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Synopsis for Table of Contents

Prompt reorganization of activities enabled to preserve oncological surgical procedures of a tertiary referral hospital in Northwestern Italy despite strict COVID-19 lockdown measures. No reduction of the oncological surgical pathology caseload was observed for most tumor types. Staging/grading characteristics of the samples showed no significant differences as well.

Abstract

Background and Objectives: Italy was severely affected by the SARS-CoV-2 pandemic. Our Institution, Piedmont's largest tertiary referral center, was designated as a non-COVID-19 hospital and activities were reorganized to prioritize critical services like oncological care. The aim of this study was to investigate the efficacy in preserving the oncological surgical practice at our Institution during the most critical months of the COVID-19 epidemic by analyzing the surgical pathology activity.

Methods: The number of oncological surgical resections submitted to histopathological examination from 9th March 2020 to 8th May 2020 were collected as well staging/grading data and compared with the previous three pre-COVID-19 years (2017-2019).

Results: Overall, no decrease was observed for most tumor sites (5/9) while breast resections showed the largest drop (109 *versus* 160; -31.9%), although a full recovery was already noticed during the second half of the period. Conversely, the selected control benchmarks showed a sharp decrease (-80.4%). Distribution of pathological TNM stages (or tumor grades for CNS tumors) showed no significant differences during the lockdown compared with previous years ($p>0.05$).

Conclusions: The present data suggest the possibility of preserving this cornerstone oncological activity during an evolving public health emergency thanks to a prompt workflow reorganization.

Keywords: COVID-19; SARS-CoV-2; surgical oncology; oncology; surgical pathology

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) disease (COVID-19), firstly identified in China at the end of 2019, rapidly spread across the globe within the first six months of 2020.

From the beginning of the epidemic, Italy has been one of the worst-affected countries. Although the first imported cases of COVID-19 date back to 30th January, the first Italian autochthonous case was registered on 20th February. The situation quickly escalated and on 4th March there were 2706 confirmed cases, mainly distributed in Northern regions of the country. Piedmont was the second most affected region[1] and on 5th March the Regional Crisis Unit of Piedmont decided to suspend all the deferrable clinical activities to focus on the growing outbreak, limiting the surgical interventions to the oncological and emergency cases. On 9th March, the Italian government imposed a national lockdown and two days later, the World Health Organization declared COVID-19 a pandemic. On 4th May, in consideration of the lowering infection rate, the Italian Government declared the "phase 2" of the emergency leading to a gradual recovery of the routine clinical activity.

During these months, many hospitals in Northern Italy were transformed into COVID-19 centers to preserve the clinical routine practice of the other clinics, but almost all the centers had to hospitalize COVID-19 patients: specific protocols had to be designed to manage both patients with and without COVID-19, often resulting in a disruption of the daily practice. Despite the will to preserve the prompt care of oncological patients, many factors like the increased workload on anesthesiology and intensive care units, availability of ventilators and of personal protective equipment or the necessity of pre-surgery SARS-CoV-2 testing hampered the regular surgical oncology practice.

Our Institution, the "Città della Salute e della Scienza" University Hospital of Turin is the main Piedmont tertiary level referral center (2,200 hospital beds) and was selected with other hospitals to carry on oncological care and other urgent health activities like transplant medicine during the lockdown. Despite this aim, multiple wards dedicated to COVID-19 patients had to be created during the lockdown months. Considering these characteristics, our Institution can be considered a representative testbed to verify the capacity to cope with a quickly escalating pandemic while preserving other priority health needs.

Multiple studies have investigated the impact of COVID-19 pandemic on both oncological and non-oncological activities with variable findings.[2-7] We thus wanted to define the real ability in preserving the

oncological surgical practice at our Institution during the most critical months of the epidemic by analyzing the surgical pathology activity of our units.

Materials and methods

Data were extracted from the pathological reporting software (Winsap, Engineering, Rome, Italy) of the Pathology Units of "Città della Salute e della Scienza" University Hospital of Turin. Specifically, the number of surgical resections samples submitted to histopathological examination from 9th March 2020 to 8th May 2020 due to a proven or suspected oncological condition were collected focusing on nine anatomical sites [breast, central nervous system (CNS), colon-rectum, lung, ovary, pancreas, prostate, uterus, and thyroid]. The specific time period was selected based on the epidemic evolution in our region.[1, 8] Incidentally diagnosed malignancies were not included.

