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TESI DI LAUREA

Surgical complications after major gastrointestinal surgery during the SARS-CoV-2 pandemic

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Sommario

Presupposti dello studio: per ridurre il rischio di esposizione alla sindrome respiratoria acuta grave indotta dal Coronavirus 2 (SARS-CoV-2), nei pazienti chirurgici più inclini a sviluppare le forme gravi di malattia da Covid 19, è stata avviata una riorganizzazione che prevedeva la creazione di ospedali o unità "COVID-19-Free".
Lo scopo di questo studio è stato quello di quantificare l'effetto dei percorsi "Covid-19 free", costruiti per ridurre il rischio di trasmissione di SARS-CoV-2, sulle complicanze postoperatorie.

Materiali e Metodi: sono stati analizzati i dati di tutti i pazienti sottoposti a interventi chirurgici per malattia del colon-retto, tra Novembre 2019 e Luglio 2020 in due centri di riferimento italiani.
I pazienti sono stati divisi in 2 gruppi: quelli che hanno subito gli interventi chirurgici da Novembre 2019 a Marzo 2020 (Gruppo 1), e quelli che hanno subito gli interventi chirurgici durante la pandemia, da Aprile a Luglio 2020 (Gruppo 2).
Le differenze tra i due gruppi sono state testate mediante test χ^2 e test t-indipendente.

Risultati: dei 264 pazienti, 168 (63,4%) hanno subito un intervento chirurgico nel periodo precedente la pandemia (Gruppo 1), mentre 96 (36,4%) durante la pandemia (Gruppo 2). Le caratteristiche preoperatorie erano simili tra questi due gruppi. Nel Gruppo 2 si è registrata una percentuale maggiore di pazienti sottoposti a procedure chirurgiche per neoplasie maligne rispetto al Gruppo 1 (92,7% vs 72%; p=0,001).
Come risultato del nostro studio, l'approccio mini-invasivo (OR 0,46; IC 95%, 0,04 – 0,83; p=0,01) e l'isolamento dei pazienti (OR 0,18; IC 95%, 0,04 – 0,83; p=0,03) sono risultati essere indipendentemente associati ad un minor rischio di complicanze postoperatorie.

Conclusioni: la morbilità postoperatoria dopo chirurgia elettiva del colon-retto si è dimostrata essere significativamente più bassa durante la pandemia, quando sono stati seguiti i percorsi liberi da COVID-19.

Abstract

Introduction: To reduce the exposition risk to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in surgical patients more prone to develop serious forms of Coronavirus disease 2019, a reorganization that previewed the creation "COVID-19-free" hospitals or units was pursued. The aim of this study was to quantify the effect of clear pathways, built to reduce the risk of SARS-Cov-2 transmission, on postoperative complications.

Methods: Data of all consecutive patients undergoing surgical procedures for colorectal diseases, between November 2019 and July 2020 in two Italian referral centers, were analyzed. Patients were divided into two groups: the ones who underwent surgical procedures from November 2019 to March 2020 (Group 1), and those who underwent surgical procedures during the pandemic, from April to July 2020 (Group 2). Differences between the two groups were tested by χ^2 test and independent t-test.

Results: Among 264 patients, 168 (63.4%) underwent surgery during the period before the pandemic (Group 1), whereas 96 (36.4%) during the pandemic (Group 2). Preoperative characteristics were similar between these two groups. In Group 2 there was a higher proportion of patients who underwent surgical procedures for malignancy if compared with Group 1 (92.7% vs 72%; p= 0.001). As a result of our study, minimally invasive approach (OR 0.46; 95% CI .04 - 0.83; p= 0.01) and isolation of patients (OR, 0.18; 95% CI, 0.04 - 0.83; p=0.03) were found to be independently associated with lower risk of postoperative complications.

Conclusions: Postoperative morbidity after colorectal elective surgery was significantly lower during the pandemic, when COVID-19-free pathways were followed.

CHAPTER 1

Introduction

The Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was identified in Wuhan, Hubei province of China in December 2019 (Guo et al., 2020). Globally, until March 20th 2021, 122.997.108 cases were confirmed, and a total of 2.715.249 patients have died from this viral infection (CDC, 2020).

