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RESEARCH ARTICLE

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Incidence of SARS-CoV-2 infection among asymptomatic patients undergoing preoperative COVID testing prior to cancer surgery: ASPECT study

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Abstract

Background and Objectives: The COVID-19 pandemic, with high rate of asymptomatic infections and increased perioperative complications, prompted widespread adoption of screening methods. We analyzed the incidence of asymptomatic infection and perioperative outcomes in patients undergoing cancer surgery. We also studied the impact on subsequent cancer treatment in those with COVID-19.

Methods: All patients who underwent elective and emergency cancer surgery from April to September 2020 were included. After screening for symptoms, a preoperative test was performed from nasopharyngeal and oropharyngeal swabs before the procedure. Patients were followed up for 30 days postoperatively and complications were noted.

Results: 2108 asymptomatic patients were tested, of which 200 (9.5%) tested positive. Of those who tested positive, 140 (70%) underwent the planned surgery at a median of 30 days from testing positive, and 20 (14.3%) had ≥ Grade III complications. Forty (20%) patients did not receive the intended treatment; 110 patients were retested in the Postoperative period, and 41 (37.3%) tested positive and 9(22%) patients died of COVID-related complications.

Conclusion: Routine preoperative testing for COVID-19 helps to segregate patients with asymptomatic infection. Higher complications occur in those who develop COVID-19 in postoperative period. Prolonged delay in surgery after COVID infection may influence planned treatment.

KEYWORDS

asymptomatic, cancer surgery, incidence, SARS-CoV-2 infection

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1 | INTRODUCTION

The COVID-19 pandemic has had a major impact on the conduct of cancer surgeries, with an estimated 2.3 million procedures being canceled worldwide.[1] Studies have documented higher pulmonary complications and mortality in patients with perioperative severe acute respiratory syndrome coronavirus (SARS-CoV-2) infection.[2] Aerosol-generating procedures in infected patients place operating room staff at greater risk of infection. As the pandemic progressed, it became apparent that many of the infections were asymptomatic, and these asymptomatic individuals could still transmit the infection to other patients and healthcare workers. Studies have shown the incidence of asymptomatic infection in the range of 1.6%–56.5%.[3,4] This has important clinical implications, as asymptomatic individuals are also infectious,[5] besides being at risk of developing the severe disease later. Early detection may reduce cross-infection and, also help manage resources more effectively.[6] To continue time-sensitive cancer surgeries while minimizing the risk of postoperative morbidity in patients, and the risk of infection in hospital personnel, we implemented routine preoperative testing for SARS-CoV-2 for all elective and emergency surgical procedures at our institute.

Currently, data from routine preoperative testing of asymptomatic individuals is available from small studies only.[6–8] Moreover, there is scarce data on the impact of a positive COVID-19 diagnosis, on treatment for patients with cancer originally planned for surgical resection. In our study, we sought to ascertain the incidence of asymptomatic COVID-19 infection in patients scheduled for elective and emergency cancer surgery in a high-volume cancer center. We also assessed the early postoperative (30-day) complications and the impact on subsequent cancer treatment in those who tested positive.

2 | METHODS

We conducted a retrospective analysis of a prospectively maintained database of patients who underwent preoperative testing for COVID-19 infection at the Tata Memorial Hospital, between April 2020 and September 2020. All patients who were scheduled to undergo elective and emergency cancer surgery under general anesthesia during this period were included in the study.

Patients planned for elective cancer surgery were contacted telephonically and screened for symptoms at a dedicated "fever clinic" in the out-patient department (OPD). Only those who were asymptomatic were planned for surgery and underwent a mandatory preoperative test from nasopharyngeal and oropharyngeal swabs collected in the viral transport medium (VTM) within 48 h before the scheduled surgery. The samples were subjected to ribonucleic acid (RNA) extraction and subsequent one-step reverse transcription-polymerase chain reaction (RT-PCR) using the Indian Council of Medical Research (ICMR) approved viral RNA extraction and COVID PCR kits (with primers for at least two target viral genes—S/N/E/ORF genes). The tests were run with at least one known (kit provided) positive control, no template (plain VTM) control, and one control of water, that is, no template no VTM control. The tests were interpreted as negative, inconclusive, and positive as per standard criteria laid by the kit protocol.

