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ORIGINAL RESEARCH

Impact of COVID-19 Pandemic on the Clinical and Pathologic Characteristics of Colorectal Cancer: A Retrospective Multicenter Study in South Korea

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Purpose: The COVID-19 pandemic has influenced various aspects of colorectal cancer (CRC) patient care, including diagnosis, treatment, and outcomes. This study assesses the pandemic's impact on CRC patients.

Methods: We performed a retrospective analysis of medical records for CRC patients who underwent surgery at five hospitals affiliated with Hallym University from January 2017 to December 2022. Patients were divided into two groups: the pre-COVID group (2017–2019) and the COVID group (2020–2022).

Results: Among 2038 patients, 987 (48.4%) were in the pre-COVID group, and 1051 (51.6%) were in the COVID group. The COVID group had more patients with two or more comorbidities ($P < 0.001$) and a higher incidence of rectal cancer ($P = 0.010$). While the rates of laparoscopic surgeries were similar, the COVID group had increased emergency surgeries ($P = 0.005$) and diversion procedures ($P = 0.002$). Additionally, the COVID group faced more overall complications ($P < 0.001$) and severe complications (Grade III–V, $P = 0.004$). There was a rise in lymphovascular invasion ($P < 0.001$) and T4 stage tumors ($P < 0.001$) within the COVID group. Despite these differences, both groups had similar 2-year overall survival rates ($P = 0.409$).

Conclusion: Although patients treated during the COVID period experienced more frequent stoma formation, complications, and adverse prognostic factors, there were no differences in short-term oncologic outcomes, which was likely due to the follow-up period being insufficient to detect differences in OS.

Keywords: colorectal cancer, COVID-19 pandemic, characteristics

Introduction

In December 2019, the novel coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first reported in Wuhan, China. The World Health Organization declared COVID-19 a pandemic on March 11, 2020, due to its global spread.[1,2]

The COVID-19 pandemic has had a significant impact on cancer management, affecting diagnosis, treatment, and prognosis. Many countries implemented restrictions on access to national healthcare systems to prevent the spread of COVID-19, leading to a reduction in national cancer screening programs. Additionally, individuals were hesitant to visit hospitals during the pandemic due to concerns about SARS-CoV-2 infection,[3] resulting in a global decrease in outpatient numbers, particularly in Italy and South Korea.[4,5] Although screening tests for colorectal cancer, such as colonoscopy and fecal occult blood tests, are crucial for early diagnosis and detection, their numbers decreased due to the clinical challenges posed by COVID-19.[6–8]

Several countries have observed a reduction in colorectal cancer incidence since the onset of the COVID-19 pandemic.[9,10] Delays in treatment increased the risk of complications such as obstruction, perforation, and hemorrhage in colorectal cancer patients, often necessitating emergency surgeries, which are linked to higher morbidity and mortality rates.[11,12] Additionally, delayed treatment resulted in more advanced disease stages, including higher tumor stages,

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perineural invasion (PNI), and lymphovascular invasion (LVI), leading to poorer prognoses.[11–15] A retrospective analysis of 166 colorectal cancer patients showed that those treated during the pandemic incurred higher costs for laboratory tests, anesthesia, and other medical expenses, resulting in greater overall treatment costs compared to those treated at other times.[16]

Moreover, the restrictions on inpatient visitors, which were intended to prevent the infection of patients and medical staff, can lead to acute social isolation, which can affect the outcomes of patients due to increased mental stress.[17,18] Consequently, patients may wish to be discharged early, even if they do not meet the discharge criteria, leading to shorter hospital stays but increased risk of readmission. Previous studies have described the impact of visitor restriction policies on pediatric patients, obstetrics, palliative care facilities, and intensive care units.[19,20] However, few studies have examined the impact of social isolation on the outcomes after colorectal cancer surgery.[21]

At the onset of the COVID-19 pandemic, several surgical societies, including the Society of the American Gastrointestinal and Endoscopic Surgeons, the European Association for Endoscopic Surgery, the Association of Coloproctology of Great Britain and Ireland (ACPGBI), and the American College of Surgeons, provided guidelines to assist surgeons in making treatment decisions for cancer patients.[22–24] For instance, the ACPGBI recommended Hartmann's procedure instead of resection with primary anastomosis to lower the risk of anastomotic leakage and advised against laparoscopic surgery due to concerns about aerosol transmission of COVID-19. However, these recommendations are based on limited evidence.[22]

This study aims to evaluate the impact of the COVID-19 pandemic on the treatment and clinical outcomes of colorectal cancer patients.

