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The effect of delays in cancer surgery due to the COVID-19 pandemic on cancer resectability and postoperative mortality in different tumor entities

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Abstract

Background During the COVID-19 pandemic, prioritization of COVID-19 patients led to delays in oncological surgery, potentially impacting patient outcomes. This analysis examines the effects of surgical delays in various tumor entities on resectability and postoperative mortality.

Methods Data from the COVIDSurg Cancer Collaborative, an international prospective cohort study with 19,676 patients, collected between March 26, 2020, and September 16, 2020, were analyzed. Postoperative mortality and complete resection (R0) were the outcomes, with tumor entity, stage and delay to surgery as key exposures.

Results 17,486 patients underwent surgery during the study period, at a median time of three weeks after decision to operate (IQR = 4). 172 (1.0%) patients died within 30 days postoperatively. 15,143 (90.5%) patients had an R0 resection, 1352 (8.1%) an R1 resection and 230 (1.4%) had an R2 resection. Postoperative mortality was highest for oesophageal cancer (3.9%) and UICC stage IV (1.5%). For the overall population, there was no association between delay to surgery and resectability. There was an association between delay to surgery and postoperative mortality ($p < 0.001$), with the highest 30-day postoperative mortality observed for operations within two weeks following surgical decision.

Conclusion Tumor resectability and postoperative mortality in oncological surgeries are influenced by various factors. During the COVID-19 pandemic, moderate delays in surgeries were observed, with differences across tumor types, UICC stages and regions. While no tangible effects on resectability were found, postoperative mortality was higher after a shorter delay to surgery.

Keywords Delay to surgery, Cancer operations, COVID-19 pandemic



1 Introduction

The COVID-19 pandemic posed enormous challenges to healthcare systems worldwide. Resources were mobilized to manage the growing number of COVID-19 patients [1–6]. Patients with COVID-19 and corresponding staff and ward capacities, in particular intensive care unit (ICU) capacities, were prioritized, leading to significant restrictions in other areas of healthcare, especially so in elective surgery [2, 6, 7]. Hospitals were urged to postpone planned surgeries to accommodate COVID-19 patients, resulting in delays for many surgical procedures [3]. This had possible serious consequences for affected patients and the entire healthcare system [6, 8]. While focusing on COVID-19 patients was necessary to prevent ICU and emergency services overload, it also meant that the treatment of many individuals with chronic conditions, including cancer, was de-prioritized [7]. Planned procedures were often postponed or even canceled, delaying treatment [1]. This is particularly concerning for cancer patients, as timely surgical intervention is crucial for treatment success and survival. Delayed surgeries can lead to tumor progression, complicating treatment and reducing effectiveness [8]. Additionally, the psychological impacts of uncertainty and the fear of delayed treatment can severely affect patients' well-being [3].

In this analysis, we assess waiting time until elective cancer surgery during the initial phase of the COVID-19 pandemic and analyze its association with resectability and postoperative mortality.

2 Methods

Our analysis is based on data from the COVIDSurg Cancer Collaborative (CSCC). Any hospital worldwide performing elective cancer surgery in areas affected by the COVID-19 pandemic was eligible to participate. Patients scheduled for elective surgery for solid cancers with curative intent were included [1]. Data were collected by local collaborators and entered into a central database through a web application between March 26, 2020 and September 16, 2020, which corresponds with the initial phase of the COVID-19 pandemic. Patients were followed up to the time of surgery or September 16, 2020. For patients who underwent surgery, outcome data were collected for up to 30 days postoperatively. For those not undergoing surgery, their most recent known status was recorded. The study enrolled 19,676 patients from 466 hospitals in 59 countries, divided into seven regions: East Asia & Pacific, Europe & Central Asia, Latin America & the Caribbean, Middle East & North Africa, North America, South Asia and Sub-Saharan Africa. The 15 most common solid cancer types were included: colon, rectal, oesophageal, gastric, head and neck, lung, liver, pancreatic, prostate, bladder, urothelial, gynecological, breast, soft-tissue and bone malignancies.

For this analysis, delay to surgery, i.e., time from decision for surgery to the operation, 30-day postoperative mortality, resectability and Union for International Cancer Control (UICC) stage were analyzed. In the CSCC, delay to surgery was recorded in two-week intervals up to 26 weeks, but alternative intervals (0–2, 3–4, 5–6, 7–10, >11 weeks) were used in this analysis. R0 resection was defined as the absence of microscopically or macroscopically detectable tumor tissue at the resection margins. R1 resection indicated microscopic tumor remnants at the margins. R2 resection was defined by macroscopically visible tumor remnants. Tumors were classified according to the UICC staging system from stage 0 (no detectable tumor) to stage IV (metastatic) [9]. Patients with UICC

stage 0, i.e., patients with complete response after neoadjuvant therapy, were included. Hospitals were categorized into four types: designated COVID-treatment "hot" hospitals; designated COVID-free "cold" hospitals; and undesignated hospitals, which were further divided into with or without emergency department. Additionally, hospitals were classified into five surge levels according to utilization of intensive care capacities: normal, low, medium, high and triage surge level.