To verify if the COVID-19 epidemic significantly hampered the oncological surgical activity, we compared these data with the number of surgical procedures performed during the same time period (9th March – 8th May) in the previous three years (2017-2019). Tumor staging data according to pathological UICC TNM criteria (VIII Edition) (or WHO grading for CNS tumors) were also compared to identify potential differences in the type of resected samples.

Lastly, to compare these results with the non-oncological surgical activity, data regarding two common non-oncological procedures were extracted and analyzed (lipoma resection and cholecystectomy due to cholelithiasis).

The study was conducted in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans and within the guidelines and regulations defined by the Research Ethics Committee of the University of Turin. Considered that data were anonymously collected and that the study had no impact at all on patients' care, no specific written informed consent was required.

Statistical analyses were performed using Stata/MP 15.0 Statistical Software (StataCorp, College Station, TX, USA) and results were compared using the Fisher exact test with two tailed p-values.

Results

During the previous three years (2017-2019), the total number of oncological surgical procedures was substantially steady in the analyzed bimester (9th March – 8th May), with a median of 422 surgical interventions (range: 420-424) (Table 1 and Figure 1). In 2020, a 11.8% decrease in total samples was observed (372 samples *versus* 422). Conversely, the selected benchmark non-oncological procedures (lipoma resection and cholecystectomy due to cholelithiasis) were 41 in 2020 compared with a median of 209 in past years (80.4% decrease).

	Number of surgical procedures (9th March – 8th May)								
Anatomic site	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	**1st half 2017-2019 (median)**	**1st half 2020**	**2nd half 2017-2019 (median)**	**2nd half 2020**
Lung	37	41	30	37	39 (+ 5.4%)	22	20	14	19
Pancreas	15	12	16	15	17 (+ 13.3%)	6	9	8	8
Prostate	32	28	37	32	27 (- 15.6%)	15	14	17	13
Uterus	14	23	16	16	24 (+ 50%)	9	13	7	11
Ovary	17	13	10	13	14 (+ 7.7%)	6	8	7	6
Colon	57	63	47	57	50 (- 12.3%)	28	38	28	12
Thyroid	20	11	9	11	12 (+ 9.1%)	6	9	6	3
CNS	70	88	94	88	80 (- 9.1%)	42	48	46	32
Breast	160	145	161	160	109 (- 31.9%)	87	43	70	66
Total oncological procedures	**422**	**424**	**420**	**422**	**372 (- 11.8%)**	**219**	**182**	**201**	**151**
Lipoma excision	55	60	90	60	10 (- 83.3%)	29	7	31	3
Cholecystectomy for cholecystitis	154	147	155	154	31 (-79.9%)	83	12	64	19
Total non-oncological procedures	**209**	**207**	**245**	**209**	**41 (- 80.4%)**	**112**	**19**	**98**	**22**

Table 1. Number of oncological and non-oncological surgical procedures performed in the different time periods.