Methods

We performed a retrospective analysis of medical records for colorectal cancer patients who had surgery at five hospitals associated with Hallym University from January 2017 to December 2022. The hospitals included Hallym Sacred Heart Hospital, which is a tertiary care center, and four secondary care centers: Kangdong Sacred Heart Hospital, Kangnam Sacred Heart Hospital, Dongtan Sacred Heart Hospital, and Chuncheon Sacred Heart Hospital. Kangdong and Kangnam Sacred Heart Hospitals are situated in Seoul, while Hallym Sacred Heart and Dongtan Sacred Heart Hospitals are in Gyeonggi Province, and Chuncheon Sacred Heart Hospital is in Gangwon Province. Patients were divided into two groups: the pre-COVID group (2017–2019) and the COVID group (2020–2022), based on whether their diagnosis and treatment took place before or during the COVID-19 pandemic. The study was approved by the Institutional Review Board of Dongtan Sacred Heart Hospital (IRB 2024–01-005) and complies with the Helsinki Declaration. The requirement for informed consent was waived by the Institutional Review Board due to the study's retrospective nature.

Patients with incomplete medical records, a history of familial adenomatous polyposis, Lynch syndrome, or recurrent colorectal cancer were excluded from the study. Moreover, individuals diagnosed with malignant tumors such as neuroendocrine tumors, gastrointestinal stromal tumors, or lymphoma were not included; only those diagnosed with adenocarcinoma were part of the study. All patients scheduled for surgery underwent preoperative COVID-19 screening through real-time polymerase chain reaction tests conducted in an outpatient clinic or emergency department. Surgeries proceeded as planned if the test result was negative. If the result was positive, the surgery was postponed until the patient had fully recovered from COVID-19. The hospitals included in our study also restricted visits to the ICU, emergency room, and inpatient wards. Each patient was limited to one caregiver, who was required to test negative for COVID-19 before entering the hospital.

We gathered and analyzed data on patient characteristics, surgical details, postoperative outcomes, and pathological findings from the medical records of both the pre-COVID and COVID groups. Patient characteristics encompassed age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, comorbid conditions, tumor location, and carcinoembryonic antigen (CEA) levels. Surgical variables included whether the surgery was laparoscopic, conversions to open surgery, operation duration, emergency surgeries, diversion procedures, length of postoperative hospital stay (POS), and complications. The severity of complications was assessed using the Clavien–Dindo classification, with grades of 3 or higher deemed severe.[25] Pathological data included histological type, T stage, N stage, TNM stage, presence of PNI, LVI, and the count of harvested lymph nodes. Tumor stages were determined according to the 8th

edition of the American Joint Committee on Cancer (AJCC) TNM staging system.[26] The primary endpoint was to assess changes in TNM staging between the pre-COVID and COVID periods. Secondary endpoints included comparing the rates of emergency surgeries, laparoscopic procedures, and pathological features such as LVI and PNI between the two periods.

Statistical Analysis

Statistical analyses were performed using SPSS version 26.0 (SPSS Inc., Chicago, IL, USA). Fisher's exact test was utilized to compare categorical variables between the two groups, while the Mann–Whitney test was used for continuous variables. Continuous data are reported as medians with ranges, and categorical data are shown as counts and percentages. The Kaplan–Meier method was employed to assess overall survival (OS), and comparisons between the groups were made using the Log rank test. To evaluate the robustness of the findings, we performed sensitivity analyses by adjusting for key covariates, such as age, sex, ASA class (I/II vs III/IV), and presence of comorbidity in a multivariable analysis, using linear regression analysis for continuous variables and logistic regression analysis for binary variables. A P-value of less than 0.05 was considered statistically significant.

Results

Throughout the study period, 2103 patients underwent surgery for colorectal cancer at the five university-affiliated hospitals. We excluded 14 patients with neuroendocrine or gastrointestinal tumors, 21 patients with synchronous colorectal cancer, 25 patients with incomplete medical records, and 5 patients with familial adenomatous polyposis or Lynch syndrome. This left 2038 eligible patients: 987 in the pre-COVID group (48.4%) and 1051 in the COVID group (51.6%).

