Long Term Implications in Surgical Re-assisting (L.I.S.A. study) During Covid-19 Outbreak: A Retrospective Observational Study on a Rural Population.

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Research Article

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Abstract

Background

The spread of the COVID-19 is having a worldwide impact on surgical treatment. Our aim was to investigate the impact of the pandemic in a rural hospital in a low densely populated area.

Methods

We investigated the volume and type of surgical operations during the pandemic (March 2020 - February 2021) versus pre-pandemic period (March 2019 - February 2020) as well as during the first and second pandemic waves compared to the pre-pandemic period. We compared the volume and timing of emergency appendectomy and cholecystectomy during the pandemic versus pre-pandemic period, the volume, timing and stages of elective gastric and colorectal resections for cancer during the pandemic versus the pre-pandemic period.

Results

In the prepandemic versus pandemic period, 42 versus 24 appendectomies and 174 versus 126 cholecystectomies (urgent and elective) were performed. Patients operated on before as opposed to during the pandemic were older (58 vs. 52 years old, p=0.006), including for cholecystectomy (73 vs. 66 years old, p=0.01) and appendectomy (43 vs. 30 years old, p = 0.04).

The logistic regression analysis with regard to cholecystectomy and appendectomy performed in emergency showed that male sex and age were both associated to gangrenous type histology, both in pandemic and prepandemic period. Finally, we found a reduction in cancer stage I and IIA in pandemic versus prepandemic period, with no increase in the more advanced stages.

Conclusions

the reduction in services imposed by governments during the first months of

total lock down did not justify the whole decrease in surgical interventions in the year of the pandemic. Data suggest that greater "non-operative management" for cases of appendicitis and acute cholecystitis does not lead to an increase in cases operated over time, nor to an increase in the "gangrenous" pattern, which seems to depend on age advanced and male population.

Background

The rapid spread of the new Coronavirus causing the COVID-19 disease is having a worldwide impact on the remodelling of surgical treatment (1,2). Before the pandemic declaration by the WHO, it was already clear that postponing elective activities was a fundamental step in order to preserve patients’ safety and to limit the viral spread. This measure increases the resources for COVID-19 patients, clearing ward and intensive care unit (ICU) beds. Moreover, it avoids unnecessary patient traffic in the hospital and reduces the risk of cross-infection between elective patients, hospital visitors, and COVID-19 patients, preventing spread of infection from the hospital to the community (3). To conserve resources and to limit the spread of the virus, many hospitals were forced to delay elective surgical operations. Nearly 38% of cancer surgeries are estimated to have been postponed worldwide during the 12-week peak of the pandemic (4). Recent studies suggest that postponing elective colorectal cancer (CRC) surgery by more than four weeks after diagnosis is associated with poorer outcomes (4,5). However, the lack of evidence-based standards for what is considered a delay in cancer surgery has led to inconsistent study designs and few attempts at meta-analysis (4). A 2007 meta-analysis found delays in surgery for CRC did not worsen survival; however, the interpretation of these results is limited since colon and rectal cancers were not evaluated separately (6). The state of

the art and most triage guidelines discourage delaying curative-intent surgery for colon cancer (7,8). For resectable colon cancer, curative intent surgery should be carried out, while preoperative chemotherapy could be considered for locally advanced colon cancer. For rectal cancer, all preoperative treatment options should be considered (3). As for gastric cancer, instead, priority should be given to surgical resection of tumour stage cT1b and patients with ongoing perioperative treatment, while patients with cT2 cancer or higher should undergo preoperative therapy (3).

Other aspects involve emergency surgery during COVID-19 pandemic. Based on recent published literature, urgent surgery should be performed for: obstructive or nearly obstructive CRC (prefer diversion in rectal cancer), acutely transfusion-dependent tumours, cancers with pending evidence of local perforation and sepsis, and post-surgical and post-colonoscopy complications (3). Non-operative or conservative management of acutely ill patients should be considered when feasible and safe, and it is strongly encouraged with COVID-19 patients (3).

As the rate of new COVID-19 cases decrease, a progressive reopening of elective procedures will be necessary. To date, the information on the long-term effects of the reorganization during the COVID-19 pandemic of the surgical units serving rural population basins is scant. However, such information may contribute to improve the management of health care resources during new COVID-19 pandemic waves as well as other pandemics. Our research group has already analysed the first effects of the COVID-19 pandemic on surgical activities in a University Hospital serving mainly an urban area and in the emerging setting (1,9).

Our aim was now to investigate the impact of the Pandemic on general surgery operations, including emergency and cancer surgeries, in a district hospital serving a wide, low densely populated rural area.

