RESEARCH ARTICLE

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Impact of preoperative COVID infection on the outcomes of planned curative-intent cancer surgeries in the second wave of the pandemic from a tertiary care center in India

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Abstract

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic was an unforeseen calamity. Sudden disruption of nonemergency services led to disruption of treatment across all specialties. Oncology revolves around the tenet of timely detection and treatment. Disruption of any sort will jeopardize cure rates. The time interval between coronavirus infection and cancer surgery is variable and needs to be tailored to avoid the progression of the disease.

Methods: We analyzed the impact of preoperative coronavirus disease 2019 (COVID-19) infection on the planned cancer surgery, delay, disease progression, and change of intent of treatment from April 1 to May 31, 2021 at a tertiary care center. All preoperative positive patients were retested after 2 weeks and were considered for surgery if the repeat test was negative and asymptomatic.

Findings: Our study included 432 preoperative patients of which 91 (21%) were COVID-19 positive. Amongst this cohort, 76% were operated and the morbidity and mortality were comparable to the COVID-19 negative cohort. Around 10% of the COVID-19 positive were lost to follow up and 10% had disease progression and were deemed palliative

Interpretation: SARS-CoV-2 infection has adversely impacted cancer care and a 2-week waiting period postinfection seems to be a safe interval in asymptomatic individuals to consider radical cancer surgery.

KEYWORDS

cancer surgery, morbidity, outcome, preoperative COVID-19, second wave

1 | INTRODUCTION

The first case of novel coronavirus infection in India was reported on January 30, 2020. There have been 23 million people infected as of May 12, 2021.¹ The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant B.1.617 was the driver of the second wave of the pandemic also known as delta variant and has now been classified as a variant of concern by the World Health

Organisation (WHO).² The rates of transmission of this variant are about 40% higher than the previous strains leading to the increasing caseload in India.² With the ongoing second wave and increased infectivity of the virus, delivering cancer care amidst this pandemic has been an extremely challenging task. There has been a reduction of more than half the patients from the healthcare system as regards new registration, major and minor surgeries all across major cancer hospitals in India.¹ Oncology revolves around the tenet of timely

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detection, diagnosis, and treatment completion. Delay of any sort will lead to stage migration and jeopardize cure rates. Experience gained from the first wave suggests that with suitable guidelines major cancer surgeries can be performed without increase morbidity or mortality.³ However, with routine use of preoperative SARS-CoV-2 testing, the precise timing of surgery after infection is still not established. The increasing infection rates due to enhanced infectivity of the delta strain in India led to increasing preoperative positive rates of real-time reverse transcriptase-polymerase chain reaction (RT-PCR), sometimes with persistent positivity for 3-4 weeks. Major cancer surgeries during the asymptomatic infection are generally avoided due to chances of infection and postoperative complications.⁴ This has possibly led to inordinate delay from decision making to the actual execution of surgery. This leads to a long treatment gap and possible disease progression. We followed a protocol of repeating an RT-PCR two weeks after a positive report and considering patients for surgery with a negative report. In this article, we have analyzed short-term outcomes for patients who were detected to be coronavirus disease 2019 (COVID-19)-positive during initial preoperative testing and had delayed surgery after testing negative and compared them with COVID-19-negative patients operated during the same timeframe. We have also assessed the impact of delay due to preoperative COVID-19 infection on disease progression and intent of treatment.

2 | MATERIALS AND METHODS

We conducted a retrospective analysis of a prospectively maintained database of April and May 2021 that was the peak of the second wave with massive numbers of daily positive reports in the state of Uttar Pradesh. We restricted our analysis to those cancer patients who were planned for surgery with curative intent. Our policy, in general, was to repeat a COVID-19 RT-PCR test after 2 weeks of a positive report and consider surgery if the patient was asymptomatic and had turned negative on repeat RT-PCR. Patients with a negative RT-PCR were admitted within 72 h of the report, most patients being admitted within 24 h. All patients in the initial preoperative positive group were assessed by a complete cardiopulmonary workup including chest X-ray or computed tomography thorax, two-dimensional echocardiography, and a 6min walk test. If deemed unfit they were optimized and then operated. We analyzed the number of patients in whom the intent of treatment changed from curative to palliative due to the delay in treatment, patients lost to follow-up, and operative morbidity of such patients as compared with COVID-19 RT-PCR negative patients operated in the same timeframe. Delay to surgery from COVID-19 was calculated from the date of COVID-19 positive report to the date of surgery. Postoperative patients were retested if clinical symptoms were suggestive of COVID-19 infection. For postoperative patients, the time to COVID-19 infection was taken as the postoperative day it was detected. Morbidity was measured using the Clavein-Dindo scoring. The study was approved by the Institutional Ethics Committee.

2.1 | Statistical analysis

The data was recorded in the prospective database of the disease management groups, and complete records for delay in surgery were added using Statistical Product and Service Solutions (SPSS), IBM Corp, for Windows version 21.0, (SPSS Inc.). Descriptive analyses were performed for age, sex, surgery performed, and delay due to COVID-19, while intraoperative and postoperative parameters were compared between patients with and without preoperative infection.