The mean ages of the patients in the pre-COVID and COVID groups were 67.4 and 68.0 years, respectively (P = 0.443; Table 1). There were no significant differences between the two groups concerning sex, BMI, presence of symptoms, or serum CEA levels. However, a higher proportion of patients in the COVID group were classified as ASA class III or V (48.0% vs 33.8%, P < 0.001). Additionally, the COVID group had more patients with two or more comorbidities (41.2% vs 33.1%, P < 0.001) and a higher percentage of rectal cancer cases (12.5% vs 8.9%, P = 0.010).

Both groups had comparable durations of POS (12.8 days vs 12.4 days, P = 0.365) and similar proportions of patients undergoing laparoscopic surgery (77.5% vs 77.8%, P = 0.209) or converting to open surgery (Table 2). However, the

Table 1 Patient Characteristics Before and During COVID-19 Pandemic

	Pre-COVID-19 (n=987)	COVID-19 (n=1051)	P
Age (years)	67.4 (12.4)	68.0 (12.0)	0.443
Sex			0.154
Male	578 (58.6)	648 (61.7)	
Female	409 (41.4)	403 (38.3)	
BMI (kg/m^2)	23.5 (3.4)	23.6 (3.6)	0.525
CEA	23.6 (190.3)	52.5 (720.7)	0.236
ASA			<0.001
I/II	653 (66.2)	546 (52.0)	
III/IV	334 (33.8)	505 (48.0)	
Comorbidities	665 (67.4)	747 (71.1)	0.070
Comorbidities ≥ 2	327 (33.1)	433 (41.2)	<0.001
Location of tumor			0.212
Right colon	334 (33.9)	357 (34.0)	
Left colon	563 (57.2)	563 (53.6)	
Rectum	88 (8.9)	131 (12.5)	0.010
Presence of Symptom	190 (19.3)	199 (18.9)	0.856

Notes: Data are presented as the number of patients (%) or mean (standard deviation) unless otherwise stated.

Abbreviations: n, number; BMI, body mass index; CEA, carcinoembryonic antigen; ASA, American Society of Anesthesiologists.

Table 2 Perioperative Outcome Before and During COVID-19 Pandemic

	Pre-COVID-19 (n=987)	COVID-19 (n=1051)	P	$P_{adjusted}$
Operation time (min)	214.9 (90.6)	200.1 (86.7)	<0.001	0.003
Laparoscopic surgery	768 (77.8)	793 (75.5)	0.209	0.746
Conversion	56 (5.7)	62 (5.9)	0.828	0.844
Emergent operation	78 (7.9)	122 (11.6)	0.005	0.094
Stoma formation	211 (21.4)	288 (27.4)	0.002	0.005
Duration of POS (days)	12.4 (8.5)	12.8 (10.2)	0.365	0.910
Complications	154 (15.6)	284 (27.0)	<0.001	<0.001
Clavien–Dindo classification			0.004	0.041
0/I/II	916 (92.8)	937 (89.2)		
III/IV	71 (7.2)	114 (10.8)		
Use of CTx	486 (49.2)	480 (51.1)	0.424	0.199

Notes: Data are presented as the number of patients (%) or mean (±standard deviation) unless otherwise stated.
Abbreviations: POS, postoperative stay; CTx, Chemotherapy.

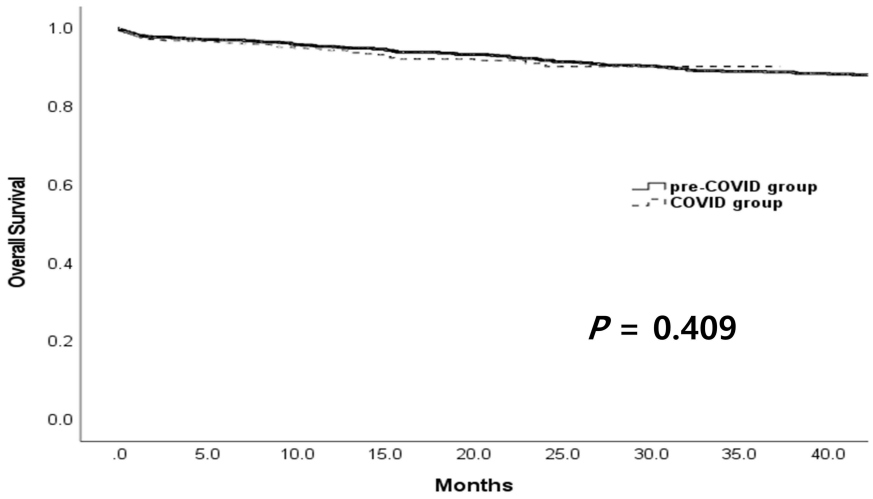
COVID group had significantly more patients with stoma formation (27.4% vs 21.4%, P = 0.002) and emergency surgeries (11.6% vs 7.9%, P = 0.005) compared to the pre-COVID group. Additionally, the incidence of complications was higher in the COVID group (27.0% vs 15.6%, P < 0.001), with a greater proportion of severe complications (grades III–V) according to the Clavien-Dindo classification (10.8% vs 7.2%, P = 0.004). In the sensitivity analysis, the perioperative outcomes remained unchanged, except for emergent surgery, for which the statistical significance changed from P = 0.005 to $P_{adjusted}$ = 0.094.