Methods And Materials

This is an observational, retrospective cohort study conducted in a hospital serving a wide least densely populated rural area in the Province of Ferrara, in North-eastern Italy.

To investigate the impact of the Pandemic on general surgery operations in such a hospital we specifically evaluated:

1) The volume and type of surgical operations during the pandemic versus pre-pandemic periods as well as during the first and second pandemic waves compared to the pre-pandemic period;

2) The volume and timing of emergency appendectomy and cholecystectomy during the pandemic versus pre-pandemic period;

3) The volume and timing of elective gastric and colorectal resections for cancer during the pandemic versus the pre-pandemic period.

We considered prepandemic period from March 2019 to February 2020 and pandemic period from March 2020 to February 2021, the two 12-month time intervals before and during the COVID-19 pandemic, respectively.

We also focused on all surgical operations performed in the first quarter (January-April) of the year 2019 (prepandemic), 2020 (first pandemic wave), and 2021 (second pandemic wave).

We collected data on all adult patients undergoing elective or emergency surgery for the pandemic period (March 2020 - February 2021), from a prospective database, and prepandemic period (March 2019 - February 2020), retrospectively.

To evaluate the impact of the COVID-19 pandemic on emergency surgery we elected cholecystectomies and appendectomies for the possibility of "non-operative-management" of cholecystitis and appendicitis as compared to other diseases. In particular, we evaluated patients' age, surgical approach (i.e., open or laparoscopic technique), and final pathology to detect gangrenous cholecystitis and appendicitis.

As far as cancer surgery is concerned, we evaluated the patients' age, the use of preoperative chemotherapy, and TNM tumour stage (AJCC 8th edition) of both colorectal and gastric cancers. We also evaluated the need of neoadjuvant and adjuvant therapies in the two periods (prepandemic and pandemic).

Finally, in order to detect any delay attributable to the pandemic burden, we reviewed the data of the multidisciplinary colorectal cancer team to detect the time elapsed between endoscopic cancer diagnosis and the preoperative computerized tomography (CT) staging, surgery, and final pathology reporting.

Statistical analysis

The normal distribution of the continuous variables was analysed using Kolmogorov-Smirnov and Shapiro-Wilk tests, while not normally distributed variables were log-transformed before entering the parametric statistical analysis. Categorical variables were summarized by using frequencies and percentages, while continuous data were presented as both mean ± standard deviation (SD) and median. The Mann-Whitney U test was used for continuous variables, and the $\chi 2$ test or the Fisher exact test was used for categorical variables. The Wilcoxon signedrank test was used in case of comparison of two related matched samples, while the analysis of variance (ANOVA) was performed to compare two or more groups of data by analysing their intrinsic variability and comparing it among groups.

In order to evaluate the predictive role of each variable toward the outcome chose, all variables with a $p < 0.05$ in the univariate analyses were entered into multivariate logistic regression analyses. All $p < 0.05$ were considered statistically significant.

Data analyses were performed by using SPSS 26.0 software (IBM SPSS Statistics, IBM Corporation).

Table 1
prepandemic (2019, blue) and pandemic (2020, red) emergency surgery. Age median and gangrenous pattern. Total of cases (grey tab)

Prepandemic 2019 (N = 93)		**Pandemic 2020 (N = 63)**		**Total of patients (N = 156)**		***P*value between groups**
Age, mean ± SD (median)	Min-max	Age, mean ± SD (median)	Min-max	Age, mean ± SD (median)	Min-max	0.006
56 ± 22 (58)	18–91	52 ± 22 (52)	17–86	55 ± 22 (55)	17–91	
Gangrenous histologic pattern (yes, %)	Gangrenous histologic pattern (no, %)	Gangrenous histologic pattern (yes, %)	Gangrenous histologic pattern (no, %)			0.89
29 (31.2)	64 (68.8)	19 (30.2)	44 (69.8)			

Table 2
prepandemic (2019, blue) and pandemic (2020, red) urgent cholecystectomies. Age median and gangrenous pattern. Total of cases (grey tab).

Prepandemic 2019 (N = 51)		**Pandemic 2020 (N = 39)**		**Total of patients (N = 90)**		***P*value between groups**
Age, mean ± SD (median)	Min-max	Age, mean ± SD (median)	Min-max	Age, mean ± SD (median)	Min-max	0.01
67 ± 19 (73)	21–89	63 ± 17 (66)	25–86	65 ± 18 (71)	21–89	
Gangrenous Cholecystitis (yes, %)	Gangrenous Cholecystitis (no, %)	Gangrenous Cholecystitis (yes, %)	Gangrenous Cholecystitis (no, %)			0.90
19 (37.3)	32 (62.7)	14 (35.9)	25 (64.1)			

Table 3
prepandemic (2019, blue) and pandemic (2020, red) urgent appendectomy. Age median and gangrenous pattern. Total of cases (grey tab).

