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RESEARCH ARTICLE

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Outcomes of elective cancer surgery in COVID-19 survivors: An observational study

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Abstract

Background and Objectives: Guidelines recommend deferral of elective surgery after COVID-19. Delays in cancer surgeries may affect outcomes. We examined perioperative outcomes of elective cancer surgery in COVID-19 survivors. The primary objective was 30-day all-cause postoperative mortality. The secondary objectives were 30-day morbidity, and its association with COVID-19 severity, and duration between COVID-19 and surgery.

Methods: We collected data on age, gender, comorbidities, COVID-19 severity, preoperative investigations, surgery performed, and intra and postoperative outcomes in COVID-19 survivors who underwent elective cancer surgery at a tertiary-referral cancer center.

Results: Three hundred and forty-eight COVID-19 survivors presented for elective cancer surgery. Of these, 332/348 (95%) patients had mild COVID-19 and 311 (89%) patients underwent surgery. Among patients with repeat investigations, computerized tomography scan of the thorax showed the maximum new abnormalities (30/157, 19%). The 30-day all-cause mortality was 0.03% (1/311) and 30-day morbidity was 17% (54/311). On multivariable analysis, moderate versus mild COVID-19 (odds ratio [OR]: 1.95; 95% confidence interval [CI]: 0.52–7.30; $p = 0.32$) and surgery within 7 weeks of COVID-19 (OR: 0.61; 95% CI: 0.33–1.11; $p = 0.10$) were not associated with postoperative morbidity.

Conclusions: In patients who recover from mild to moderate COVID-19, elective cancer surgery can proceed safely even within 7 weeks. Additional preoperative tests may not be indicated in these patients.

KEYWORDS

cancer, COVID-19, operative, postacute COVID-19 syndrome, postoperative complications, surgical procedures

1 | INTRODUCTION

As on 8th July 2022, India has seen more than 43 million cases of COVID-19 with over 500 000 deaths.[1] Patients with cancer are at higher risk of getting infected with COVID-19 and are likely to have more severe disease and worse outcomes.[2] Guidelines recommend various waiting periods and evaluation strategies in patients recovered from COVID-19 who are planned for elective surgery.[3–5] However, cancer surgery is usually semi-urgent and any delays may compromise oncological outcomes.[6] There is no guidance on physiological evaluation or waiting times for patients with cancer who have recovered from COVID-19 and are scheduled for time-sensitive surgery. The aim of this study was to look at the perioperative outcomes of patients with cancer who recovered from COVID-19 and underwent elective cancer surgery at a tertiary referral cancer center.

2 | METHODS

This was an ambi-directional (retrospective and prospective) study of patients with cancer who were diagnosed to have COVID-19 between 1st April 2020 and 31st December 2021. The study was approved by the Institutional Ethics Committee and carried out in accordance with good clinical research practices. We included patients with a confirmed diagnosis of cancer and a confirmed COVID-19 diagnosis (by reverse transcriptase polymerase chain reaction [RT-PCR]), who were planned for surgery as part of their cancer treatment plan. Patients with clinical or radiological suspicion of COVID-19 without a positive RT-PCR test were excluded. We used various data sources to identify eligible patients: preanaesthesia check-up (PAC) documentation on the electronic medical records, lists of patients who tested positive for COVID-19 on routine preoperative testing and review of daily operating room schedules to identify patients with a previous history of COVID-19 infection. For eligible patients, we captured data on age, gender, comorbidities, American Society of Anesthesiologists (ASA) physical status, surgery planned, date of PAC, date of test positivity for COVID-19, severity of COVID-19 as per the ordinal scale for clinical improvement suggested by the World Health Organization (WHO) (Table S1),[7] details of treatment received for COVID-19, whether PAC was repeated after COVID-19, details of repeat investigations done after recovery from COVID-19, date of surgery, intra and postoperative complications, reasons for any cancellation or deferral of surgery and status at hospital discharge or 30 days after surgery (whichever was earlier). We classified complexity of surgeries based on an institutional grading system with complexity increasing from Grades 2 to 6 (examples of grades are given in Table 1). The primary objective of this study was to look at 30-day all-cause postoperative mortality in COVID-19-recovered patients who underwent elective cancer surgery. The secondary objectives were to measure 30-day morbidity in these patients, and to