We performed analysis of the overall CSCC cohort and stratified by tumor entity, UICC stage, region, hospital type and surge level, with regard to delay to surgery, post-operative mortality and resectability. The association between delay to surgery and post-operative mortality and resectability was analyzed in the overall cohort and stratified by tumor entity. For the analysis of categorical variables, the chi-square test was used. Statistical significance was set at $p \leq 0.05$. This study was registered on November 5, 2020, at ClinicalTrials.gov with the registration number NCT04384926 [1]. Clearance from the competent ethics committee (Medical Faculty, University of Halle, reference 2020–080) was obtained.

Local principal investigators obtained all required ethical approvals according to local and national regulations. In most settings, a waiver of individual informed consent was granted by the ethics committee. Where required, written or verbal informed consent was obtained from participants or their legal guardians, based on local ethics committee recommendations. All data collection activities were performed in accordance with relevant guidelines and regulations.

3 Results

3.1 Overall cohort

11,190 (56.9%) patients were women and 8486 (43.1%) were men. The average age was 62 years. 7966 (40.5%) patients had a normal BMI, 6394 (32.5%) were overweight, 4209 (21.4%) obese and 625 (3.2%) underweight. The majority of patients (11,570; 58.8%) were physically fully active. 88.9% of patients underwent surgery during the survey period. Most patients had to wait three to four weeks for an operation after the decision to operate was made (Table 1).

1.2% of patients died during the observation period. 0.2% of patients died before a scheduled operation and 1.0% of patients died within 30 days postoperatively. 90.5% of patients had an R0 resection, 8.1% had an R1 resection and 1.4% had an R2 resection (Table 1).

3.2 Tumor entity

The largest proportion were patients with breast cancer (19.4%) and the smallest proportion were patients with bone sarcoma (0.4%) (Table 1).

There was an association between tumor entity and waiting time for surgery ($p < 0.001$). In all tumor entities except oesophageal cancer, prostate cancer and bone sarcoma, most operations were performed three to four weeks after the decision for surgery. In oesophageal and prostate cancer, as well as in bone sarcoma, most operations took place more than 11 weeks after the decision (Table 1).

The highest postoperative 30-day mortality was observed in patients with oesophageal cancer (3.9%) and bladder cancer (3.7%) while the lowest was found in patients with prostate cancer and bone sarcoma (0%) (Table 1). R0 resection was achieved most

Table 1 Postoperative mortality, resectability and interval from decision to operation stratified by tumor entity