SARS-CoV-2 mainly affects the respiratory tract. The virus firstly binds to the ACE2 cell receptor located in the upper respiratory tract and then, secondly, in the lower respiratory tract. As shown in recent studies, the infection can become generalized and involve different systems (e.g. gastrointestinal, central nervous, cardiac, and dermatologic ones) (Deidda et al., 2021; Alam et al., 2020; Larson et al., 2020; Gottlieb et al., 2020; Gupta et al., 2020). Affecting the respiratory system, Covid-19 can cause a persistent state of hypoxia that can lead to the over production of pro-inflammatory mediators (known as a cytokine storm) that worsen the systemic clinical picture; high levels of pro-inflammatory cells and molecules (INF-G, TNF-A and IL-6) have been found in the blood of infected patients (Mazzoni et al., 2020).

Covid-19 infection mainly manifests itself with respiratory symptoms such as cough and dyspnea, but also with generalized symptoms such as fever and malaise, loss of taste and smell.

Some studies have also pointed out some atypical manifestations: patients can present with abdominal pain resembling an attack of acute pancreatitis (Saeed et al., 2020) or with vague gastrointestinal symptoms such as nausea, vomiting and diarrhea (Goyal et al., 2020).

Patients can also present with cardiovascular complications. In many cases Covid-19 infection occurred together with an acute cardiovascular syndrome (Bangalore et al., 2020) and, even more frequently, with episodes of venous and pulmonary thromboembolism (Connors et al., 2020).

The Central Nervous System can also be involved: the virus has the ability to enter the CNS via the olfactory nerve (Zubair et al., 2020).

Clinical manifestations and out-comes vary greatly between patients depending on different comorbidities: older age, overweight and obesity are the most important risk factors affecting survival (Docherty et al., 2020; Goyal et al., 2020).

In this scenario, hospitals urgently needed to change their organizations, in order to free standard and intensive care unit beds for COVID-19 patients. Subsequently, these changes in the health system organization necessitated a sudden mutation in the management of patients with diseases other than COVID-19, with a worrying reduction of elective surgical activities (Zarrintan et al., 2020; Francis et al., 2020; CovidSurg Collaborative, 2020).

Several studies have shown how Covid-19 infection has damaged the entire preventive, diagnostic and surgical system of abdominal and colorectal surgery: CRC diagnoses and screening had decreased significantly (Smith et al., 2021) and, as demonstrated by the multicentric study COVID-CRC, in the time span March-December 2020, patients with colorectal cancer have come to clinical observation with a disease in a more advanced stage, with worse clinical symptoms and with a higher probability of liver metastases (Rottoli et al., 2022).

Given this, a reform of the hospitalization system was necessary in order to allow the safe maintenance of elective surgery for patients with life threatening diseases such as oncologic patients (Liang et al., 2020; Philouze et al., 2020; Spolverato et al., 2020). A reorganization that previewed the creation of "COVID-19-free" hospitals or units was pursued in order to resume elective surgical procedures limiting the exposition risk to SARS-CoV-2 in surgical patients more prone to develop serious forms of Covid-19 (Restivo et al., 2020; Spolverato et al., 2020; Cavaliere et al., 2021; Royal College of Surgeons, 2020; Glasbey et al., 2020).

As some studies have shown, these conditions were posed considering that postoperative risk of morbidity and mortality was increased with postoperative diagnosis of SARS-CoV-2 infection especially in centers that were not organized

as “COVID-free” (COVIDSurg Collaborative, 2020; Lei et al., 2020; Abate et al., 2020; Jessop et al., 2020).

Surgical complications are a series of events that alter normal physiological healing after surgery and can significantly affect patient's recovery after surgery: they increase the length of hospitalization, worsen the clinical condition and may also require further medical prescriptions, instrumental investigations and, in some cases, even re-surgery. All these aspects have an impact on both the patient's outcome and the economic health system (Townsend et al., 2021).

Surgical Site Infections (SSIs) are one the most common complications seen after surgery and reported in 2% to 5% of surgical patients in the US (World Health Organization, 2018). The term SSI refers to incisional skin infection but also to infection of deeper tissues and organs; the Centers for Disease Control and Prevention (CDC) groups SSIs into superficial, deep, and organ/space (Townsend et al., 2021).