TABLE 1 Details of surgery

Status of surgery	
Operated	311 (89%)
Awaiting surgery	8 (2%)
Deferred	25[a] (8%)
Canceled	4[a] (1%)
Grade of surgery performed (for 311 operated pts)	
2 (e.g., endoscopy, chemoport insertion, radiofrequency ablation, brachytherapy)	19 (6%)
3 (e.g., oral surgery with primary closure, simple mastectomy, above or below knee amputation, colostomy or ileostomy closure)	47 (15%)
4 (e.g., radical mastectomy, oral cancer surgery with pedicled flap reconstruction, simple hysterectomy, transurethral bladder resection	114 (37%)
5 (e.g., tumour prostheses, partial esophagectomy, radical hysterectomy, cholecystectomy, gastrectomy, colorectal surgery, oral cancer surgery with free flap reconstruction, total thyroidectomy)	63 (20%)
6 (e.g., nephrectomy, total esophagectomy, pancreatico-duodenectomy, major lung resections, multi-visceral resections, minimally invasive gastrectomy, minimally invasive colorectal surgery)	68 (22%)
Duration between COVID-19 and surgery	
0–2 weeks	5 (1%)
2–4 weeks	73 (24%)
4–7 weeks	95 (30%)
More than 7 weeks	138 (45%)

[a]Out of 29 patients whose surgeries were deferred/canceled, 10 were due to patients' personal reasons, 14 had progression of cancer necessitating neoadjuvant therapy and 5 were for other reasons.

correlate postoperative morbidity with severity of COVID-19 and duration between COVID-19 and surgery.

Data were entered into a statistical software (SPSS 25.0) for analysis. Since this was an observational study, no formal sample size was calculated, and we included all patients who met the eligibility criteria during the study period. We used a multivariable logistic regression analysis to look at the association of duration between COVID-19 and surgery with postoperative outcomes, adjusting for age, complexity of surgery, ASA physical status and severity of COVID-19. All results were interpreted at the 5% level of significance.

3 | RESULTS

Between 28th May 2020 and 16th November 2021, we identified 348 patients with cancer who had recovered from COVID-19 and were scheduled for surgery. Table 2 shows the baseline characteristics of the patients. Most patients (332/348, 95%) had mild COVID-19 (WHO scale Grades 1–3), with no patient having COVID-19 severity beyond Grade 5. Of these, 311 (89%) patients underwent surgery during the study period. The median duration between COVID-19 diagnosis and surgery was 45 days (interquartile range [IQR]: 28–87 days). Table 1 lists the details of the surgeries.

Among patients who had repeat investigations done before surgery, only few patients had fresh abnormalities on electrocardiography (ECG), echocardiography (2D ECHO), chest radiograph (CXR) and 6-min walk test (6MWT). Almost 20% of those who had a repeat computerized tomography (CT) scan of the thorax showed new abnormalities. Very few patients underwent specialized tests such as assessment of D-dimer, C-reactive protein (CRP), fibrinogen, N-terminal pro-brain natriuretic peptide (NT-proBNP), and troponin I (Trop I) levels. Figure 1 shows the proportions of patients who had repeat tests, and the results of those tests.

Only 1 patient died within 30 days after surgery (postoperative 30-day all-cause mortality rate 0.3%). Intraoperative complications occurred in 14 (5%) of patients and postoperative complications in 54 (17%) patients. Table 3 shows the details of the intra- and postoperative complications. Thirteen (4%) patients needed re-exploration within 30 days after surgery. The median postoperative intensive care unit stay was 0 days (IQR: 0–1), and the median postoperative hospital stay was 5 days (IQR: 2–8). Table 4 lists the unadjusted intra- and postoperative complication rates for various patient and surgery-related factors. On multivariable analysis, none of the factors were significantly associated with increased risk of postoperative complications (Table 5).

4 | DISCUSSION

In this study, we found that patients who recovered from COVID-19 and underwent elective cancer surgery had low and acceptable rates of intra- and postoperative complications. Among patients who underwent repeat PAC after recovery from COVID-19, only a small proportion showed abnormal parameters. Postoperative complication rates were not different in patients who underwent surgery within or after 7 weeks after COVID-19, after adjusting for confounders.