	Patients (%)	30-day postoperative mortality (%)	Resectability (%)			Interval from decision to operation in weeks (%)					Patients with no operation (%)
			R0	R1	R2	0–2	3–4	5–6	7–10	> 11	
All patients	19,676 (100)	172 (1.0)	15,143 (90.5)	1352 (8.1)	230 (1.4)	3942 (22.5)	5172 (29.6)	3119 (17.8)	2667 (15.3)	2586 (14.8)	2190 (11.1)
<i>Tumor entity</i>											
Colon	2942 (15.0)	44 (1.6)	2623 (97.4)	55 (2.0)	15 (0.6)	674 (24.3)	825 (29.8)	511 (18.4)	446 (16.1)	316 (11.4)	170 (5.8)
Rectal	1695 (8.6)	9 (0.6)	1363 (93.7)	83 (5.7)	9 (0.6)	264 (17.5)	397 (26.3)	265 (17.6)	233 (15.5)	349 (23.1)	187 (11.0)
Gastric	638 (3.2)	12 (2.1)	510 (92.7)	37 (6.7)	3 (0.6)	112 (19.9)	161 (28.6)	94 (16.7)	62 (11.0)	134 (23.8)	75 (11.8)
Oesophageal	488 (2.5)	14 (3.9)	306 (87.7)	41 (11.7)	2 (0.6)	51 (14.0)	60 (16.5)	67 (18.5)	45 (12.4)	140 (38.6)	125 (25.6)
Liver	882 (4.5)	18 (2.2)	631 (86)	87 (11.9)	16 (2.1)	122 (15.2)	217 (27)	154 (19)	177 (22)	135 (16.8)	77 (8.7)
Pancreatic	737 (3.7)	20 (3.4)	463 (83.1)	90 (16.2)	4 (0.7)	157 (26.5)	182 (30.7)	93 (15.7)	85 (14.4)	75 (12.7)	145 (19.7)
Kidney or upper tract urothelial	454 (2.3)	2 (0.5)	338 (93.8)	20 (5.6)	2 (0.6)	74 (19.2)	90 (23.4)	79 (20.5)	75 (19.5)	67 (17.4)	69 (15.2)
Bladder	388 (2.0)	6 (3.7)	122 (89.7)	12 (8.8)	2 (1.5)	26 (16.3)	42 (26.2)	34 (21.2)	31 (19.4)	27 (16.9)	228 (58.7)
Prostate	592 (3.0)	0 (0.0)	327 (75.5)	102 (23.6)	4 (0.9)	42 (8.4)	65 (13.0)	76 (15.0)	144 (29.1)	172 (34.5)	93 (15.7)
Soft-tissue sarcoma	361 (1.8)	2 (0.6)	250 (83.9)	43 (14.4)	5 (1.7)	62 (19.4)	78 (24.5)	55 (17.2)	49 (15.4)	75 (23.5)	42 (11.6)
Bone sarcoma	88 (0.4)	0 (0.0)	73 (93.6)	4 (5.1)	1 (1.3)	15 (18.5)	19 (23.5)	10 (12.3)	14 (17.3)	23 (28.4)	7 (7.9)
Lung	1300 (6.6)	13 (1.1)	1051 (94.6)	52 (4.7)	8 (0.7)	234 (19.9)	409 (34.8)	242 (20.6)	174 (14.8)	117 (9.9)	124 (9.5)
Head and neck	3124 (15.9)	18 (0.6)	2208 (83.0)	370 (13.9)	82 (3.1)	840 (30.0)	931 (33.6)	423 (15.3)	321 (11.6)	265 (9.5)	344 (11.0)
Breast	3803 (19.4)	6 (0.2)	3152 (92.4)	240 (7.0)	21 (0.6)	756 (21.7)	1051 (30.2)	624 (17.9)	566 (16.3)	485 (13.9)	321 (8.4)
Gynecological	2184 (11.1)	8 (0.4)	1726 (90.9)	116 (6.1)	56 (3.0)	513 (25.7)	645 (32.2)	392 (19.6)	245 (12.2)	206 (10.3)	183 (8.4)

frequently in colon and least frequently in prostate cancer, while R1 resection occurred most frequently in prostate cancer (Table 1).

3.3 UICC stage

Most patients were UICC stage I (38.0%) and fewest patients UICC stage 0 (3.3%).

Although there was a statistically significant association between tumor stage and delay to surgery ($p < 0.001$), no clear pattern of earlier operations in higher tumor stages or vice versa could be detected. In all UICC stages, most surgeries took place three to four weeks after the decision to operate (Table 2).

The highest 30-day postoperative mortality was observed in UICC stage IV (1.5%) and the lowest in UICC stage I (0.5%). There was an association between tumor stage and resection status, with a higher proportion of R0 resections being achieved in earlier tumor stages and vice versa (Table 2).

3.4 Region

The largest proportion of patients was from Europe & Central Asia (69.5%) and the smallest from Sub-Saharan Africa (1.1%) (Table 5). There was an association between region and delay to surgery ($p < 0.001$). In East Asia & Pacific, Europe & Central Asia and North America, most operations took place three to four weeks after decision and least operations were performed after more than 11 weeks. In Latin America & the Caribbean, Middle East & North Africa and South Asia, most surgeries were performed within two weeks. In Sub-Saharan Africa most patients were operated on more than 11 weeks after the decision for surgery was made (Table 3).

The highest 30-day postoperative mortality was observed in South Asia (1.6%) while no patient died in Sub-Saharan Africa within 30 days postoperatively (Table 5). The proportion of R0 resections was highest in South Asia, and lowest in North America. The highest R1 resection rate was observed in North America. The largest proportion of R2 resections were in the Middle East & North Africa (Table 3).