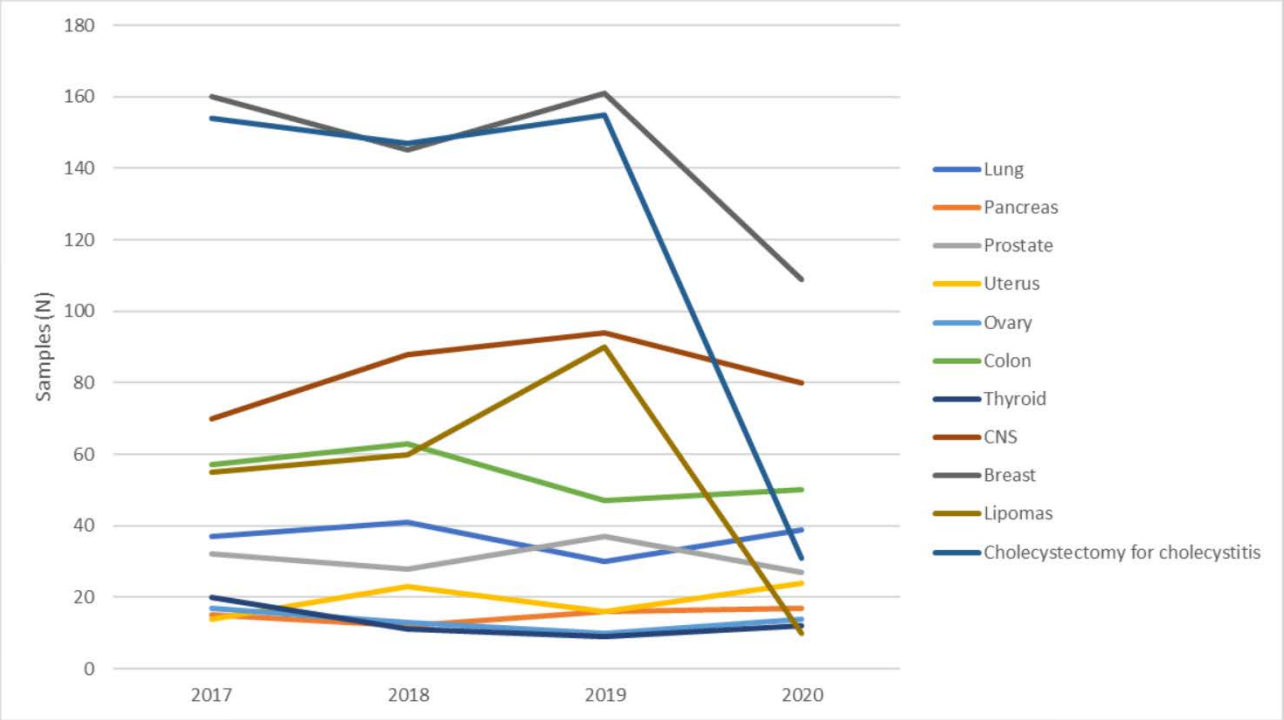

Figure 1. Number of surgically resected specimens according to sample type during the COVID-19 lockdown and in the pre-COVID-19 years.

Considering each anatomical site separately, neoplastic surgery was substantially steady during the investigated bimester of the 3 previous years 2017-2019 (Table 1). Unexpectedly, an increase was observed in most sample types (5/9) in 2020; by converse, a significant reduction was identified in breast surgery with 109 resections in 2020 versus a median of 160 in March-May 2017-2019 (-31.9%). Considering separately the first and the second half of the lockdown period, we noticed that breast surgery mainly decreased during the first month of the COVID-19 emergency compared with the control period (43 *versus* 87; -49.4%), while it recovered during the second half (66 *versus* 70).

We also wanted to assess if, due to restrictions imposed by the COVID-19 pandemic, there were significant variations in the characteristics of resected tumors according to pathological UICC TNM staging criteria (VIII Edition) (or WHO grading for CNS tumors). For instance, the closing of many outpatient clinics and the lower access rates to the emergency departments could have affected the stage of surgically resected neoplasms. Interestingly, no significant differences were observed in the distribution of T and N stages across the tumor types here investigated ($p>0.05$) (Table 2).

Lung						
T	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	
1	9	7	9	9	9	
2	8	17	8	8	12	
3	7	5	6	6	5	
4	3	1	3	3	6	
Total	27	30	26		32	p=0.773
N	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	
x	1	1	0	1	0	
0	14	13	16	14	22	
1	7	10	4	7	5	
2	5	6	6	6	5	
Total	27	30	26		32	p=0.408
Pancreas						
T	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	
1	2	0	1	1	5	
2	2	3	7	3	7	
3	9	7	4	7	4	
4	0	0	1	0	0	
Total	13	10	13		16	p=0.163
N	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	
x	0	1	0	0	1	
0	2	0	3	2	6	
1	3	2	5	3	7	
2	8	7	5	7	2	
Total	13	10	13		16	p=0.067
Prostate						
T	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	
2	17	17	17	17	13	
3	15	11	20	15	14	
4	0	0	0	0	0	
Total	32	28	37		27	p=0.796
N	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	
x	4	2	7	4	4	
0	24	22	25	24	20	
1	4	4	5	4	3	
Total	32	28	37		27	p=1.000
Uterus						
T	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	
is	0	0	0	0	1	
1	8	15	13	13	20	
2	2	3	3	3	1	

3	3	5	0	3	2	
4	0	0	0	0	0	
Total	13	23	16		24	p=0.372
N	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	
x	3	6	8	6	12	
0	15	12	7	12	11	
1	5	4	1	4	1	
2	0	1	0	0	0	
Total	23	23	16		24	p=0.153
Ovary						
T	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	
1	3	0	2	2	4	
2	7	4	1	4	2	
3	6	8	6	6	8	
4	0	0	0	0	0	
Total	16	12	9		14	p=0.662
N	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	
x	9	7	6	7	8	
0	3	3	2	3	5	
1	4	2	1	2	1	
Total	16	12	9	12	14	p=0.860
Colon						
T	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	
is	0	0	1	0	0	
1	3	3	1	3	2	
2	10	13	8	10	6	
3	33	38	28	33	27	
4	11	8	7	8	13	
Total	57	62	45		48	p=0.443
N	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	
0	39	41	27	39	20	
1	13	13	10	13	17	
2	5	8	8	8	11	
Total	57	62	45	57	48	p=0.053
Thyroid						
T	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	
1	7	3	6	6	6	
2	1	0	1	1	2	
3	6	1	0	1	1	
4	1	0	0	0	0	
Total	15	4	7		9	p=1.000
N	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	