Different surgical procedures have different risks of developing SSIs; depending on the risk of infection and the type of antibiotic prophylaxis needed they are classified in clean, clean contaminated, contaminated and dirty (Culver et al.,1991; Ehrenkranz et al., 1981; Page et al., 1993).

In the specific case of colorectal surgery, the most frequent complications are hemorrhages (related to the incorrect clamping of vessels during surgery), intestinal obstruction, and acute wound failure. In this last group we can find fascial dehiscence, evisceration, acute hemorrhage, incisional hernia, anastomotic leaks, and fistulas. Dehiscence consists of a spontaneous reopening of a sutured portion; it is a serious complication that can lead to the formation of intra-abdominal collections requiring surgery while fistulas are non-anatomical communications between adjacent organs (Townsend et al., 2021; Spolverato et al., 2021).

A whole series of medical systemic complications can also occur after surgery affecting the renal, respiratory, cardiovascular and cerebrovascular systems. Among these: deep vein thrombosis and pulmonary embolism, favored by

immobility and pro-inflammatory status, urinary infections, fever, hemorrhagic or septic shock and renal failure (Goldhaber et al., 1998; Lennard et al., 1982; Spolverato et al., 2021).

We aimed to identify whether specific protocols to decrease the risk of SARS-Cov-2 transmission resulted in a reduction of postoperative morbidity and mortality, comparing patients undergoing surgery during the pandemic with those who underwent the same surgical procedure in a control period.

CHAPTER 2

Materials and methods

2.1 Patients' Selection

All consecutive patients undergoing surgical procedure for colorectal diseases, between November 2019 and July 2020, were retrospectively selected from a prospectively maintained database of two high-volume referral centers for Colorectal Surgery: the department of Surgical science of Cagliari and Padova University hospitals.

Patients were divided into two groups: the ones who underwent surgical procedures from November to March 2020 (Group 1), and those who underwent surgical procedure from April to July 2020 during the pandemic (Group 2).

All patients undergoing elective surgery, who were tested negative for SARS-CoV-2 before surgery and did not develop COVID-19 during hospitalization, were included.

Group 2 patients were carefully selected and contacted the day before admission to ask if they had experienced, in the 15 days before, the most common symptoms of COVID-19 infection, such as fever, cough, dyspnea, anosmia, or other respiratory symptoms. Moreover, it was investigated if they had strict contact with anyone who presented COVID-19 manifestation or who tested positive for SARS-CoV-2. During the pre-hospitalization period all patients undergoing elective surgery must have had a negative serology test and swab test within 48 hours before the day of the scheduled hospitalization.

During the perioperative period the daily ward rounds were limited and performed by a single surgeon, visits were prohibited or limited, and in one of the two centers patients were isolated and hospitalized in a single room. All healthcare staff used maximal individual protective measures, including personal protective equipment (PPE) such as surgical or FFP2 masks, frequent hand sanitation and gloves. Emergency hospitalizations were continued in one of the two institutions even during the pandemic.

Demographics (age, sex) and clinical characteristics including BMI, American Society of Anesthesiology (ASA) status classification, smoking, medications history, diagnoses, surgery details, intraoperative complications, length of stay, and intensive care unit (ICU) admission were recorded. The severity of complications was determined using the Clavien-Dindo classification(Dindo et al., 2004). Data concerning post-operative 30-days complications, including both surgical and medical ones, as well as data reguarding 30-days postoperative mortality were collected.

The following complications were recorded: wound infection, intra-adominal collection, anastomotic leakage, ileus, bleeding, infectious colitis, chest infection, urinary tract infection, renal failure, myocardial infarction, polmonary embolism and cerebrovascular complications. Postoperative surgical complications were classified into superficial, deep, or organ/space SSI.

2.2 Statistical analysis

Statistical analysis was performed using Stata version 13 for Mac (StataCorp, Texas, USA). Continuous variables were expressed as mean [± standard deviation (SD)]; categorical variables as frequencies and percentage. Significant differences between the two groups were tested by χ^2 test and independent t-test for continuous one. The possible relationship between the two groups and postoperative complications was analyzed using a logistic regression model; results are shown as odds ratio (OR) and 95% confidence interval (CI). Univariate and multivariate logistic regression analyses were performed to study the risk of postoperative complications for patients who had undergone surgery.
All tests were two-sided with a level of significance set at $p<0.05$.