Surgery within 2–6 weeks of recovery after even mild respiratory viral infections is a risk factor for pulmonary complications.[8] Since the beginning of the COVID-19 pandemic, there have been concerns

TABLE 2 Baseline characteristics of participants

Gender	
Female	183 (53%)
Male	165 (47%)
Age (years)	46.8 (±16)
Surgery	
Breast	68 (20%)
Bone/soft tissue	33 (9%)
Gastro-intestinal	81 (23%)
Gynecology	29 (8%)
Head and neck	67 (20%)
Neurosurgery	3 (1%)
Pediatric	6 (2%)
Reconstructive	1
Thoracic	27 (8%)
Urology	33 (9%)
ASA status	
I	193 (55%)
II	132 (38%)
III	23 (7%)
Comorbidities	
Hypertension	36
Diabetes	23
Cardiovascular	6
Pulmonary	4
Other	35
Multiple	51
COVID severity (WHO 8-point ordinal scale)	
1	258 (74%)
2	19 (6%)
3	55 (16%)
4	12 (3%)
5	3 (1%)
Missing	1

Abbreviations: ASA, American Society of Anesthesiologists; WHO, World Health Organization.

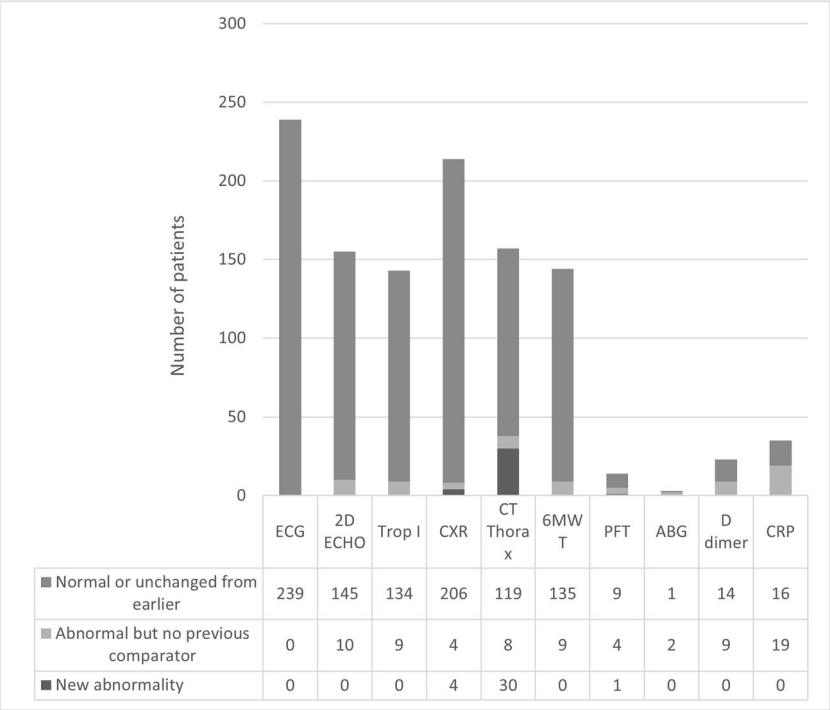

FIGURE 1 Investigations performed after COVID-19 before surgery. ABG, arterial blood gas; CRP, C-reactive protein; CT Thorax, computerized tomography of thorax; CXR, chest radiograph; 2D ECHO, two-dimensional echocardiography; ECG, electrocardiogram; 6MWT, 6-min walk test; PFT, pulmonary function test; Trop I, troponin I

TABLE 3 Details of intra- and postoperative complications

Intraoperative complications	
Bleeding	7 patients had massive intraoperative blood loss (more than 1 blood volume)
Renal	1 patient had intraoperative oliguria
Respiratory	2 patients had bronchospasm
Cardiovascular	3 patients
	1—intraoperative hypotension needing vasopressor support
	1—severe bradycardia
	1—pacemaker malfunction leading to hemodynamic instability
Postoperative complications	
Cardiovascular	4 patients (2 patients had changes on ECG suggestive of myocardial ischemia, 1 patient had hypertensive crisis, 1 patient had pulmonary embolism)
Pulmonary	5 patients (3 patients had pleural effusion with lung collapse, 1 patient developed a pneumonia-and 1 patient had a pneumothorax)
Renal	1 patient—acute kidney injury
Liver	3 patients—postoperative liver dysfunction
Surgical	34 patients—surgical site infection, re-exploration, venous thrombosis, chyle leak, seroma
Multiorgan failure	7 patients

about the outcomes of patients with perioperative COVID-19 who undergo surgery. Early data from the COVIDSurg Collaborative suggested that such patients were at high risk of pulmonary complications and mortality.[9] However, these data included very few patients who underwent elective surgery after COVID-19.[9] Most patients in this study had either emergent procedures or postoperative COVID-19, and the severity of COVID-19 and complexity of surgery was not specified.[9] Subsequent data from the same group of researchers suggested that surgery within 7 weeks of COVID-19 was associated with increased adverse outcomes, and that patients who had surgery performed 7 weeks or more after COVID-19 had outcomes similar to uninfected patients.[10] The study also suggested that patients with prolonged symptoms may need longer periods of waiting. Another paper from the COVIDSurg collaborative reported higher rates of venous thrombo-embolism, pneumonia and mortality among patients undergoing surgery within 1–6 weeks after COVID-19

