare policies for future medical crises, it is crucial to thoroughly analyze the long-term consequences of the COVID-19 pandemic. As we transition into a post-mask era, which is gradually happening worldwide, it is important to prepare for potential future infectious diseases, including those transmitted through contact or droplets, much like COVID-19. Given the necessity of developing colorectal cancer treatment guidelines in anticipation of infectious disease pandemics, further research and considerations will be essential in the times ahead.

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## Acknowledgements

Not applicable.

### Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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### Author Contribution

The article is prepared by a single author.

### Ethics Approval and Consent to Participate

Not applicable.

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