x	2	2	4	2	0	
0	5	1	2	2	4	
1	8	1	1	1	5	
Total	15	4	7	7	9	p=0.236
CNS						
Grade (gliomas)	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	
1	3	5	7	5	3	
2	6	2	5	5	5	
3	2	3	3	3	3	
4	4	14	8	8	12	
Total	15	24	23		23	p=0.761
Grade (meningiomas)	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	
1	10	19	20	19	17	
2	2	6	2	2	3	
3	0	1	1	1	2	
Total	12	26	23		22	p=0.741
Breast						
T	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	
is	18	8	18	18	15	
1	83	73	72	73	63	
2	31	21	29	29	22	
3	3	3	4	3	2	
4	1	1	2	1	0	
Total	136	106	125		102	p=0.993
N	**2017**	**2018**	**2019**	**Median 2017-2019**	**2020**	
x	24	14	13	14	14	
0	70	56	64	64	58	
1	26	25	29	26	18	
2	3	4	2	3	5	
3	4	2	3	3	5	
Total	127	101	111		100	p=0.705

Table 2. Number of surgical oncological samples submitted to histopathological examination (2017-2019 versus 2020) according to tumor stage/grade.

Discussion

The SARS-CoV-2 pandemic produced a huge impact on global health care and Italy was both early and severely affected. To preserve the prompt addressing of other urgent health needs, COVID-19 hospitals were

created in areas with high SARS-CoV-2 incidence so that other health care centers could carry on these activities (hub-and-spoke model). Among these, oncological care is a deeply integrated clinical setting and surgery represents both a diagnostic and therapeutic cornerstone for these patients, thus any delay could jeopardize their overall outcomes.

Our data show that, despite the pandemic-induced restrictions, the creation of dedicated tracks allowed to preserve the oncological surgical activity of our Institution. For most tumor types, the number of samples submitted to our Pathology units were similar to pre-COVID-19 years; breast surgery showed the largest drop, but a full recovery was already observed since the second half of the lockdown period. The sharp decrease of elective non-oncological surgeries supports a prompt and good compliance with regional/national directives.

Other recently published reports show a variable efficacy in preserving routine health services during these critical months.[6, 9, 10] As it could be expected, their more serious deterioration was reported in regions with higher SARS-CoV-2 infection rates. Although Piedmont was initially the second most affected Italian region, our hospital reorganized health services according to the constant evolving needs through flexible interventions on individual medical and surgical units. The decision to promptly suspend all elective surgical procedures and deferrable outpatient clinics enabled to preserve as much as possible a timely oncological therapeutic workflow as well as to tackle other urgent needs like transplantation procedures (issue not reviewed in this paper).[11] It should also be noted that this result was achieved despite the creation of 9 dedicated COVID-19 wards (including intensive care, internal medicine and pneumology units) and the overall treatment of 375 patients with SARS-CoV-2 infection during the analyzed period.

Future studies should compare the efficacy of the specific models (e.g. hub-and-spoke hospitals) by taking into account both the local epidemic course and the surgical outcomes in order to identify the best approach for each setting. Surgery delivery had also to be prioritized according to tumor features like malignancy and/or the risk of evolution into an unresectable lesion. For this reason, we also assessed if resected tumors were differently distributed in terms of TNM stage or grade compared to pre-COVID-19 years, but no significant discrepancies were detected. Nevertheless, a significant decrease of newly diagnosed cancers during these months has been reported.[12] Correlation of COVID-19 impact on diagnostic procedures with future sample characteristics is warranted to verify if this diagnostic delay will translate into worse TNM stages at time of resection and/or higher cancer deaths in the future.[13]

Analysis of a single-center experience should be cautiously interpreted and should be incorporated in and/or compared with larger datasets. Nevertheless, these data support the possibility of preserving the prompt treatment of oncological patients despite a quickly evolving public health emergency, thanks to a prompt assessment of priorities and workflow reorganization.

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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Conflict of Interest

The authors declare they have no conflict of interest.

Ethics approval statement

The study was conducted in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans and within the guidelines and regulations defined by the Research Ethics Committee of the University of Turin. Considered that data were anonymously collected and that the study had no impact at all on patients’ care, no specific written informed consent was required.

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