TABLE 4 Complication rates for various factors (unadjusted)

	Intraoperative complication rate	*p* value	Postoperative complication rate	*p* value
Gender				
Female	7/163 (4%)	0.85	23/163 (14%)	0.15
Male	7/148 (5%)		31/148 (21%)	
Age (in years)				
More than 60	2/54 (4%)	0.76	9/54 (17%)	0.73
Less than 60	12/257 (5%)		45/257 (18%)	
ASA status				
I	10/173 (6%)	0.40	28/173 (16%)	0.90
II	3/120 (2.5%)		22/120 (18%)	
III	1/18 (5.5%)		4/18 (22%)	
Severity of COVID-19				
Mild (Grades 1–3)	12/298 (4%)	0.11	53/298 (18%)	0.27
Moderate (Grades 4–5)	2/13 (15%)		4/13 (31%)	
Complexity of surgery				
Grade 2	0/19	0.02	1/19 (5%)	0.01
Grade 3	0/47		5/47 (11%)	
Grade 4	3/114 (3%)		14/114 (12%)	
Grade 5	3/63 (5%)		18/63 (29%)	
Grade 6	8/68 (12%)		19/68 (28%)	
Duration from COVID-19 to surgery				
0–2 weeks	0/5 (0%)	0.17	0/5 (0%)	0.06
2–4 weeks	2/73 (3%)		12/73 (16%)	
4–7 weeks	3/95 (3%)		13/95 (14%)	
More than 7 weeks	9/138 (7%)		29/138 (21%)	

Abbreviation: ASA, American Society of Anesthesiologists.

TABLE 5 Multivariable analysis for risk factors for postoperative complications

	OR (95% CI)	*p* value
Age more than 60 years	0.75 (0.32–1.79)	0.52
Complexity of surgery		
Grades 1–2	Ref	Ref
Grades 3–4	2.49 (0.31–19.88)	0.39
Grades 5–6	7.24 (0.92–56.79)	0.06
ASA physical status		
I	ref	ref
II	1.11 (0.58–2.12)	0.76
III	1.54 (0.41–5.78)	0.53
Severity of COVID-19		
Mild	ref	ref
Moderate	1.95 (0.52–7.30)	0.32
Duration between COVID-19 and surgery less than 7 weeks	0.61 (0.33–1.11)	0.10

Abbreviation: CI, confidence interval.

with the risk decreasing in those operated after 7 weeks.[11] Deng et al.[12] reported results from the COVID-19 Research Database which also showed that elective surgery within 8 weeks after recovery from COVID-19 was associated with increased adverse events.[12] Based on these data, recent updated guidelines recommend a waiting period of 7–8 weeks for elective surgery after COVID-19.[13] However, other studies have shown that surgery performed earlier than 8 weeks after a COVID-19 diagnosis is safe. Kane[14] reported on a subset of 13 patients who tested positive for COVID-19 during preoperative screening, of whom 6 subsequently underwent elective surgery within 36 days after infection. None of them had mortality or major morbidity. Baiocchi studied 49 patients who underwent elective surgery at a median of 25 days after their COVID-19 diagnosis, with no increase in complications compared to matched controls.[15] A recent review identified 10 studies that looked at surgical outcomes in patients with perioperative SARS CoV2 infection.[16] However, the studies were heterogeneous (different countries, retrospective vs. prospective, inclusion of patients with pre and postoperative infection, variable techniques of testing for COVID-19, small sample sizes, elective and emergency procedures and surgeries of varying complexity) making the interpretation of their results difficult.[16]

Surgery for cancer (solid tumors) is a key treatment modality, is often complex and may be associated with significant perioperative morbidity. Oncological surgery is considered semi-urgent since any delays could result in progression of cancer, potentially rendering the patient inoperable. A recent systematic review found that even a 4-week delay in cancer surgery was associated with an increased risk of mortality.[6] Thus, the timing of surgery after COVID-19 in cancer patients is crucial and recommended waiting times of 7–8 weeks may not be generalizable to these surgeries. There are limited data on the outcomes of COVID-19 survivors undergoing cancer surgery. The COVIDSurg-Cancer study looked at 122 patients undergoing elective cancer surgery who had a previous SARS CoV2 infection.[17] Surgery within 4 weeks after the infection was associated with a higher risk of pulmonary complications and mortality.[17] In contrast, Kothari et al.[18] reported on 112 patients undergoing elective cancer surgery after recovery from COVID-19. The duration between COVID-19 and surgery was 52 days on an average but was as low as 20 days in some patients. Compared to matched controls, there was no difference in complication rates, and within the group of COVID-19 survivors, increased complications were seen only in those who needed in-patient hospitalization for COVID-19.