Prepandemic 2019 (N = 42)		**Pandemic 2020 (N = 24)**		**Total of patients (N = 66)**		***P*value between groups**
Age, mean ± SD (median)	Min-max	Age, mean ± SD (median)	Min-max	Age, mean ± SD (median)	Min-max	0.04
43 ± 19 (43)	18–91	35 ± 17 (30)	17–78	40 ± 18 (37)	17–91	
Gangrenous Appendicitis (yes, %)	Gangrenous Appendicitis (no, %)	Gangrenous Appendicitis (yes, %)	Gangrenous Appendicitis(no, %)			0.78
10 (23.8)	32(76.2)	5 (20.8)	19 (79.2)			

Table 4
Logistic regression analyses of gangrenous histologic patterns among surgical urgencies. Variables in relation to gangrenous histology. OR = Odds Ratio; 95% CI = 95% Confidential Interval.

Variable	**OR**	**95% CI (lower-upper)**	***p*value**
Sex (Male)	3.14	1.47–6.70	0.008
Age	1.02	1.01–1.04	0.003
Year of surgery (2020)	1.05	0.50–2.20	0.89

Table 5
Logistic regression analyses of gangrenous histologic patterns among urgent cholecystectomies. Variables in relation to gangrenous cholecystectomies. OR = Odds Ratio; 95% CI = 95% Confidential Interval.

Variable	**OR**	**95% CI (lower-upper)**	***p*value**
Sex (M)	4.30	1.61–11.50	0.004
Age	1.03	1.02–1.06	0.04
Year of surgery (2020)	1.03	0.40–2.63	0.96

Table 6
Logistic regression analyses of gangrenous histologic patterns among urgent appendectomies. Variables in relation to gangrenous appendectomies. OR = Odds Ratio; 95% CI = 95% Confidential Interval.

Variable	OR	95% CI (lower-upper)	*p*value
Sex (M)	2.00	0.59–6.74	0.26
Age	1.01	0.98–1.04	0.50
Year of surgery (2020)	0.96	0.27–3.39	0.95

Table 7
prepandemic (2019, blue) and pandemic (2020, red) partial gastrectomies. Median age, tumor diameter, postoperative lymph node staging. Total of cases (grey tab).

prepandemic 2019 (N = 10)		**pandemic 2020 (N = 9)**		**Total of patients (N = 19)**		***P*value between groups**
Age, mean ± SD (median)	Min-max	Age, mean ± SD (median)	Min-max	Age, mean ± SD (median)	Min-max	0.25
77 ± 5 (79)	64–82	74 ± 6 (73)	62–81	75 ± 6 (78)	62–82	
Tumor diameter (mm ± SD)						
47.2 ± 27.3		52.1 ± 27.1		49.4 ± 26.5		0.71

Table 8
prepandemic (2019, blue) and pandemic (2020, red) partial gastrectomies. Comparison of neoadjuvant and adjuvant therapy.

Prepandemic 2019 (N = 10)		**Prepandemic 2020 (N = 9)**		***P*value between groups**
Neoadjuvant therapy (yes, %)	Neoadjuvant therapy (no, %)	Neoadjuvant therapy (yes, %)	Neoadjuvant therapy (no, %)	0.47
1 (10.0)	9 (90.0)	2 (22.2)	7 (77.8)	
Adjuvant therapy (yes, %)	Adjuvant therapy (no, %)	Adjuvant therapy (yes, %)	Adjuvant therapy (no, %)	0.85
4 (40.0)	6 (60.0)	4 (44.4)	5 (55.6)	

Table 9
diagnostic and therapeutic pathway for colon cancer. Pre-pandemic period (2019, blue) versus pandemic (2020, red). Median of the ages, time interval between: CT and intervention, intervention and histology, colonoscopy and CT, colonoscopy and intervention. Total of cases (grey tab).