CHAPTER 3

Results

3.1 Patients' clinicopathological characteristics

Two hundred and sixty-four patients were included in the analysis. One hundred and sixty-eight (63.4%) underwent surgery during the period before the pandemic, whereas ninety-six (36.4%) during the pandemic. Patients distribution in different groups is shown in Figure 1.

Mean age was 66.5 (SD, ±13.9), mean BMI 24.4 (SD, ±3.9), 253 (95.8%) patients were smokers and 139 (52.6%) of the patients were male.

According to the ASA score most patients were ASA II [139 (52.6%)], and the most common diagnoses were malignancy 210 (79.5%). Other diseases recorded included Stoma 23 (8.7%), Diverticular disease 19 (7.2%) and Inflammatory Bowel disease 12 (4.5%). Most of the patients were taking Steroids 259 (98.1%), Anticoagulants 245 (92.8%), but only 38 patients were taking Antiplatelets (14.4%). The demographics and clinical characteristics for Group 1 and Group 2 were homogeneous. As expected, during the pandemic there was a higher proportion of patients who underwent surgical procedures for malignancy if compared with the period before pandemic (92.7% vs 72%; p= 0.001). (Table I)

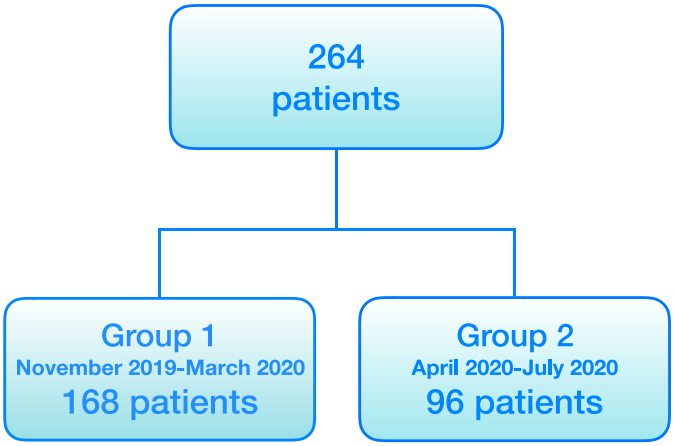

Figure 1. Patients distribution in different groups.

Table I. Characteristics of patients treated within pandemic period and before the pandemic.

		Total 264	Group 1 168 (63.4%)	Group 2 96 (36.4%)	P
Age, mean (±SD)		66.5 (±13.9)	66.9 (±13.5)	65.9 (±14.8)	0.55
Gender, n(%)					
	Male	139 (52.6)	93 (55.4)	46 (47.9)	0.35
	Female	125 (47.3)	75 (44.6)	46 (47.9)	
BMI, mean (±SD)		24.4 (±3.9)	24.7 (±4.2)	24 (±3.4)	0.17
Smoking, n(%)					
	Yes	11 (4.2)	5 (3)	6 (6.2)	0.20
	No	253 (95.8)	163 (97)	90 (93.7)	
ASA, n(%)					
	1	16 (6.1)	13 (7.7)	3 (3.1)	0.40
	2	139 (52.6)	86 (51.2)	53 (55.2)	
	3	104 (39.4)	65 (38.7)	39 (40.6)	
	4	5 (1.9)	4 (2.4)	1 (1.04)	
Steroids, n(%)					
	No	5 (1.9)	3 (1.8)	2 (2.1)	0.86
	Yes	259 (98.1)	165 (98.2)	94 (97.9)	
Anticoagulants, n(%)					0.49
	No	19 (7.2)	12 (6.5)	7 (8.9)	
	Yes	245 (92.8)	173 (93.5)	72 (91.1)	
Antiplatelets, n(%)					0.52
	No	226 (85.6)	142 (84.5)	84 (87.5)	
	Yes	38 (14.4)	26 (15.5)	12 (12.5)	
Diseases, n(%)					0.001
	Malignancy	210 (79.5)	121 (72)	89 (92.7)	
	Inflammatory Bowel disease	12 (4.5)	11 (6.5)	1 (1.04)	
	Diverticular Disease	19 (7.2)	15 (8.9)	4 (4.2)	
	Stoma	23 (8.7)	21 (12.5)	2 (2.1)	

Abbreviations: SD, standard deviation; BMI, body mass index; ASA, American Society of Anesthesiology

3.2 Patients' perioperative characteristics

Table II showes perioperative characteristics of all patients. Hygiene and safety measures like PPE, Hand sanitizer and isolation, were adopted only during the pandemic, in Group 2.