3 | RESULTS

There were a total of 432 preoperative patients who underwent RT-PCR testing in the defined study period (April 1–May 31, 2021) at our center. Of these, 331 (76.6%) were RT-PCR negative and underwent surgery as planned. Ninety-one patients (21%) tested RT-PCR positive, and surgery/definitive treatment was delayed in them by variable intervals depending on their symptoms and time to turn RT-PCR negative. In addition, there were 10 patients (2.4%) who had tested RT-PCR negative in the initial preoperative test and were operated as planned but were detected to be RT-PCR positive in the postoperative setting.

Amongst the COVID-19-positive cohort (preoperative + postoperative positives) 77 out of 101 (76.2%) were operated as shown in Figure 1. While assessing the remaining preoperative COVID-19-positive patients, six had their plan changed to neoadjuvant therapy, nine were lost to follow up and nine were deemed palliative due to disease progression. Patients rendered palliative took 24-60 (median 32) days to turn COVID-19-negative following which restaging revealed disease progression. The demographic characteristics of operated patients are summarized in Table 1. Most patients (89%) had an asymptomatic COVID-19 infection and were detected on routine preoperative testing. While comparing operated cases between the COVID-19-positive cohort and those who were always COVID-19-negative, the age group was similar (47.3 vs. 47.7 years), there was a preponderance of male sex, oral cavity, and breast primary in both groups, the duration of hospital stay (7.8 vs. 6 days) as well as the in-hospital morbidity (12.9% vs. 12.7%) were comparable between the two groups. The 30-day mortality was 2.5% in the COVID-19-positive group, while it was 0.6% in the COVID-19negative group. The median delay in surgery in those 67 patients who were tested COVID-19-positive in their initial preoperative RT-PCR but could undergo surgery later was 23 days (7-60).

In the COVID-19-positive group, there were two postoperative mortalities; both were due to severe ARDS as a result of SARS-CoV-2 infection. One patient was operated on for oral cavity malignancy and the other patient for radical cholecystectomy. Both mortalities were in the group of 10 patients who were initially COVID-19-negative on preoperative testing but were detected to be COVID-19-positive in the postoperative period. No patient among the 67 patients (the initial preoperative positive group who had delayed surgery) died in the postoperative period.

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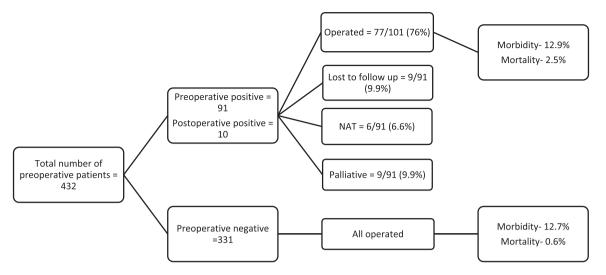


FIGURE 1 Surgical oncology COVID-19-positive patients' outcome. NAT, neoadjuvant therapy

4 | DISCUSSION

The novel SARS-CoV-2 pandemic created an overwhelming healthcare crisis that required a vision to maintain effective cancer care services along with COVID-19 healthcare facilities to be ahead of time. Lessons learned to tackle the pandemic included the creation of a COVID-19 action group, screening patients at entry points, preparedness to deal with infected patients, consciously taking treatment decisions based on riskbenefit ratio, and extensive use of telemedicine to reduce inhospital visits.^{5,6} However, decisions were impacted by a surge of digital information with multiple discordant guidelines for the management of patients with cancer.⁷ Perioperative outcomes for major cancer surgeries reported during the first wave of the pandemic from several centers including ours did not reveal a significant rise in morbidity or mortality.^{3,8-11} However, there have been delays from referrals to diagnoses to definitive treatment including surgeries which has resulted in the loss of lives.¹²⁻¹⁶ The paramount fact to be gathered is that unless we continue cancer care as routine, we will be losing lives over and above the lives lost due to the pandemic. To the best of our knowledge, the impact of delays due to preoperative COVID-19 infection and follow-up of these patients has not been published. Post novel coronavirus infection, recent COVID-19Surg Collaborative international prospective study has defined more than or equal to 7 weeks intervals for surgery to reduce perioperative mortality to baseline.¹⁷ However, National Cancer Database has calculated a safe postponement period for cancer surgeries to be 4 weeks without adversely affecting survival or disease progression.¹⁸ This implies that we need a middle ground for cancer surgeries accepting the possible slightly increased morbidity to balance disease progression. We also need to be cognizant of the fact that different cancers have different biological clocks, and the extrapolation of data will be erroneous.