prepandemic 2019 (N = 65)		**pandemic 2020 (N = 46)**		**Total of patients (N = 111)**		***P*value between groups**
Age, mean ± SD (median)	Min-Max	Age, mean ± SD (median)	Min-Max	Age, mean ± SD (median)	Min-Max	0.27
76 ± 12 (80)	41–102	73 ± 10 (73)	46–95	75 ± 11 (76)	41–102	
Days from CT scans to surgery, mean ± SD (median)	Min-Max	Days from CT scans to surgery, mean ± SD (median)	Min-Max	Days from CT scans to surgery, mean ± SD (median)	Min-Max	0.85
26 ± 25 (22)	1-164	25 ± 17 (22)	1–82	26 ± 22 (22)	1-164	
Days from histologicanalysis to surgery, mean ± SD (median)	Min-Max	Days from histologicanalysis to surgery mean ± SD (median)	Min-Max	Days from histologicanalysis to surgery mean ± SD (median)	Min-Max	0.23
36 ± 25 (33)	4-121	30 ± 18 (27)	1–84	33 ± 23 (30)	1-121	
Days from colonscopy to CT scans, mean ± SD (median)	Min-Max	Days from colonscopy to CT scans, mean ± SD (median)	Min-Max	Days from colonscopy to CT scans, mean ± SD (median)	Min-Max	0.43
14 ± 19 (7)	1–96	12 ± 9 (10)	1–49	13 ± 16 (8)	1–96	
Days from colonscopy to surgery, mean ± SD (median)	Min-Max	Days from colonscopy to surgery, mean ± SD (median)	Min-Max	Days from colonscopy to surgery, mean ± SD (median)	Min-Max	0.43
42 ± 29 (36)	1-160	37 ± 19 (36)	2–88	40 ± 26 (36)	1-160	

Results

Between March 2019 and February 2020 (prepandemic period), a total of 663 surgical operations were performed at our institution as opposed to 493 between March 2020 and February 2021 (pandemic period). Fig. 1 summarizes the number of surgical procedures performed in the two periods, detailing the type of surgical operations. In the prepandemic

compared to pandemic period, 42 versus 24 appendectomies and 174 versus 126 cholecystectomies (urgent and elective) were performed.

In the first quarters of 2019, 2020, and 2021 the total number of elective surgical operations was 137, 116, and 130, respectively (p=0.79, Fig. 2). There was no statistical difference in the total number of procedures performed in the first quarters of 2019 versus 2020 (p=0.21) and 2020 versus 2021 (p=0.21), although a reduction in lower G.I. Surgery (13 vs 18) and cholecystectomies (28 vs. 46) were observed in 2020 versus 2019, while inguinal hernia repair and haemorrhoidectomies increased in 2021 versus 2020.

Regarding emergency appendectomies and cholecystectomies, 93 operations were performed in the prepandemic period compared to 63 in the pandemic period (Tab. 1). Patients operated on before as opposed to during the Pandemic were older (58 vs. 52 years old, p=0.006), both for cholecystectomy (73 vs. 66 years old, p=0.01) (Tab. 2) and appendectomy (43 vs. 30 years old, p = 0.04) (Tab. 3). In the prepandemic versus pandemic period, the rate of gangrenous cholecystitis at final pathology report was 37.3% (19 out of 51) and 35.9% (14 out of 39) (p=0.90), while for gangrenous appendicitis was 23.8% (10 out of 42) and 20.8%(5 out of 24) (p=0.78) (Tab. 1-3).

There were no substantial differences in the number of laparotomic appendectomy operations performed during the period 2019-2020 (3 out of 42; 7,1%) versus 2020-2021 (2 out of 24; 8,3%).

In prepandemic period, 6 out of 51 laparotomic cholecystectomies were performed (11,7%) compared to 3 out of 39 (7,7 %) during the pandemic period.

The logistic regression analysis, performed to evaluate factors associated to gangrenous pattern in emergency cholecystectomy and appendectomy, showed that the male sex (OR 3.14, 95% CI 1.47-6.10; p = 0.008) and age (OR 1.02, 95% CI 1.01-1.04; p = 0.003) were associated to a

gangrenous type histology both in pandemic and prepandemic period (Tab. 4).

Similar results were obtained in a subgroup analysing considering cholecystectomies (Tab. 5) and appendectomy (Tab. 6) separately. Fig. 3 reports the total volumes of urgent procedures performed in the prepandemic (2019) and pandemic (2020), differentiated by type of surgery (cholecystectomies and appendectomies).

Ten patients underwent gastric resection for cancer in the prepandemic period compared to 9 in the pandemic period, with no difference between groups in terms of age, comorbidities, and tumour size (Tab. 7).

We also evaluated the need of neoadjuvant and adjuvant therapies in the two periods and from the analysis of these subgroups, no significant differences emerged (Tab. 8).

Sixty-five patients underwent colorectal cancer surgery in the prepandemic period compared to 46 in the pandemic period.