Although there were no significant differences in overall stage (P = 0.112), T classifications (P = 0.703), or N classifications (P = 0.973) between the groups, the proportion of patients with T4 tumors was higher in the COVID group compared to the pre-COVID group (19.4% vs 13.9%)(Table 3). The number of harvested lymph nodes was slightly greater in the pre-COVID group (23.9 vs 22.6, P = 0.041), but the proportion of patients with ≥12 harvested lymph nodes was similar in both groups. Furthermore, the COVID group had a higher proportion of patients with LVI compared to the

Table 3 Pathologic Outcome Before and During COVID-19 Pandemic

	Pre-COVID-19 (n=987)	COVID-19 (n=1051)	P	$P_{adjusted}$
Histologic grade			0.162	0.164
Well/Moderate	923 (94.2)	956 (92.6)		
Poorly/Undifferentiated	57 (5.8)	76 (7.4)		
Stage			0.112	0.155
0/1/2	580 (58.8)	581 (55.3)		
3/4	407 (41.2)	470 (44.7)		
T classifications			0.703	0.696
0/1/2	281 (28.5)	291 (27.8)		
3/4	704 (71.5)	757 (72.2)		
Only T4	137 (13.9)	203 (19.4)	< 0.001	0.006
N classifications			0.973	0.934
0/1	838 (85.2)	888 (85.3)		
2/3	145 (14.8)	153 (14.7)		
N of harvested LN	23.9 (15.0)	22.6 (12.7)	0.041	0.100
LN ≧ 12	917 (93.5)	961 (92.8)	0.526	0.509
LVI	368 (37.5)	483 (46.6)	<0.001	<0.001
PNI	226 (23.1)	250 (24.1)	0.572	0.466

Notes: Data are presented as the number of patients (%) or mean (standard deviation) unless otherwise stated.
Abbreviations: n number, lymph nodes; LVI, Lymphovascular invasion; PNI, Perineural invasion.



N at risk									
Pre-COVID-19	986	913	864	827	776	718	668	576	463
COVID-19	1049	883	588	350	214	93	27	6	0

Figure 1 Overall survival rate between the COVID-19 group and pre-COVID group (2 years-OS rate: COVID-19 group: 91.1% vs pre-COVID group: 91.8%, P = 0.409).

pre-COVID group (46.6% vs 37.5%, P < 0.001). In the sensitivity analysis, there were no differences in the results of the pathological variables between the two groups, except for the number of harvested lymph nodes for which the statistical significance changed from P = 0.041 to $P_{adjusted}$ = 0.100.

The mean follow-up period was 24.1 months overall (ranging from 1 to 72 months), with 36.7 months for the pre-COVID group and 12.2 months for the COVID group. The 2-year overall survival rate was similar between the COVID and pre-COVID groups (91.1% vs 91.8%, P = 0.409; Figure 1).

Discussion

In this study, although the frequencies of laparoscopic surgeries were similar, the COVID group had higher proportions of patients with rectal cancer, emergency surgeries, stoma formation, and complications, including severe grade III–V complications according to the Clavien-Dindo classification, compared to the pre-COVID group. Despite these differences, the 2-year OS rate remained comparable between the two groups. However, the COVID group showed a higher incidence of LVI and T4 tumor classifications.