3.5 Hospital type and surge level

Most patients were operated on in undesignated hospitals with emergency departments (39.0%) and in hospitals with a low surge level (34.3%), while fewest patients underwent surgery in undesignated hospitals without emergency departments (5.9%) and in

Table 2 Postoperative mortality, resectability and interval from decision to operation stratified by baseline UICC stage

UICC stage	Patients (%)	30-day postoperative mortality (%)	Resectability (%)			Interval from decision to operation in weeks (%)					Patients with no operation (%)
			R0	R1	R2	0–2	3–4	5–6	7–10	> 11	
0	556 (3.3)	3 (0.6)	424 (92.6)	28 (6.1)	6 (1.3)	121 (23.4)	144 (27.8)	106 (20.5)	88 (17.0)	59 (11.3)	38 (6.8)
1	6334 (38.0)	27 (0.5)	5403 (94.7)	279 (4.9)	25 (0.4)	1275 (21.8)	1840 (31.5)	1072 (18.4)	896 (15.3)	758 (13.0)	493 (7.8)
2	3695 (22.2)	34 (1.0)	2934 (91.4)	248 (7.7)	29 (0.9)	769 (23.4)	914 (27.5)	588 (17.6)	531 (16.0)	518 (15.5)	375 (10.1)
3	4502 (27.0)	45 (1.1)	3455 (88.9)	358 (9.2)	75 (1.9)	973 (24.1)	1135 (28.1)	667 (16.6)	548 (13.6)	709 (17.6)	470 (10.4)
4	1588 (9.5)	21 (1.5)	1058 (81.1)	182 (13.9)	65 (5.0)	334 (24.3)	428 (31.1)	240 (17.4)	174 (12.6)	201 (14.6)	211 (13.3)

Table 3 Postoperative mortality, resectability and interval from decision to operation stratified by region

Region	Patients (%)	30-day postoperative mortality (%)	Resectability (%)		Interval from decision to operation in weeks (%)						Patients with no operation (%)
			R0	R1	R2	0–2	3–4	5–6	7–10	> 11	
East Asia & Pacific	1292 (6.6)	7 (0.6)	1034 (91.1)	88 (7.6)	13 (1.3)	275 (23.6)	398 (34.1)	223 (19.1)	154 (13.2)	116 (10.0)	126 (9.8)
Europe & Central Asia	13,671 (69.5)	126 (1.0)	10,639 (90.1)	1030 (8.7)	136 (1.2)	2579 (20.9)	3812 (30.8)	2309 (18.7)	1922 (15.5)	1740 (14.1)	1300 (9.5)
Latin America & Caribbean	831 (4.2)	9 (1.2)	700 (94.5)	33 (4.4)	8 (1.1)	197 (25.7)	195 (25.5)	150 (19.5)	117 (15.3)	107 (14.0)	65 (7.8)
Middle East & North Africa	743 (3.8)	9 (1.5)	492 (89.8)	33 (6.0)	23 (4.2)	215 (35.2)	127 (20.8)	68 (11.1)	85 (13.9)	116 (19.0)	132 (17.8)
North America	1685 (8.6)	9 (0.6)	1300 (86.8)	153 (10.2)	44 (3.0)	337 (21.6)	452 (28.9)	278 (17.8)	258 (16.5)	237 (15.2)	123 (7.3)
South Asia	1243 (6.3)	14 (1.6)	847 (98.3)	12 (1.4)	3 (0.3)	327 (37.6)	161 (18.5)	63 (7.2)	99 (11.4)	219 (25.3)	374 (30.1)
Sub-Saharan Africa	211 (1.1)	0 (0.0)	131 (95.6)	3 (2.2)	3 (2.2)	10 (7.1)	20 (14.2)	26 (18.4)	26 (18.4)	59 (41.9)	70 (33.2)

hospitals with triage level (0.1%) (Table 6). There was an association between hospital type and surge level and delay to surgery ($p < 0.001$, $p = 0.015$). In all types of hospitals and across all surge levels, with the exception of the triage surge level, the majority of surgeries were performed three to four weeks after decision to operate. In triage surge level hospitals, most surgeries were conducted within two weeks (Table 4).

The highest 30-day postoperative mortality was observed in undesignated hospitals without emergency department (1.2%) and in hospitals with a high surge level (1.5%), while it was lowest in “cold” hospitals (0.6%) and hospitals with a triage level (0.0%) (Table 6). R0 resection was achieved in 90% or more of patients in all hospital types with the exception of undesignated hospital type without emergency department, where it was achieved only in 84.7% of patients (Table 4).

3.6 Association of delay to surgery with resectability and postoperative mortality

For the overall population, there was no linear association between delay to surgery and resectability, with R0 resection rates being highest after a very short (0–2 weeks) and a long (>11 weeks) delay, but very small absolute differences in R0 rates between the single intervals. The highest R0 resection rate was observed after a long delay (>11 weeks) in many tumor entities including pancreatic, lung, head and neck, breast and bone sarcoma. For liver and prostate cancer as well as for soft tissue sarcoma, the highest R0 resection rate was noted after a delay of 0–2 weeks, and R0 resection rates were considerably lower after >11 weeks. (Table 5).