For patients who underwent to colorectal resection for colonic cancer, the time elapsed between endoscopic diagnosis, preoperative staging (contrast enhanced CT of the thorax, abdomen, and pelvis), surgery, and final pathology during the prepandemic and pandemic period did not show a significant difference (Tab. 9). Finally, we considered any differences between the groups in terms of the need for neoadjuvant therapy.

Discussion

This study shows that Covid-19 pandemic has change our activity in emergency surgery, while elective surgery did not significantly change. As the COVID-19 pandemic has put the Italian national health care system under pressure, we hypothesized three possible scenarios after the reopening of surgical activities at the end of the total lockdown between March and May 2020 (first pandemic period):

1) A rapid increase in hospital admission of surgical patients compared to the same period

in2019;

2) A progressive increase in surgical patients' admission distributed over a several months period of time;

3) A non-recovery of unoperated surgical patients' admission, compared to the same period in 2019.

The data analysed shows a reduction in operating volumes in the first quarter of 2020 (first pandemic wave), as a consequence of government restrictions (Fig. 1), which was not followed by an increase in cases in the following months, until the interruption of the observation period in April 2021 (Fig. 1-2).With the reopening of the main activities in Italy, starting from May 2020, separate diagnostic-therapeutic paths for positive Covid-19 patients and negative Covid-19 patients were instituted. Comparing the first quarters of the three consecutive years (i.e., 2019, 2020, and 2021), there was an overall recovery in terms of volumes of surgical interventions during the second pandemic wave (2021) as compared to the prepandemic period (2019) (Fig. 2).

Regarding emergency surgery, we focused on emergency appendectomy and cholecystectomy. Data shows that patients operated on during the pandemic (March - May 2020) were younger as compared to the prepandemic period (March - May 2019) (Tab. 1-3). In pandemic versus prepandemic period, both urgent cholecystectomies (51 vs. 39, p) and appendectomies (42 vs. 24, p) decreased, but There were no significant changes in the age of colon and stomach cancer patients (Tab. 7,8). we did not detect a greater number of histological exams with a "gangrenous" pattern. We identified, however, an association between gangrenous pattern of the gallbladder and older age and male sex (Tab. 5). This data has not been identified in the appendices. The decline in emergency operated patients for appendectomy and appendicectomy is in accordance with other district hospitals in the Province of Ferrara.

The number of cases of stomach cancer who had surgery remained constant in between periods. Interestingly, the number of patients who underwent preoperative chemotherapy in the prepandemic period compares well with the prepandemic period.

The curative treatment of colon cancer did not show a delay in the diagnostic-therapeutic path during pandemic versus prepandemic period (Tab. 9). In particular, there were no statistically significant differences in time intervals between endoscopic diagnosis, preoperative contrast enhanced CT, surgery, and definitive histological report. In prepandemic period, 62 patients had surgery, compared to 44 cases in pandemic. Four patients in pandemic underwent neoadjuvant chemotherapy, while in prepandemic we did not register any cases. Of note, looking at the stages of colonic tumours of patients undergoing surgery, there was a clear reduction in stage I and IIA in the pandemic versus prepandemic period (Fig. 4).

The presence of a pre-established multidisciplinary team and a perioperative pathway for colorectal cancer patients may have helped to preserve the diagnostic and treatment steps during the Pandemic.

A possible explanation for the drop in surgical admissions in the pandemic period may rely on the advanced age of Covid-19 patients, who is the population with highest incidence of colon cancer and cholelithiasis. The increase in mortality and morbidity in the elderly during the Pandemic, could explain the decline in surgical admission as well as the reduction in the age of patients who underwent emergency surgery during the Pandemic.

Another possible explanation, however, could be the fear of the population, in particular the elderly, to go to the hospital during the Pandemic due to the risk of contagion in crowded environments. This could explain the decline in hospitalizations for acute appendicitis in pandemic and the younger age, as younger people may have less fear of Covid-19 as compared to the elderly as they were affected by a mild form of the disease.

Finally, as the decrease of surgical activity in the first quarter of 2020 was not recovered subsequently, including urgent appendectomy and cholecystectomy, may suggest greater use of medical treatment or non-operational management.

The limitations of the study are related to the retrospective nature which introduces bias.

Conclusion

The decrease in surgical interventions in the Pandemic due to the reduction in services imposed by the health reorganization to face the Covid-19 spread was not recuperated in the following months, although the subsequent reopening with Covid-free pathways.

Increased medical treatment and non-operative management for acute appendicitis and acute cholecystitis may have occurred operated in the Pandemic, but no increase in the "gangrenous" pattern could be detected.

The curative treatment of colon cancer was not delayed during the Pandemic, possibly for the presence of a multidisciplinary team and a consolidated perioperative pathway for such patients.