Delays during the pandemic have resulted in an increase in neoadjuvant chemotherapy for pancreatic cancer and colorectal liver metastases and locoregional treatment for hepatocellular carcinoma.¹⁹ During the peak second wave of the pandemic, our data shows that approximately 10% of patients were rendered palliative even though our services were fully functioning without any reduction in capacity. The average waiting time between the decision to actual execution of surgery at our center is about 3-4 weeks because of various factors including patient load, manpower issues, number of operating rooms, the time required for the patients to be prepared for surgery, etc. An additional delay due to the diagnosis of COVID-19 in the routine preoperative testing can potentially change the intent of treatment from curative to palliative. Amongst our two hospitals in Varanasi, Uttar Pradesh under the Tata Memorial Centre, one (Homi Bhabha Cancer Hospital) was converted into an L2/L3 COVID-19 facility while the other (Mahamana Pandit Madan Mohan Malviya Cancer Centre) continued cancer care services in full strength. This resulted in the segregation of COVID-19 and COVID-19-free pathways with separate wards, intensive care units, and operation theaters which has shown to provide safe elective cancer surgeries with lower postoperative pulmonary complications.²⁰ Published literature identifies the fact that perioperative infection with SARS-CoV-2 either preoperatively or postsurgery can lead to mortality as high as 33%.^{21,22} Mortality defined by published literature for COVID-19 infected patients varies significantly by the specialty discussed.²² Our data show that the COVID-19-positive group (those with initial preoperative infection and delayed surgery, or those with postoperative infection in the hospital) did not have a very significant increase in mortality as compared to COVID-19-negative patients. Both the postoperative mortalities in the COVID-19-positive group were among those 10 patients who tested positive postoperatively despite having a negative RT-PCR preoperatively, implying that either the initial preoperative RT-PCR was false-negative or the patients acquired the infection around the time of their admission into the hospital.

TABLE 1 Distribution and outcome of surgical oncology patients

Variables	COVID-19 RT-PCR positive	COVID-19 RT-PCR negative
n = 432	Preoperative-91 (21%)	331
	Postoperative-10	
COVID-19 symptoms (n = 91)	Asymptomatic-81 (89%)	NA
	Mild symptoms-9	
	Hospitalized-1	
Delay to surgery from COVID-19 (n = 67 in initial preoperative positive group who were later operated)	23 (7-60)	NA
Postoperative day on which RT-PCR was positive ($n = 10$)	4 (1-20)	NA
n	77 (preop and postop)	331
Age (years)	47.3 (20-72)	47.7 (16-82)
Sex M:F	40:37 (60:40)	181:150 (55:45)
ASA I	61	147
ASA II	15	24
ASA III	1	4
Procedure/site		
Oral cavity	27	161
Thyroid	0	6
Larynx	0	2
Breast conservation	8	25
Mastectomy	11	56
TAH + BSO + omentectomy	10	25
Esophagectomy	2	2
Lobectomy/pneumonectomy	1	4
Radical cholecystectomy	10	9
Whipples	2	3
Gastrectomy	2	6
Colectomy/LAR/APR	2	14
CRS + HIPEC	0	2
Hepatectomy	0	1
Others	2	15
Intraoperative blood loss (ml)	50-3000	10-6000
Duration of hospital stay	7.8 (2-28)	6 (1-60)
Clavien-Dindo > /=IIIa	10 (12.9%)	42 (12.7%)
30-day mortality	2 (2.5%)	2(0.6%)

Abbreviations: APR, abdominoperineal resection; COVID-19, coronavirus disease 2019; CRS + HIPEC, cytoreductive surgery + heated intraperitoneal chemotherap; LAR, low anterior resection; RY-PCR, real-time reverse transcriptase-polymerase chain reaction; TAH + BSO, total abdominal hysterectomy with bilateral salphingoophorectomy.

We would like to propose that curative-intent surgical candidates should not be referred for neoadjuvant treatment just because of the fear of the continuing pandemic, and routine surgical care should be undertaken. Our wait period of 2 weeks for retesting COVID-19 RT-PCR positive preoperative patients did not result in prohibitive morbidity and mortality for asymptomatic patients operated after a negative RT-PCR. This should be considered along with the patient's performance status, age, disease status, and comorbidities while planning surgery. Another major stressing point to prevent either preoperative or postoperative infection amongst patients is to reduce hospital visits, strict reinforcement of wearing masks and hand hygiene and admitting patients one day prior or on the same day of surgery followed by discharge as soon as feasible to avoid contracting the infection in the hospital. We need to continue providing cancer care at its optimum along with treating and preventing the spread of the pandemic to maintain the survival advantage our treatment is likely to offer.

An integral part of disaster management is preparedness to mitigate another hit. Unfortunately, India has been one of the worst-hit nations in the second wave of the pandemic. To get ahead of the pandemic we need to create virus-free zones and declare cancer care as a priority rather than wait for the surge to decline.^{23,24} We also need a better and comprehensive guideline for infected and recovered patients to guide treatment decisions that are time sensitive.

5 | CONCLUSION

SARS-CoV-2 infection has adversely impacted cancer care and a 2-week waiting period post-SARS-CoV-2 infection seems to be a safe interval in asymptomatic individuals to consider radical cancer surgery. This will ensure the safe and timely delivery of curative-intent treatment.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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How to cite this article: Pandrowala S, Ramraj D, Shankar R, et al. Impact of preoperative COVID infection on the outcomes of planned curative-intent cancer surgeries in the second wave of the pandemic from a tertiary care center in India. J Surg Oncol. 2022;125:107-112. https://doi.org/10.1002/jso.26697