Patients in Group 2 had a lower rate of postoperative complications (21.9% vs 34.5%; p=0.03) and a nearly statically significant lower rate of surgical complications (14.6% vs 25%; p=0.05). Moreover, patients in Group 2 had a shorter length of stay than patients in Group 1 (11.9 days vs 20.5 days; p<0.001).

Patients in Group 2 had a slightly lower rate of medical complications (6.2% vs 7.7%; p=0.65), infections (18.7% vs 27,4%; p=0.10), intraoperative complications (1% vs 4.2%; p=0.15) but a slightly higher rate of ICU admissions (11.5% vs 7.1%; p=0.23). Post-operative complications were graded according to the Clavien-Dindo Classification: most patients had a complication grade equal to 0 (102, 38.6%) and 1 (102, 38.6%); 27 (10.2%) were graded 2, 27 (10.3%) were graded 3, only 4 (1.5%) were graded 4 and 2 (0.8%) were graded 5.

Most patients underwent surgery with a laparoscopic approach (155, 58.7%), 98 (37.1%) had an open surgery and 11 (4.2%) patients had a robotic approach.
No patients died in Group 2, while, the mortality rate in Group 1 was 2.4%.
Data related to the number of emergency admissions were also recorded: during the pandemic period the rate showed to be higher than the previous one (62.5% vs 41.1%; p=0.001). (Table II)

Table II. Operative and postoperative results of patients treated within pandemic period and before the pandemic.

		Total 264	Group 1 168 (63.4%)	Group 2 96 (36.4%)	P
Operative time, n(%)		4.2 (±1.7)	4.1 (±1.6)	4.4 (±1.9)	0.12
Intraoperative complications, n(%)					0.15
	Yes	8 (3)	7 (4.2)	1 (1)	
	No	256 (97)	161 (95.8)	95 (99)	
ICU admission, n(%)					0.23
	Yes	23 (8.7)	12 (7.1)	11 (11.5)	
	No	241 (91.3)	156 (92.9)	85 (88.5)	
Surgical approach, n(%)					0.59
	Open	98 (37.1)	65 (38.7)	33 (34.4)	
	Robotic	11 (4.2)	8 (4.8)	3 (3.1)	
	Laparoscopic	155 (58.7)	95 (56.5)	60 (62.5)	
Postoperative complications, n(%)					0.03
	Yes	79 (29.9)	58 (34.5)	21 (21.9)	
	No	185 (70.1)	110 (65.5)	75 (78.1)	
Surgical Complications, n(%)					0.05
	Yes	56 (21.2)	42 (25)	14 (14.6)	
	No	208 (78.8)	126 (75)	82 (85.4)	
Medical Complications, n(%)					0.65
	Yes	19 (7.2)	13 (7.7)	6 (6.2)	
	No	245 (92.8)	155 (92.3)	90 (93.7)	
SSI, n(%)					0.10
	No	200 (75.8)	122 (72.6)	78 (81.2)	
	Superfic./incisional	22 (8.3)	14 (8.3)	8 (8.3)	
	Deep/incisional	9 (3.4)	9 (5.4)	0	
	Organ/space	33 (12.5)	23 (13.7)	10 (10.4)	
Clavien-Dindo Classification, n(%)					0.45
	0	102 (38.6)	67 (39.9)	35 (36.5)	
	1	102 (38.6)	60 (35.7)	42 (43.7)	
	2	27 (10.2)	17 (10.1)	10 (10.4)	
	3	27 (10.23)	18 (10.7)	9 (9.4)	
	4	4 (1.5)	4 (2.4)	0	
	5	2 (0.8)	2 (1.42)	0	
Hospital Stay (days), mean (±SD)		17.4 (±19.1)	20.5 (±21.9)	11.9 (±11.1)	<0.001
Mortality, n(%)					0.12
	Yes	4 (1.5)	4 (2.4)	0	
	No	260 (98.4)	164 (97.6)	96 (100)	
PPE, n(%)					0.000
	Yes	83 (31.4)	0	83 86.46	
	No	181 (68.6)	168 100.00	13 13.54	
Hand sanitizer, n(%)					0.000
	Yes	83 (31.4)	0	83 (86.5)	
	No	181 (68.6)	168 (100)	13 (13.5)	
Isolation, n(%)					0.000
	Yes	34 (12.9)	0	34 (35.4)	
	No	230 (87.1)	168 (100)	62 (64.6)	
Emergency admission, n(%)					0.001
	Yes	129 (48.9)	69 (41.1)	60 (62.5)	
	No	135 (51.1)	99 (58.9)	36 (37.5)	