Finally, new pathogen affecting more the elderly may have influenced the reduction of surgical interventions in pandemic compared to prepandemic.

Abbreviations

AJCC: *American Joint Committee on Cancer*

ANOVA: analysis of variance

COVID-19: CoronaVirus Disease-19

CRC: colorectal cancer

CT: computerized tomography

ICU: intensive care unit

SD: standard deviation

STROBE: Strenghtening the Reporting of Observational Studies in Epidemiology

WMA: World Medical Association

Declarations

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Ethics approval and consent to participate

This study was approved by Institutional Review Board, Azienda USL di Ferrara, Italy.

Consent for publication

Not applicable.

Competing interests

The authors have no relevant financial or non-financial interests to disclose.

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Figures

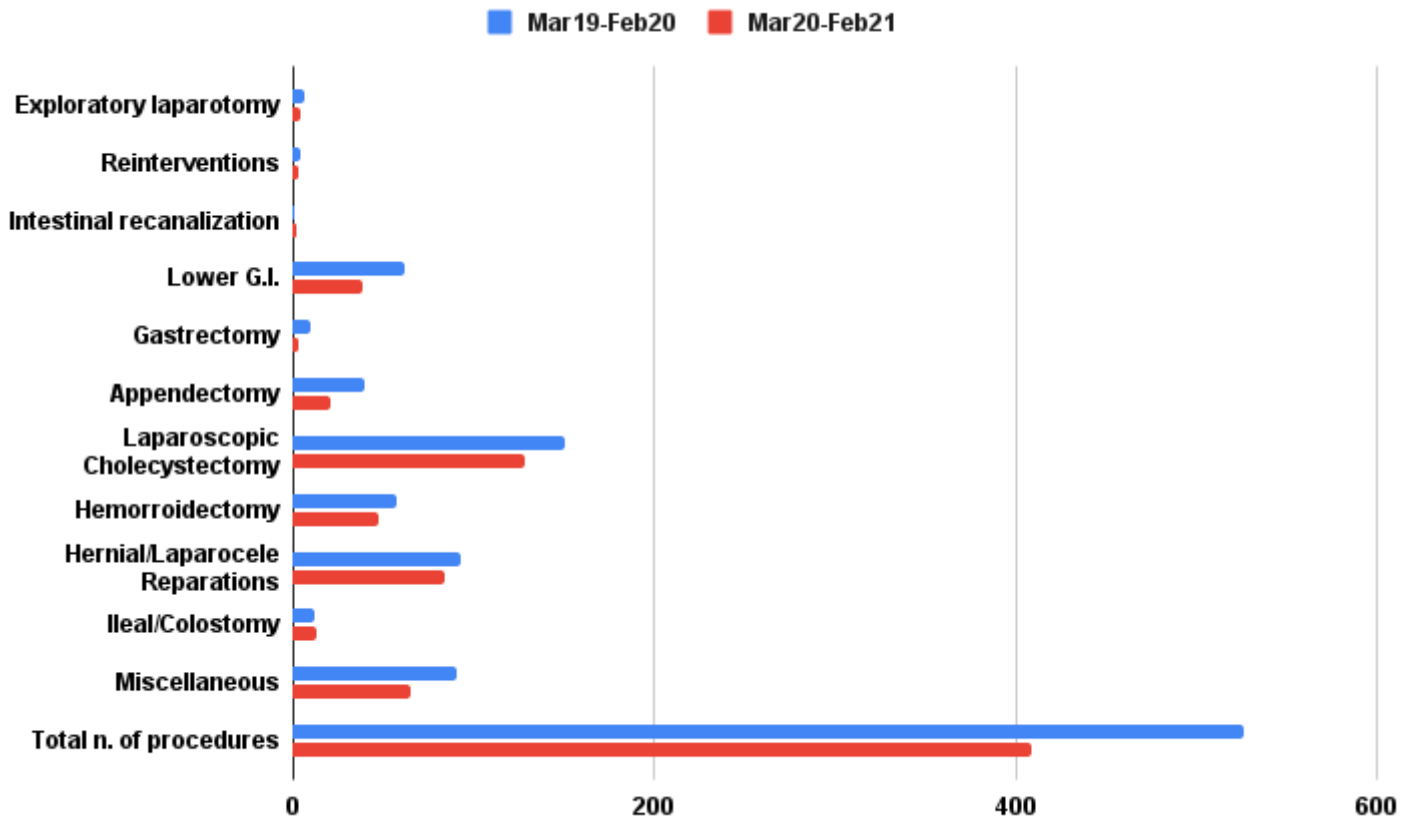

Figure 1

Surgical operations performed by the Department of General Surgery of the Delta hospital, stratified by type of surgeries (blue: prepandemic; red pandemic).