Patients with negative tests were admitted and underwent surgery as planned in the same indoor admission. Patients with an inconclusive report had a repeat test and two consecutive inconclusive reports were considered as a positive result according to institute protocol. Patients who tested positive, and were scheduled to undergo elective surgery, were admitted to a dedicated COVID-19 isolation ward and monitored for symptoms and disease severity, or isolated at home if they had the facility. Patients opting for home isolation were counseled to report telephonically in case of worsening of symptoms. After an isolation period of 15 days, patients were retested and those with two consecutive negative results more than 24 h apart without symptoms were considered suitable to resume surgical treatment as planned. In the event of a persistent positive result, the test was repeated at weekly intervals till the patient tested negative twice.

Patients who required emergency surgery had the swabs collected and the surgery was performed in a designated "COVID" operating room taking universal precautions, while awaiting the test result. Based on the result, patients with a positive test were segregated to an intensive care unit/isolation ward and those with a negative test were subsequently shifted to a regular postoperative care unit.

Following surgery and postoperative recovery, patients were followed up for 30 days either telephonically or via outpatient visits, and any complication was noted as per the Clavien–Dindo classification system.[9] Impact of the SARS-CoV-2 infection on patients' original surgical plan was evaluated.

The Institutional Ethics Committee (IEC) approved the study with a waiver of consent, in view of the retrospective design. Data collection were in accordance with the Declaration of Helsinki and the trial has been registered in the Clinical Trials Registry-India (CTRI), bearing Unique Identification Number (UIN)- CTRI/2021/04/032965.

Statistical analysis was performed by using IBM SPSS® Statistics 25.0. Proportions and descriptive statistics were used. χ^2 test or Fischer's exact test were used to compare categorical variables where appropriate, with $p < 0.05$ being significant.

3 | RESULTS

3.1 | Asymptomatic positivity rate

A total of 2108 asymptomatic patients were tested preoperatively for SARS-CoV-2 by RT-PCR between April 21st and September 30th, 2020. Of these, 2034 (96.5%) were planned for elective surgery and 74 (3.5%) needed to undergo emergency surgery. One hundred and ninety-four (9.2%) patients tested positive, and 15 patients (0.7%) had inconclusive reports (Table 1). Of the 15 patients with inconclusive results, a repeat swab was performed in all, of which six

tested inconclusive again, and hence were considered positive as per institute protocol and advised isolation. Nine patients tested negative and were admitted for the planned surgery. Therefore, the overall asymptomatic positivity rate was 9.5%. (200/2108). Adults (>15 years) had a positivity rate of 9.7% (198/2032) while the lowest positivity rate was seen among pediatric patients (n = 2/76; 2.6%)

3.2 | Impact of SARS-CoV-2 on oncological plan

Of the 200 patients who tested positive, 140 (70%) underwent the prior planned surgery at our institute during the study period; 15 (10.7%) of these were emergencies. The median interval between the initial positive test and surgery in 125 patients who subsequently underwent elective surgery was 30 days (range, 14–124 days). Of the remaining 60 (30%), 13 (6.5%) patients underwent surgery after the period of this study, 7 (3.5%) underwent surgery elsewhere, 19 (9.5%) patients had progressive disease with change in oncological treatment plan and, 21 (10.5%) patients either defaulted the planned treatment or were lost to follow-up. Thus, 40 (20%) patients eventually did not undergo planned surgery (Figure 1).

3.2.1 | Postoperative course after SARS-CoV-2 infection

Of the 140 patients who had tested positive for SARS-CoV-2 and eventually underwent surgery (at our institute during the study period), 20 patients (15 elective and five emergency surgeries—overall 14.3%) had major (Clavien–Dindo Grade III and above) postoperative complications (Table 2). Notably, 5/15 (33.3%) patients who underwent emergency surgery despite testing positive had major complications and 4/15 (27%) died in the postoperative period.

Among the 125 patients who underwent elective surgery after a period of isolation and subsequent two negative tests, there was no significant difference in the frequency of major (Grade III and above) complications when operated at <30 days (n = 7/61, 11.5%) and >30 days (n = 8/64, 12.5%) from the date of a positive result (OR: 0.91, 95% CI: 0.31–2.68; p = 0.86).

Five patients (3.6%) died of postoperative complications. Of the 125 patients undergoing elective surgery, one patient (0.8%) had cardiac arrest after surgery (suspected pulmonary embolism). The other four patients who were being treated with the best supportive care due to poor performance status and advanced nature of disease had undergone emergency surgery (two palliative tracheostomies, one palliative gastrojejunostomy, one exploratory laparotomy and ureterostomy for bladder perforation and ureterostomy). Two of these patients died of COVID.