There was an association between delay to surgery and postoperative mortality ($p < 0.001$). The highest 30-day postoperative mortality rate was observed within two

Table 4 Postoperative mortality, resectability and interval from decision to operation stratified by hospital type and surge level

	Pa- tients (%)	30-day postopera- tive mortal- ity (%)	Resectability (%)			Interval from decision to opera- tion in weeks (%)				
			R0	R1	R2	0–2	3–4	5–6	7–10	> 11
<i>Hospital type</i>										
Designated COVID-free “cold” hospitals	4788 (27.4)	29 (0.6)	4195 (91.0)	355 (7.7)	59 (1.3)	988 (20.6)	1319 (27.5)	911 (19.0)	846 (17.7)	724 (15.2)
Designated COVID- treatment “hot” hospitals	4852 (27.7)	54 (1.1)	4235 (90.8)	343 (7.4)	85 (1.8)	1252 (26.6)	1413 (29.1)	796 (16.4)	623 (12.9)	728 (15.0)
Undesignated hospital type with emergency department	6817 (39.0)	77 (1.1)	5892 (90.9)	521 (8.0)	71 (1.1)	1452 (21.3)	2082 (30.5)	1206 (17.7)	1062 (15.6)	1015 (14.9)
Undesignated hospital type without emer- gency department	1029 (5.9)	12 (1.2)	818 (84.7)	133 (13.8)	15 (1.5)	216 (21.0)	355 (34.5)	203 (19.7)	131 (12.7)	124 (12.1)
<i>Surge level</i>										
Level 0 – normal	3940 (22.7)	38 (1.0)	3416 (90.9)	295 (7.8)	49 (1.3)	877 (22.3)	1226 (31.1)	719 (18.2)	540 (13.7)	578 (14.7)
Level 1 – low surge	5962 (34.3)	57 (0.9)	5209 (91.0)	446 (7.8)	70 (1.2)	1246 (20.9)	1640 (27.5)	1051 (17.6)	975 (16.4)	1050 (17.6)
Level 2 – medium surge	5757 (33.1)	52 (0.9)	4936 (89.7)	488 (8.9)	76 (1.4)	1359 (23.6)	1702 (29.6)	1056 (18.3)	891 (15.5)	749 (13.0)
Level 3 – high surge	1705 (9.8)	25 (1.5)	1489 (91.0)	114 (7.0)	34 (2.0)	436 (25.6)	552 (32.4)	270 (15.9)	241 (14.1)	206 (12.0)
Level 4 – triage	20 (0.1)	0 (0.0)	17 (89.5)	2 (10.5)	0 (0.0)	8 (40.0)	1 (5.0)	2 (10.0)	7 (35.0)	2 (10.0)

Table 5 Interval from decision to operation and resectability, stratified by tumor entity