Previous research has also observed a higher proportion of rectal cancer patients in COVID groups compared to pre-COVID groups.[1,13,27] Patients with rectal cancer typically exhibit symptoms such as anal pain, bleeding, and tenesmus, which lead to earlier detection and medical intervention compared to patients with proximal colon cancer, regardless of the availability of screening programs.[28] In this study, the COVID group had a significantly higher proportion of rectal cancer patients compared to the pre-COVID group (11.5% vs 6.4%, P < 0.001).

Multiple studies have observed a significant rise in emergent surgeries during the COVID-19 pandemic.[11,29] Many countries restricted access to their national healthcare system to prevent the spread of COVID-19 and to utilize limited resources more effectively in essential areas. In addition, people avoided hospital visits due to fear of COVID-19 infection.[3] These events led to reductions in national cancer screenings and outpatient visits.[4,5] Shinkwin et al reported a decrease in cancer diagnostic activity and an increase in large bowel obstruction in 2020 compared with 2018–2019.[11] In this study, although the COVID group had a higher frequency of emergent surgeries compared to the pre-COVID group (11.6% vs 7.9%, P = 0.005), after sensitive analysis, only a higher trend was observed in the COVID-19 group (P = 0.094).

Previous research has shown that postoperative complications and mortality rates following emergent colorectal surgery are significantly higher compared to elective procedures.[30] In our study, this higher frequency of emergent

surgery in the COVID group could be linked to the higher incidence of postoperative complications (27.0% vs 15.6%, $P < 0.001$, $P_{adjusted} < 0.001$). Furthermore, the proportion of patients with severe complications, classified as Clavien–Dindo Grade III–V, was higher in the COVID-19 group ($P = 0.004$, $P_{adjusted} = 0.041$). Several studies have reported the severity of complications using the Clavien–Dindo classification, and most of them found no significant difference.[27,29,31,32] However, Dong et al reported a higher proportion of complications classified as Grade I–IIIa in the COVID-19 group compared with the routine group (28% vs 12%, $P = 0.046$). This discrepancy might be attributed to the smaller sample size and the differences in the classification of severe complications compared with our study where severe complications were classified as grade III–IV.[33]

The rate of stoma formation has varied in previous studies.[7,12,13] Despite recommendations from several major societies to adopt low-risk strategies in colorectal surgery, including the construction of stomas to reduce the risk of anastomotic leakage,[16,22] a meta-analysis involving 11,082 patients found that the frequencies of anastomotic leakage were similar in both pre-pandemic and pandemic periods. This meta-analysis indicated that routine stoma formation might not be necessary.[34] However, our study observed a significant increase in stoma formation from 21.4% in the pre-COVID period to 27.4% during the COVID period ($P = 0.002$, $P_{adjusted} = 0.005$). This rise could be due to the higher proportion of rectal cancer and emergent surgery in the COVID group. In emergent surgery situations, the lack of bowel preparation may increase the risk of anastomotic leakage, which could explain the higher rate of stoma formation observed in the COVID group.[35]

The use of laparoscopic surgery became a significant concern during the COVID-19 pandemic. Previous studies have highlighted the presence of various bacteria and activated viruses, such as Corynebacterium and human immunodeficiency virus, in surgical smoke.[36,37] While direct evidence linking SARS-CoV-2 transmission to medical staff through aerosols is lacking, several guidelines issued during the early stages of the pandemic recommended minimizing laparoscopic procedures.[22,38] However, Xu et al argued that laparoscopic surgery, conducted within a confined surgical space, reduces the risk of bodily fluid or tissue exposure, thereby lowering the risk of COVID-19 transmission.[39] A more recent guideline suggested that both laparoscopic and open surgeries in patients with COVID-19 were associated with similar rates of COVID-19 among surgical staff, with laparoscopy demonstrating lower perioperative mortality.[40] Since the patients included in our study underwent screening and tested negative for COVID-19 infection, we continued to practice laparoscopic surgery during the pandemic. Consequently, there was no observed change in the proportion of patients undergoing laparoscopic surgery between the pre-COVID and COVID groups (77.8% vs 75.5%, $P = 0.209$).