3.2.2 | Retesting for SARS-CoV-2 in the postoperative period

Hundred and ten patients were retested (after a negative preoperative test and subsequent surgery) in the 30-day postoperative period (median: 9 days; range: 1–30 days) due to symptoms suspicious of COVID like fever, persistent cough, dyspnea, and/or fall in oxygen saturation. Of these, 41 patients tested positive

TABLE 1 Initial results of SARS-CoV-2 RT-PCR test among the entire cohort

Result	Frequency	%
Positive	194	9.2
Negative	1899	90.1
Inconclusive	15	0.7
Total	2108	100

Abbreviation: RT-PCR, reverse transcription-polymerase chain reaction.

TABLE 2 Perioperative complications in patients who underwent surgery after testing positive

CD grade	*N* (%)
I	4 (10.8)
II	13 (35.1)
IIIa	6 (16.2)
IIIb	7 (18.9)
IVa	2 (5.4)
V	5 (13.6)

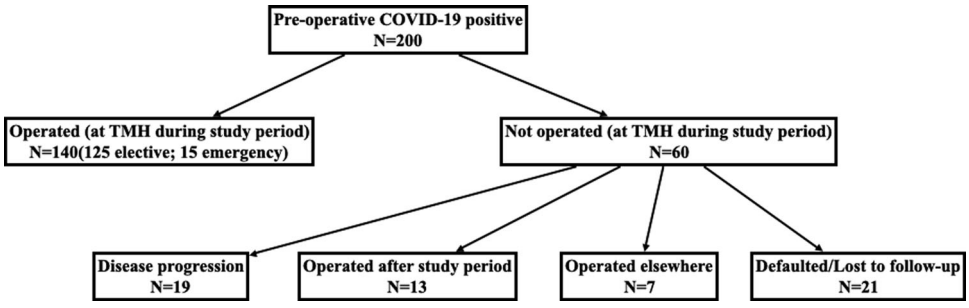

FIGURE 1 Status of patients who tested positive in preoperative period

(perioperative COVID infection rate of 2.1%). Seventeen patients (41.4%) among these had significant postoperative complications (Grade III and above) including nine (22%) COVID-19-related acute respiratory distress syndrome (ARDS) deaths. One patient died of septic shock.

Among the elective procedures, patients who did not have the SARS-CoV-2 infection (1808), had a major complication rate of 9.9% compared to the 12% ($n = 15/125$) in those with preoperative COVID-19 (odds ratio [OR]: 1.24, 95% confidence interval [CI]: 0.71–2.18; $p = 0.45$). The postoperative mortality of patients who underwent elective surgery and did not have symptoms of COVID-19 in the postoperative period or retested negative for SARS-CoV-2 in the perioperative period was 11/1808 (0.6%) compared to those who retested positive, which was 10/41 (24.4%), (OR: 52.7, 95% CI: 20.9–133.2; $p < 0.0001$). The perioperative outcomes, of different subsets in the entire cohort, are depicted in Table 3.

4 | DISCUSSION

Our study showed that a substantial proportion of asymptomatic preoperative patients harbored infection with SARS-CoV-2 on testing. COVID infection resulted in a change in cancer treatment delivery in close to one-fifth of the patients.

Perioperative risks are minimal when patients are operated on 4 weeks from an initial positive test. Patients who undergo surgery while they are COVID positive or test positive in the early postoperative period have a high rate of complications and mortality. These findings have implications in defining policies for patients undergoing elective surgery during the pandemic. The largest study to date (COVID Surg Collaborative) evaluating preoperative testing in elective cancer surgery patients showed higher pulmonary complications and mortality in those with perioperative infection, with those undergoing preoperative testing at a lower risk of pulmonary complications and death.[10]

Results of the recently published study on timing of surgery after SARS-CoV-2 infection, which included the largest cohort of >140 000 patients, showed an increased risk of mortality (odds ratio up to 4.1) when surgery was performed within 6 weeks of infection.[11] However, this timing needs to be carefully balanced with the risk of disease progression due to delay in surgery especially in an oncological setting. In a healthcare environment where patients seek specialized cancer care in centers distant from their domicile, the added challenge of logistics and cost of travel/accommodation can be hurdles to patients continuing their planned care in the face of long delays in treatment delivery. While 9.5% ($n = 19$) of our patients that were tested eventually could not undergo the previously outlined surgical treatment plan on account of progression, a total of 20% ($n = 40$) did not undergo the prior planned surgery due to a variety of reasons. This further reiterates the importance of balancing the consequences of delays in planned surgery with the possibility of increased complications of early surgery in COVID-positive patients.