		Resectability	Interval from decision to operation in weeks (%)					p-value
			0–2	3–4	5–6	7–10	> 11	
All patients	R0	3454 (91.1)	4497 (90.9)	2667 (89.1)	2287 (90.1)	2227 (91.2)	0.02	
	R1/R2	339 (8.9)	449 (9.1)	327 (10.9)	250 (9.9)	214 (8.8)		
Tumor location								
Colon	R0	643 (97.3)	778 (97.6)	486 (97.0)	423 (98.1)	293 (96.7)	0.73	
	R1/R2	18 (2.7)	19 (2.4)	15 (3.0)	8 (1.9)	10 (3.3)		
Rectal	R0	231 (92.8)	361 (95.5)	240 (93.4)	213 (93.8)	316 (92.4)	0.48	
	R1/R2	18 (7.2)	17 (4.5)	17 (6.6)	14 (6.2)	26 (7.6)		
Gastric	R0	101 (92.7)	143 (91.1)	82 (91.1)	59 (96.7)	125 (94.0)	0.6	
	R1/R2	8 (7.3)	14 (8.9)	8 (8.9)	2 (3.3)	8 (6.0)		
Oesophageal	R0	45 (91.8)	49 (84.5)	56 (84.8)	41 (95.3)	115 (86.5)	0.36	
	R1/R2	4 (8.2)	9 (15.5)	10 (15.2)	2 (4.7)	18 (13.5)		
Liver	R0	94 (89.5)	176 (88.4)	114 (79.2)	145 (88.4)	102 (83.6)	0.06	
	R1/R2	11 (10.5)	23 (11.6)	30 (20.8)	19 (11.6)	20 (16.4)		
Pancreatic	R0	126 (85.1)	143 (83.6)	65 (74.7)	68 (84.0)	61 (87.1)	0.22	
	R1/R2	22 (14.9)	28 (16.4)	22 (25.3)	13 (16.0)	9 (12.9)		
Kidney	R0	69 (93.2)	77 (90.6)	69 (98.6)	66 (91.7)	57 (96.6)	0.22	
	R1/R2	5 (6.8)	8 (9.4)	1 (1.4)	6 (8.3)	2 (3.4)		
Bladder	R0	20 (90.9)	35 (89.7)	27 (90.0)	24 (96.0)	16 (84.2)	0.93	
	R1/R2	2 (9.1)	4 (10.3)	3 (10.0)	1 (4.0)	3 (15.8)		
Prostate	R0	32 (86.5)	42 (80.8)	39 (61.9)	93 (75.0)	120 (77.4)	0.04	
	R1/R2	5 (13.5)	10 (19.2)	24 (38.1)	31 (25.0)	35 (22.6)		
Soft-tissue sarcoma	R0	51 (89.5)	59 (84.3)	44 (81.5) 10	37 (80.4)	59 (83.1)	0.74	
	R1/R2	6 (10.5)	11 (15.7)	(18.5)	9 (19.6)	12 (16.9)		
Bone sarcoma	R0	15 (100)	18 (94.7)	9 (90.0)	10 (76.9)	21 (100)	0.07	
	R1/R2	0 (0.0)	1 (5.3)	1 (10.0)	3 (23.1)	0 (0.0)		
Lung	R0	212 (95.1)	368 (96.1)	206 (91.2)	158 (94.6)	104 (96.3)	0.1	
	R1/R2	11 (4.9)	15 (3.9)	20 (8.8)	9 (5.4)	4 (3.7)		
Head and neck	R0	672 (83.4)	724 (81.9)	326 (80.3)	255 (82.5)	231 (90.6)	0.009	
	R1/R2	134 (16.6)	160 (18.1)	80 (19.7)	54 (17.5)	24 (9.4)		
Breast	R0	696 (93.3)	946 (91.2)	575 (92.7)	496 (90.7)	437 (94.8)	0.06	
	R1/R2	50 (6.7)	91 (8.8)	45 (7.3)	51 (9.3)	24 (5.2)		
Gynecological	R0	447 (90.9)	578 (93.7)	329 (88.9)	199 (87.7)	170 (89.9)	0.03	
	R1/R2	45 (9.1)	39 (6.3)	41 (11.1)	28 (12.3)	19 (10.1)		

weeks following the surgical decision in the overall study population. Only in colon and gastric cancer and soft tissue sarcoma, the highest mortality rates were recorded three to four, seven to ten or >11 weeks after decision (Table 6).

4 Discussion

Surgery is the most important treatment modality for solid cancers. For most of them, it represents the only potentially curative approach, especially when the tumor is at an early stage. Inappropriate delay in cancer surgery is concerning, as it can lead to worse outcomes [3].

Such delay poses varying risks depending on tumor type due to differing growth rates. Rapidly metastasizing cancers, such as pancreatic [10], certain types of breast [11] or lung cancers [4], require prompt intervention for optimal outcomes. A systematic review with meta-analysis showed that a surgical delay of just four weeks can adversely affect survival in patients with bladder, breast, colon, rectum, lung, cervix, and head and neck cancers, with hazard ratios ranging between 1.06–1.08 [5]. Another systematic review found decreased survival in lung and oesophageal cancer patients when surgery was delayed beyond three to six weeks, although different times might apply for the interval

Table 6 Interval from decision to operation and postoperative mortality, stratified by tumor entity

30-day postoperative mortality (%)	Interval from decision to operation in weeks (%)					p-value
	0–2	3–4	5–6	7–10	> 11	
All patients	54/3942 (1.4)	46/5172 (0.9)	26/3119 (0.8)	27/2667 (1.0)	19/2586 (0.7)	< 0.001
<i>Tumor location</i>						
Colon	9/674 (1.3)	15/825 (1.8)	6/511 (1.2)	7/446 (1.6)	7/316 (2.2)	0.83
Rectal	2/264 (0.8)	2/397 (0.5)	2/265 (0.7)	1/233 (0.4)	2/349 (0.6)	0.98
Gastric	4/112 (3.6)	3/161 (1.9)	1/94 (1.1)	3/62 (4.8)	1/134 (0.7)	0.28
Oesophageal	5/51 (9.8)	3/60 (5.0)	1/67 (1.5)	4/45 (8.9)	1/140 (0.7)	0.01
Liver	6/122 (4.9)	3/217 (1.4)	5/154 (3.2)	3/177 (1.7)	1/135 (0.7)	0.13
Pancreatic	8/157 (5.1)	6/182 (3.4)	1/93 (1.2)	3/85 (3.5)	2/75 (2.7)	0.66
Kidney	1/74 (1.4)	0/90 (0.0)	1/79 (1.3)	0/75 (0.0)	0/67 (0.0)	0.13
Bladder	2/26 (7.7)	2/42 (4.8)	0/34 (0.0)	1/31 (3.2)	1/27 (3.7)	0.63
Prostate	0/42 (0.0)	0/65 (0.0)	0/76 (0.0)	0/144 (0.0)	0/172 (0.0)	1
Soft-tissue sarcoma	0/62 (0.0)	1/78 (1.3)	0/55 (0.0)	0/49 (0.0)	1/75 (1.3)	0.7
Bone sarcoma	0/15 (0.0)	0/19 (0.0)	0/10 (0.0)	0/14 (0.0)	0/23 (0.0)	1
Lung	4/234 (1.7)	2/409 (0.5)	3/242 (1.2)	3/174 (1.7)	1/117 (0.9)	0.55
Head and neck	7/840 (0.8)	6/931 (0.6)	3/423 (0.7)	1/321 (0.3)	1/265 (0.4)	0.21
Breast	3/756 (0.4)	1/1051 (0.1)	1/624 (0.2)	1/566 (0.2)	0/485 (0.0)	0.2
Gynecological	3/513 (0.6)	2/645 (0.3)	2/392 (0.5)	0/245 (0.0)	1/206 (0.5)	< 0.001