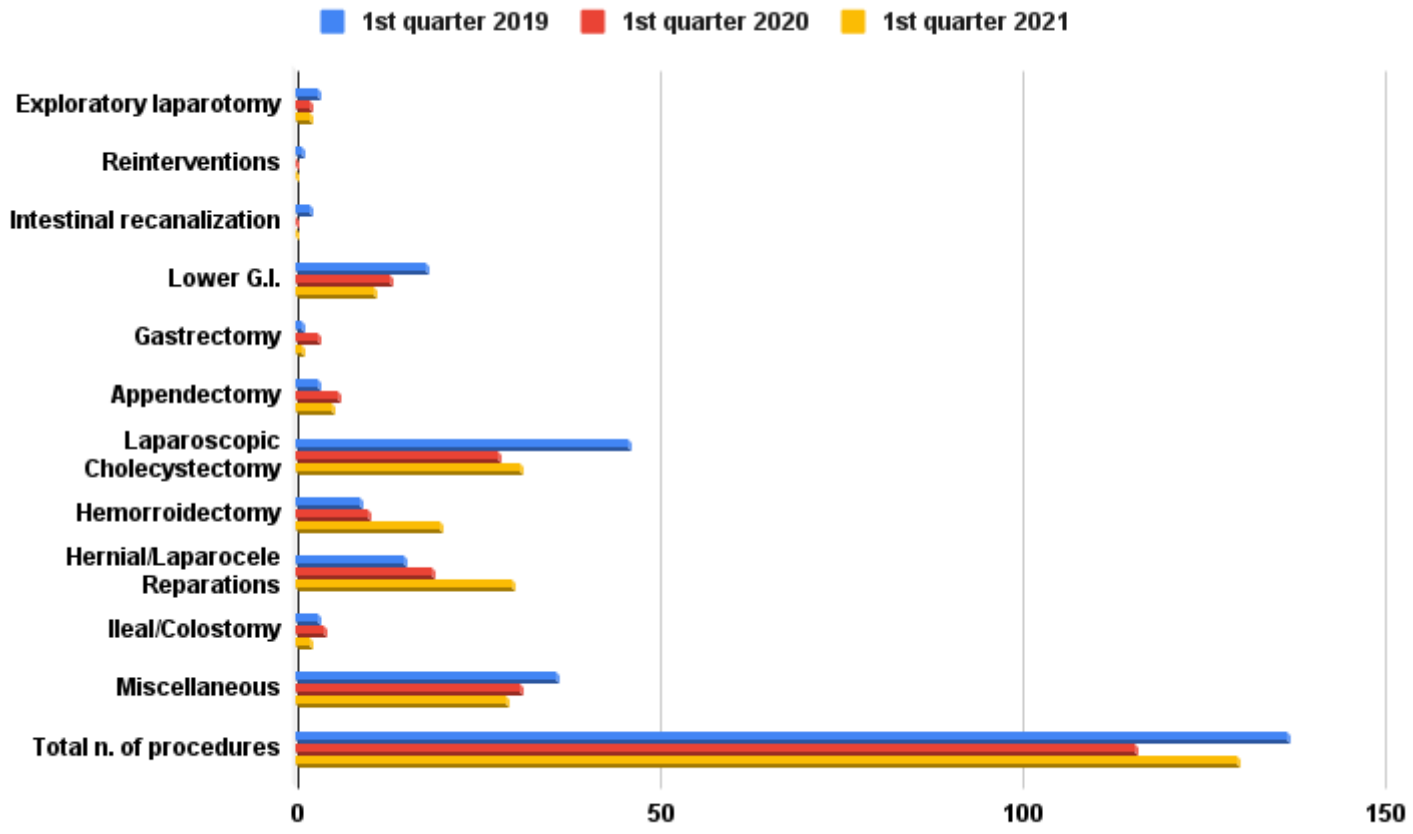

Figure 2

Surgical activity, Delta hospital, January-March quarter compared (blue: 2019; red: 2020; yellow: 2021).