Study by Sargent et al. suggested operating 10 days from the date of the positive test in asymptomatic patients or from the last day of symptoms in others.[12] Due to uncertainties in exact understanding of the disease at the time of this study (between April 2020 and September 2020) and an absence of guidelines, we exercised a more cautious approach. The COVID Surg Collaborative study had demonstrated a higher rate of pulmonary complications in patients with perioperative SARS-CoV-2 infection.[2] Though the median interval between the initial positive test and subsequent elective surgery in our study was 30 days, the median interval between an initial positive test and a subsequent negative RT-PCR in our population was only 12 days—the remaining delay was a function of patients recovering from their post-COVID-19 infection symptoms and logistics of rescheduling operation lists. Twenty percent of these patients eventually did not undergo the prior planned surgery. In hindsight, it is possible that these numbers may have been smaller had we operated earlier. However, it is also possible that earlier surgery might have adversely affected the frequency of major (Grade III and above) complications in these patients.

Previous SARS-CoV-2 infection is associated with increased odds of pulmonary complications compared to no infection. Both, pulmonary complications and mortality were lowest when surgery was performed at least 4 weeks after notification of a positive swab.[13]

In our study, major complications (Clavien–Dindo Grade III and above) were similar whether elective surgery was performed <30 days or >30 days from the date of initial positive result.

The mortality of our patients who tested positive in the postoperative period (after a negative preoperative test) is similar to the 20.4% mortality rate seen in patients who developed COVID-19 following elective surgery in the COVID Surg Collaborative study.[2]

TABLE 3 Perioperative outcomes in various subsets of patients during the study period

Subset	Patients (*n*)	Major complications	Mortality
Preoperative SARS-CoV-2 negative—elective	1808	179 (9.9%)	11 (0.6%)
Preoperative SARS-CoV-2 negative—emergency	59	9 (15.3%)	7 (11.8%)
Preoperative SARS-CoV-2 positive—elective who subsequently underwent surgery after testing negative	125	15 (12%)	1 (0.8%)
Preoperative SARS-CoV-2 positive—emergency	15	5 (33.3%)	4 (27%)
Postoperative SARS-CoV-2 positive who underwent elective surgery after an initial negative report	41	17 (41.4%)	10 (24.4%)

These results highlight the poor outcomes of those with perioperative COVID-19 infection and reiterate the need for early diagnosis and treatment.

Being a high-volume cancer center, the endeavor to sustain ongoing cancer care at our hospital relied on the implementation of a multipronged strategy.[14,15] The cornerstone of this approach was the development of COVID-19-free surgical pathways to continue cancer care, albeit at a scaled-down level, in the face of a rapidly spreading outbreak. This involved setting up a dedicated fever clinic for screening of symptomatic patients, routine preoperative testing using ICMR-approved RT-PCR kits,[16] creating isolation and segregation pathways, allocating designated operating rooms, and dedicated intensive care units for COVID positive patients. While emergency surgeries could not be deferred, we waited for patients requiring elective surgery to test negative, and completely recover from their COVID infection before undergoing surgery. We believe that this approach balances the risks of delayed cancer treatment with optimizing postoperative outcomes.

Our study should be interpreted with some caveats. The period when the testing was done coincided with the peak incidence of COVID-19 infection in the region.[17] Our results may therefore not be applicable in regions or periods when prevalence is low. Despite this limitation, it still represents one of the largest single-center cohorts with perioperative outcomes of patients planned for cancer surgery during the pandemic. Very few studies have evaluated the proportion of asymptomatic infection with SARS-CoV-2 in patients with cancer. Most studies have focused on patients with symptoms and the positivity rate among them. Our cohort was a set of consecutive patients being tested with prospectively collected data, reducing the likelihood of selection bias and missing data.

With subsequent waves of infection in several regions in the world (many that are more severe than the first wave) our study can help formulate protocols and guidelines. Accurate evaluation of asymptomatic infection would facilitate policy decisions on routine preoperative testing, reducing the risk of disease transmission and the risk of complications of undergoing surgery in infected asymptomatic patients. Optimizing the time of surgery after infection to balance the risk of complications while reducing the number of patients who may not receive the intended treatment due to delay in surgery is critical in improving oncologic outcomes. Increased awareness and sustained vigilance to diagnose perioperative COVID-19 infection may help in reducing the increased mortality in these patients.

5 | CONCLUSION

Routine preoperative testing for SARS-CoV-2 helps to identify and segregate patients with asymptomatic infection. Elective surgery following a period of isolation may minimize complications in those who test positive. Higher complications are seen in those positive in the postoperative period. Prolonged delay in surgery after COVID infection may affect oncologic outcomes as patients may not receive their planned treatment. Policies should be framed depending on the general incidence in the population, the likelihood of postoperative complications, and the consequences of delaying surgery.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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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