between neoadjuvant therapy and surgery [6]. Another systematic review found that delays exceeding 30–40 days for colon cancer and more than seven to eight weeks for rectal cancer after neoadjuvant therapy correlate with lower survival. For pancreatic cancer, delays over 30 days were associated with tumor progression and irresectability, but no effects on survival could be shown [12]. In our analysis, over 50% of breast and lung cancer patients underwent surgery within four weeks after the decision for surgery, achieving high R0 resection rates and comparatively low 30-day postoperative mortality rates.

There are presumed differences between tumor entities with regard to the relevance of delay to surgery. For example, pancreatic cancer exhibits rapid tumor growth and is often diagnosed only at advanced stages, making timely treatment even more critical [13]. In our analysis, more than half of pancreatic cancer patients underwent surgery within four weeks after surgical decision. These patients showed higher postoperative 30-day mortality and lower R0 resection rates compared to other tumor entities. Fligor et al. believe that surgery for pancreatic cancer should not be delayed beyond 30 days to avoid worse outcomes [12]. However, our results indicated that the highest R0 resection rate for pancreatic cancer occurred more than 11 weeks after the surgical decision, suggesting that delays did not have a negative impact on resectability. In contrast, prostate cancer usually develops and spreads more slowly [14]. More than one third of prostate cancer patients in our analysis underwent surgery only after >11 weeks. However, the results showed that highest R0 resection rates were achieved within two weeks following decision to operate, while delay for surgery did not affect postoperative mortality. Recent studies have shown that delays of three to six months for surgeries in prostate cancer patients have no impact on mortality [14]. In some studies, no survival differences were observed even with delays of up to twelve months [15].

When delaying cancer surgeries, not only differences in growth rates must be considered but also the UICC stage plays a crucial role. Prolonged waiting times for advanced-stage tumors can worsen the patient's physical status and prognosis to a proportionally larger extent than in earlier stages. The larger and more advanced a tumor is, the more

difficult becomes complete resection. Our data show that R0 resection rate for patients with UICC stage III tumors was lowest compared to earlier UICC stages, and that postoperative 30-day mortality was highest in UICC stage III. Bolm et al. found similar results, linking higher UICC stages to lower resectability [16].

Postoperative mortality varies significantly among different tumor types. High mortality rates are observed in oesophageal, pancreatic, bladder, liver and gastric cancers. This is likely related to the fact that surgery is more extensive and thus complication-prone for these tumors. Furthermore, patients are often diagnosed at advanced stages and in a reduced physical status, making surgery considerably more complicated. In contrast, lower mortality is seen for prostate and breast cancer and bone sarcoma. This may result from early detection, slower tumor growth, or lower-risk operations. Prior to the pandemic, the lowest postoperative mortality was reported for prostate (<1%) and breast cancer (<1%) [17]. On the other hand, highest mortality was reported for pancreatic (4–12%), liver (5%), and oesophageal (3–10%) cancer [17–19]. Our results are in line with these data.

No elevated postoperative mortality was observed during the COVID-19 pandemic, even with delays in surgery. Surprisingly, it was found that 30-day postoperative mortality was higher in almost all tumor entities within two weeks after surgical decision compared to later operations. This may be attributed to the fact that surgeries were performed when capacity was available, potentially leading to deviations from the original treatment plan, not allowing for optimal preparation for surgery. The postoperative mortality in the CSCC was lower for most tumor entities than what is reported in the literature. However, it must be considered that 11.2% of patients in the CSCC were not operated on during the observation period, which is a possible source of selection bias.