Acute social isolation due to COVID-19 may also affect the patient's mental health and ability to cope with postoperative stress.[17,18] This has led to a tendency for patients to be discharged early even if they do not meet the discharge criteria, which can increase the readmission rate. Some studies have reported a reduction in the length of stay (LOS) during the COVID-19 period compared to the pre-COVID-19 period,[41,42] but others found no difference in LOS between the pre-COVID-19 and COVID-19 periods.[27,31,43] We found no difference in the POS, which can be explained by the fact that each patient was allowed one caregiver (usually a family member, who needed to test negative for COVID-19 before entering the hospital), which reduced the sense of isolation and could explain the consistent duration of POS during the COVID-19 and pre-COVID-19 periods.

Concerning colorectal cancer, the suspension of cancer screening and treatment delays during the COVID-19 pandemic may result in a more advanced disease stage. However, findings from various studies regarding stage distribution during the pandemic period have been inconsistent. A French multicenter study found no significant differences in TNM stage distribution between the pre-SARS-CoV-2 infection period (2018–2019) and the COVID period (2020).[44] Conversely, Aguiar et al reported a higher proportion of patients with advanced clinical stage (cT4 or cN + or M1) during the COVID period compared to the pre-COVID period.[45] Similarly, other studies have noted differences in stage distribution before and during the pandemic. For instance, a multicenter study in The Netherlands reported a decrease in patients with stage I but no significant change in stage IV in the COVID group compared to the pre-COVID group.[46] In our study, while the TNM stage tended to be more advanced in the COVID group, it did not reach statistical significance ($P = 0.112$, $P_{adjusted} = 0.155$). However, the proportion of patients with pathologic T4 classification was significantly higher in the COVID group ($P < 0.001$). T4 classification indicates tumor extension through all layers of the bowel wall with infiltration of surrounding structures, signifying an advanced tumor status. Consistent with these

findings, Choi et al reported a higher proportion of patients in the COVID period requiring combined resection of adjacent organs due to bulky tumors compared to the pre-COVID period in a Korean study.[12]

When interpreting the findings of this study, it's important to acknowledge several limitations. Firstly, despite including patients from five hospitals across three regions of South Korea, which collectively represent a significant portion of the population, the study may not fully capture the overall medical landscape of the country. However, the inclusion of secondary hospitals across various regions may offer insights into regional healthcare dynamics compared to tertiary hospitals. Additionally, although this multicenter study involved a larger patient cohort compared to previous studies, the sample size might still be insufficient to comprehensively assess the impact of COVID-19 on patients with colorectal cancer. Therefore, future population-based studies are warranted. Furthermore, long-term follow-up is crucial to evaluate the oncologic outcomes of colorectal cancer patients affected by COVID-19. However, due to the pandemic's onset in early 2020, the follow-up period for patients in the COVID-19 group was unavoidably limited, and there was an inevitable difference in the follow-up period between the pre-COVID-19 and COVID-19 groups (36.7 vs 12.2 months). Consequently, few studies have reported oncologic outcomes during the COVID-19 era, and only one study has reported 1-year.[44] Some studies have used predictive models to assess oncologic outcomes.[47,48] To address this gap, our future research aims to conduct a study with an extended follow-up period to thoroughly evaluate the oncologic outcomes of colorectal cancer patients affected by COVID-19.

Although previous studies have selectively compared the outcomes of colorectal cancer patients over short periods, ranging from just 1 month to as long as 10 months before and after COVID-19,[1,12–14,16,27,34,39] this study compared the outcomes over a longer, continuous period of 3 years before and after COVID-19. This approach allows for a more accurate assessment of the impact of COVID-19 on the outcomes of colorectal cancer patients.

Conclusion

The present study revealed significantly higher rates of rectal cancer, stoma formation, and complications (including severe grade III–V complications according to the Clavien–Dindo classification) during the COVID-19 pandemic period. Although the patients encountered during this period had more adverse prognostic factors, there were no differences in short-term oncologic outcomes, which was likely due to the follow-up period being insufficient to detect differences in OS. However, the long-term impact of the COVID-19 pandemic on oncologic outcomes requires further evaluation.

Ethics Approval and Informed Consent

The study was approved by the Institutional Review Board of Dongtan Sacred Heart Hospital (IRB 2024-01-005) and complies with the Helsinki Declaration. Owing to the retrospective nature of the study, the Institutional Review Board waived the need to obtain informed consent. The researcher keeps a personal list of subject identifiers to access patient records and assigns identification codes to each patient. Clinical research documents are then secured with passwords to prevent unauthorized access, ensuring that only authorized personnel can view them.

Author Contributions

All authors made significant contributions to conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no conflicts of interest.

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