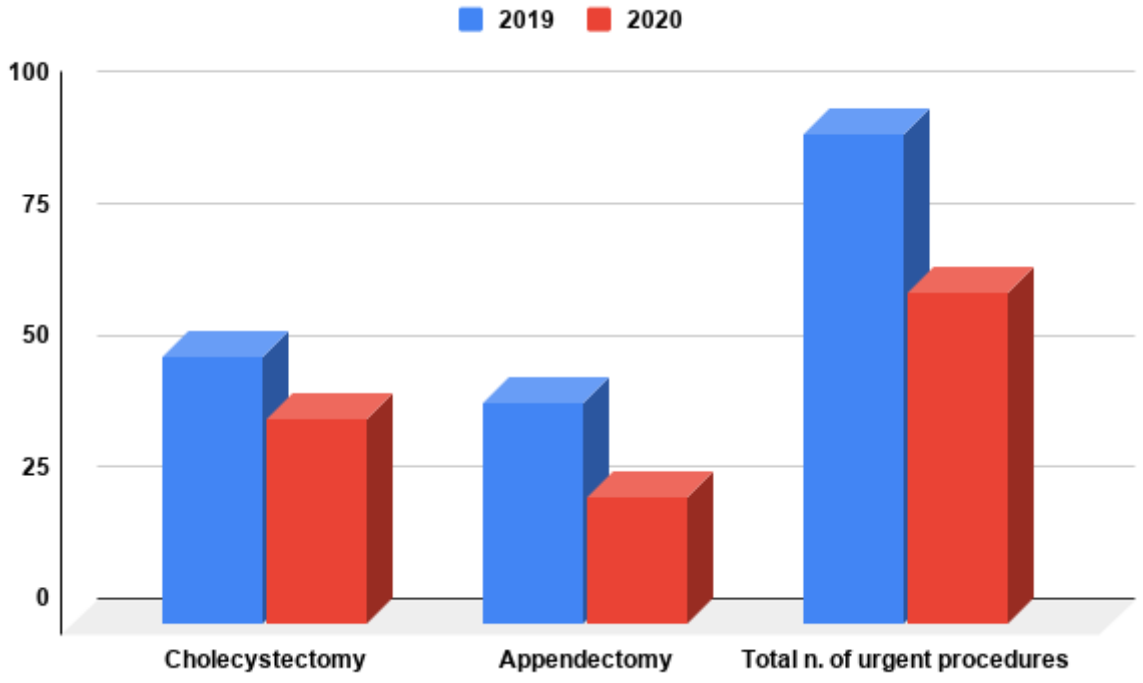

Figure 3

Urgent cholecystectomies and appendectomies (blue: year 2019; red year 2020).

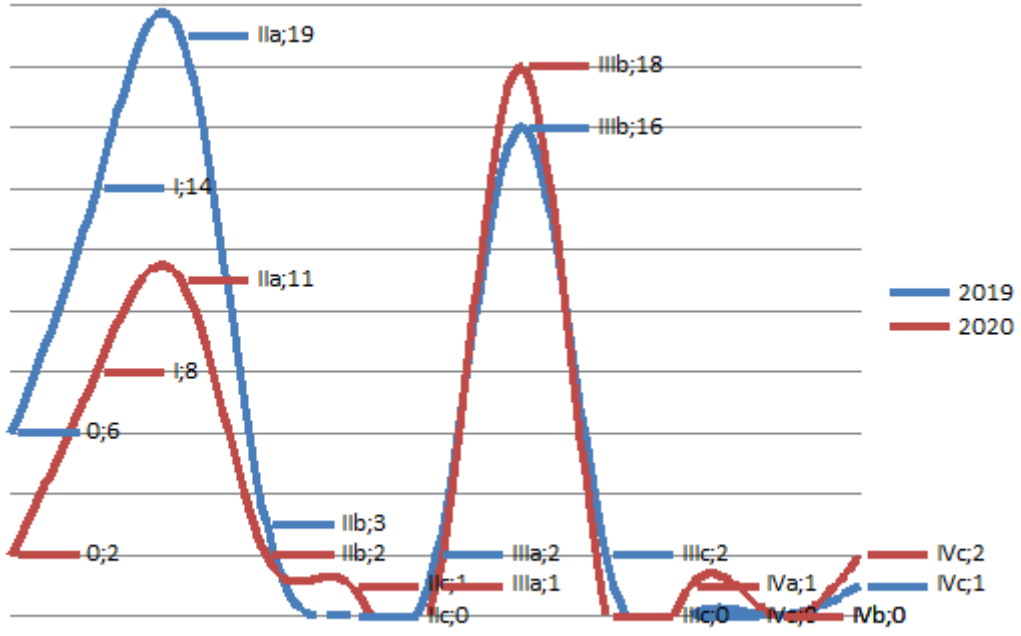

Figure 4

Colorectal cancer: comparison between histologicals 2019 vs 2020 (AJCC 8th edition).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- flowchartLISA.pdf
- manuscriptPDFLISA.pdf