Abbreviations: ICU, intensive care unit; SSI, Surgical Site Infection; PPE, personal protective equipment

3.3 Univariate analysis for postoperative complications

Table III reports univariate analysis and shows that patients with postoperative complications had a prolonged operative time (OR, 1.20; 95% CI, 1.01 – 1.37; p=0.03), and patients who had minimally invasive surgery had a lower risk of postoperative complications (OR, 0.41; 95% CI, 0.24 – 0.71; p=0.001). Also, isolation of patients was associated with lower risk of postoperative complications (OR, 0.12; 95% CI, 0.03 - 0.53; p=0.005), and emergency admission were related with higher risk of postoperative complications (OR, 1.98; 95% CI, 0.16 - 3.40; p=0.01).

Males had a slightly lower risk of postoperative complications (OR, 1.3; 95% CI, 0.75–2.18; p=0.36). An high ASA score was related with higher risk of postoperative complications, for example ASA 3 (OR 1.45; 95% CI, 0.44 – 4.85; p=0.54) or ASA 4 (OR 12; 95% CI, 1.02 – 141.34; p=0.05). Stoma was associated with lower risk of postoperative complication (OR 0.65; 95% CI, 0.23 – 1.82; p=0.41) compared to diverticular disease (OR 1.36; 95% CI, 0.51 – 3.62; p=0.54).

The presence of postoperative complications led to a longer length of stay (OR 1.01; 95% CI, 1.00 – 1.02 p=0.05). Also, the use of Hand sanitizer and PPE led to a lower risk of postoperative complications (both OR, 0.60; 95% CI, 0.32 – 1.09; p=0.09). (Table III)

Table III. Univariate analysis for postoperative complications.

		OR	CI (95%)	P
Age		1.01	0.99 - 1.03	0.35
Gender				0.36
	Female	1		
	Male	1.3	0.75 - 2.18	
BMI		0.99	0.92 - 1.06	0.81
ASA				
	1	1		
	2	1.08	0.33 - 3.58	0.89
	3	1.45	0.44 - 4.85	0.54
	4	12	1.02 - 141.34	0.05
Diseases				
	Malignancy	1		
	Inflammatory Bowel disease	1.16	0.34 - 4.01	0.81
	Diverticular Disease	1.36	0.51 - 3.62	0.54
	Stoma	0.65	0.23 - 1.82	0.41
Operative time		1.20	1.01 - 1.37	0.03
Intraoperative complications				0.76
	No	1		
	Yes	0.77	0.15 - 3.92	
ICU admission				0.32
	No	1		
	Yes	1.57	0.64 - 3.79	
Surgical approach				
	Open			
	Minimal invasive approach	0.41	0.24 - 0.71	0.001
Hospital stay		1.01	1.00 - 1.02	0.05
PPE				0.09
	No	1		
	Yes	0.60	0.32 - 1.09	
Hand sanitizer				0.09
	No	1		
	Yes	0.60	0.32 - 1.09	
Isolation				0.005
	No	1		
	Yes	0.12	0.03 - 0.53	
Emergency admission				0.01
	No	1		
	Yes	1.98	0.16 - 3.40	

Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiology; ICU, intensive care unit; SSI, Surgical Site Infection; PPE, personal protective equipment

3.4 Multivariate analysis for postoperative complications

Multivariate analysis showed that minimally invasive approach (OR 0.46; 95% CI .04 - 0.83; p= 0.01) and isolation of patients (OR, 0.18; 95% CI, 0.04 - 0.83; p=0.03) were independently associated with lower risk of postoperative complications. Instead, a longer operative time (OR, 1.14; 95% CI, 0.96 – 1.35; p=0.13) and emergency admission (OR, 1.12; 95% CI, 0.60 – 2.10; p=0.72) were independently associated with higher risk of postoperative complications.
(Table IV)

Table IV. Multivariate analysis for postoperative complications.