Prognosis is vastly different across tumor entities with particularly high five-year survival after resection of prostate cancer (nearly 100%), breast cancer (90%) and kidney cancer (75–90%) and lowest five-year survival after resection of pancreatic (10%), oesophageal (20%) or liver cancer (20%) [20]. Five-year survival would be an extremely valuable parameter in the analysis of the effects of pandemic-related surgical delays. For many patients who survive the first five years post-diagnosis, there are good chances of permanent cure, as recurrence becomes less likely thereafter. Unfortunately, the CSCC did not collect information on long-term survival. Resectability varies depending on tumor entity and stage. High probabilities of R0 resections are attributed to breast, colorectal, gastric and kidney cancer, provided the tumors are detected at an early stage [21–28]. The likelihood of R0 resection of pancreatic cancer is much lower at 68.5–81% [29, 30], primarily due to locally advanced stages complicating surgery [31, 32]. Similar results were found in our analysis. Notably, even during the pandemic, when many cancer surgeries were postponed, no considerable differences in resectability compared to what is reported in the literature from the pre-pandemic period were observed [21–30].

Surgical delays varied by region and health care systems, influenced by different hospital utilization across regions. Specific types of hospitals were established, divided into "hot" and "cold" hospitals, which helped control the spread of the virus while ensuring that patients with other health issues continued to receive necessary care. "Hot" hospitals focused on COVID-19 cases, leading to longer wait times for non-COVID surgeries, while "cold" hospitals prioritized regular care and elective procedures [33]. The availability of these hospitals varied by healthcare system, resulting in regional disparities.

Additionally, differences in postoperative mortality and resectability can be attributed to variations in infrastructure, devices, training, and treatment protocols [34].

Limitations of this analysis include unavailable data from the CSCC. Some data were collected incompletely, leading to possible bias. Long-term survival data, crucial for assessing the impact of delays in elective tumor surgeries, were not collected. Additionally, selection bias may have occurred, as participating centers could in theory selectively include patients, potentially resulting in unequal group compositions. There may also have been insufficient validation of source data at centers. In contrast, this analysis has several strengths. A large dataset was included, encompassing many regions, hospital types, tumor entities and oncological operations. Moreover, the outcomes used in this analysis, postoperative mortality and resectability, are relatively easy to collect and should therefore be rather complete and valid.

In summary, the resectability and postoperative mortality in oncological surgery are influenced by various factors that should be particularly considered in pandemic situations or during capacity shortages, which may lead to delays. During the COVID-19 pandemic, a moderate delay of surgeries was observed worldwide, with relevant differences between tumor entities, UICC stages and regions. However, no tangible effects on resectability could be observed with slightly higher postoperative mortality early after decision for surgery, possibly due to subpar preparation for the respective operation.

5 Conclusion

In this analysis, delay to surgery during the COVID-19 pandemic did not impact resectability and even showed a small elevation of postoperative mortality in operations carried out early after decision for surgery. Short-term survival data provide only partial information and further research is needed to investigate the long-term effects of surgical delays during pandemics. All efforts should be made not to unduly delay cancer surgery with curative intent within tumor entities in order to avoid negative effects on resectability and mortality in pandemic situations or in situations with limited hospital capacities, and rapidly growing tumors and higher tumor stages should be prioritized.

Supplementary Information

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Supplementary Material 1.

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Collaborating authors are listed in the online supporting information Appendix S1.

Author contributions

A.L.S. wrote the original draft of the manuscript and prepared all figures and tables. A.L.S. and U.R. performed data analysis and interpretation, statistical analysis and edited and prepared the manuscript. U.R. was responsible for supervision, funding acquisition, conceptualization and project administration. J.C.G., A.A.B., E.M.H. and the CovidSurg Collaborative were responsible for data acquisition. J.C.G., A.A.B. and E.M.H. performed data quality control. All authors reviewed the manuscript.

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Data availability

The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

Declarations**Ethics approval and consent to participate**

Clearance from the competent ethics committee (Medical Faculty, University of Halle, reference 2020–080) was obtained. The study adhered to the Declaration of Helsinki. Local principal investigators obtained all required ethical approvals according to local and national regulations. In most settings, a waiver of individual informed consent was granted by the ethics committee. Where required, written or verbal informed consent was obtained from participants or their legal guardians, based on local ethics committee recommendations.

Consent for publication

Not applicable.

Competing interests

Ulrich Ronellenfisch declares that he is an Editorial Board Member of *Discover Oncology* and confirms that he is not involved in the handling or decision-making of their own submission.

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