COVID-19 is known to cause several long-term complications. These include but are not limited to pulmonary fibrosis and interstitial lung disease, cardiac complications such as myocardial injury, myocarditis, acute myocardial infarction, heart failure and dysrhythmias, thrombotic events affecting the cardiovascular and cerebrovascular systems, profound fatigue, memory loss, and emotional disturbances.[19–21] In addition, in patients with severe COVID-19 who have a prolonged illness, there can be significant deconditioning resulting in frailty.[21] Patients with COVID-19 may receive steroids, anticoagulants or immune suppressants such as tocilizumab, all of which could impact subsequent anesthesia management. At present, there are no definite guidelines for the evaluation of COVID-19 survivors presenting for elective surgery. It has been suggested that patient assessment should include the duration since recovery from COVID-19, functional status, ruling out sequelae on various organ systems, and reviewing past or ongoing medications.[21–23] The Indian Society of Anaesthesiologists recommends estimation of effort tolerance, breath holding time, ambulatory oxygen saturation measurement and a 6MWT test in all COVID-19 survivors.[23] Further objective tests that assess individual organ systems can be chosen depending on the severity of COVID-19, functional status and complexity of planned surgery. Suggested specialized investigations include 2D ECHO, CT thorax, ABG, PFT, and assessment of D-dimer, CRP, fibrinogen, NT-proBNP, and Trop I levels. In our study, ECG, 2D ECHO, and CT thorax were the most frequently repeated tests; among these, only CT thorax showed substantial new abnormalities. Few patients underwent other specialized tests, and their results were mostly normal. It is important to note that cancer itself can lead to elevated levels of several of these cytokines, confounding the interpretation of certain laboratory results.

The strength of our study is that we included data on more than 300 patients undergoing a variety of cancer surgeries. It was a pragmatic study that looked at patients over a large time period, encompassing various phases of the pandemic. We had a 30-day follow-up on most patients to capture delayed postoperative complications. In studies reporting outcomes after COVID-19, estimating the severity of COVID-19 accurately is a key factor. We used the WHO ordinal scale for reporting severity of COVID-19 because it is a standard and universally adopted scale.[7] Kothari[18] and colleagues used the need for in-patient admission as a surrogate for severe COVID-19. However, in the Indian context, many patients with mild COVID-19 needed hospital admission for social rather than medical reasons and, therefore, this indicator may not be reliable. One of the limitations of our study is that most of the included patients had mild COVID-19, and the results may not apply to those who have recovered from moderate or severe COVID-19. This may have been due to a selection bias where patients with moderate to severe COVID-19 who had physiological disruptions were triaged and offered alternative treatments and did not present for surgery. However, our data mirrors the real-life scenario since most infections in this part of the world have been mild with good recovery.[24] Another drawback of our study is that we did not use a concurrent control group or perform propensity matching to have a comparator. However, another publication from the same institute reported a major complication rate of 9.9% and mortality of 0.6% in patients who underwent elective cancer surgery after a negative preoperative test for COVID-19 which is comparable to our findings.[25]

In summary, our study shows that at least in patients who recover from mild COVID-19, specialized testing may not be required before surgery, and that elective cancer surgery can proceed safely even before the recommended 7-week waiting period after COVID-19.

AUTHOR CONTRIBUTIONS

Priya Ranganathan: concept and design, data acquisition, data analysis, first draft of manuscript. **Bindiya Salunke**: patient recruitment, data acquisition, editing manuscript. **Anjana Wajekar**: patient recruitment, data acquisition, editing manuscript. **Aafreen Siddique**: patient recruitment, data acquisition, editing manuscript. **Kaizeen Daruwalla**: patient recruitment, data acquisition, editing manuscript. **Shreyas Chawathey**: patient recruitment, data acquisition, editing manuscript. **Devayani Niyogi**, **Prakash Nayak**: concept and design, editing manuscript. **Jigeeshu Divatia**: concept and design, data analysis, editing manuscript.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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