		OR	**CI (95%)**	**p**
Operative Time	No Yes	1 1.14	0.96 - 1.35	0.13
Surgical Approach	Open Minimal invasive approach	1 0.46	0.04 – 0.83	0.01
Isolation	No Yes	1 0.18	0.04 – 0.83	0.03
Emergency Admission	No Yes	1 1.12	0.60 – 2.10	0.72

CHAPTER 4

Discussion

This retrospective study compares postoperative morbidity rates between patients undergoing abdominal surgical procedures during the pandemic period, with those who underwent the same surgical treatments in a control period. The aim was to quantify the effect of clear pathways to reduce the risk of SARS-Cov-2 transmission, on postoperative complications.

Our results demonstrated that strict compliance on protective measures and stringent protocols allows to safely carry out elective surgical activity during pandemic without compromising short-term postoperative outcomes. Moreover, these results showed that isolation and hospitalization of the patients in a single room significantly reduced the risk of postoperative complications.

Recently, some studies have analyzed short-term postoperative outcomes in surgical patients during the pandemic and showed that complications were more common during this period. However, the primary aim of these studies was to examine early surgical morbidity and mortality in patients with COVID-19 compared with patients without the disease (Doglietto et al., 2020; Jonker et al., 2021; Lei et al., 2020; COVIDSurg Collaborative, 2020; Cano-Valderrama et al., 2020). Postoperative outcomes in SARS-CoV-2-infected patients are worse than pre-pandemic: thirty-day mortality was close to 20-25% (COVIDSurg Collaborative, 2020; Gammeri et al., 2020), and pulmonary, thrombotic and surgical postoperative complications dramatically increased (Doglietto et al., 2020).

No study has specifically analyzed the impact of anti-COVID-19 measures on elective surgical activity and postoperative outcomes in patients who did not develop the infection.

A recent study (Glasbey et al., 2020) compared patients undergoing elective surgery during the pandemic in a COVID- 19 – free surgical pathway with patients

undergoing surgery in a no defined pathway, to determine whether COVID-19–free surgical pathways were associated with lower postoperative pulmonary complication rates. Data from 9171 patients showed that complications and death after surgery were lower for patients treated in COVID-19-free units. Pulmonary complications for those in COVID-19-free units were 2.2% compared to 4.9 %, the rates of contracting COVID-19 around the time of surgery were 2.1% versus 3.6%, and the rates of death was also lower (0.7 % vs 1.7%).

Otherwise, we focused our analysis on patients who did not develop SARS-Cov-2 infection in the perioperative period and up to 30-days after surgery. Interestingly, we identified that, as well as the intraoperative period (Badia et al., 2020; Dieplinger et al., 2020; Wick et al., 2012), also the postoperative course should be implemented with some interventions in order to reduce postoperative morbidity. We specifically identified that isolation, hospitalization in a single room and visits prohibition (or limited), led to a control of postoperative complications.

Also, a minimally invasive approach showed a very positive effects and advantages on postoperative complications, as already showed by previous studies (Veldkamp et al., 2005; Chen et al., 2017; Jiang et al., 2015; Prete et al., 2018; van der Pas et al., 2013).

This represents the first available retrospective study on this topic, however, there were many acknowledged limitations. The main bias is related to the retrospective design. As with every retrospective series: there were bias related to patients' selection and heterogeneity of clinical practice among the two involved centers. The potential biases are largely compensated by the strength of numbers and by the fact that data were obtained from prospectively maintained datasets from two referral colorectal cancer centers.

CHAPTER 5

Conclusions

This retrospective study documents that postoperative morbidity after colorectal elective surgery was significantly lower during the pandemic, when COVID-19-free pathways were followed. With an implementation of intra-hospital protocols during the pandemic, we find that elective surgery could be performed safely for both patients and caregivers. Moreover, these hospitalization protocols should be validated and used in daily clinical practice.

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