The Impact of the COVID-19 Pandemic on General Surgery Acute Admissions and Urgent Operations: A Comparative Prospective Study

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ABSTRACT **Background:** As part of the effort to control the coronavirus disease-19 (COVID-19) outbreak, strict emergency measures, including prolonged national curfews, have been imposed. Even in countries where healthcare systems still functioned, patients avoided visiting emergency departments (EDs) because of fears of exposure to COVID-19.

Objective: To describe the effects of the COVID-19 outbreak on admissions of surgical patients from the ED and characteristics of urgent operations performed.

Methods: A prospective registry study comparing all patients admitted for acute surgical and trauma care between 15 March and 14 April 2020 (COVID-19) with patients admitted in the parallel time a year previously (control) was conducted.

Results: The combined cohort included 606 patients. There were 25% fewer admissions during the COVID-19 period ($P < 0.0001$). The COVID-19 cohort had a longer time interval from onset of symptoms ($P < 0.001$) and presented in a worse clinical condition as expressed by accelerated heart rate ($P = 0.023$), leukocyte count disturbances ($P = 0.005$), higher creatinine, and CRP levels ($P < 0.001$) compared with the control cohort. More COVID-19 patients required urgent surgery ($P = 0.03$) and length of ED stay was longer ($P = 0.003$).

Conclusions: During the COVID-19 period, fewer patients presented to the ED requiring acute surgical care. Those who did, often did so in a delayed fashion and in worse clinical condition. More patients required urgent surgical interventions compared to the control period. Governments and healthcare systems should emphasize to the public not to delay seeking medical attention, even in times of crises.

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KEY WORDS: acute admissions, coronavirus disease-19 (COVID-19), emergency medicine, general surgery, urgent operations

Coronavirus disease-19 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) [1-3]. The disease was first described in December 2019 in Wuhan, Hubei province, China, and has since spread globally [4,5].

The World Health Organization (WHO) declared the coronavirus outbreak a pandemic on 11 March 2020 with disease transmission in more than 200 countries. As of 23 April 2020, more than 2.5 million people have been infected worldwide with over 175,694 deaths [6,7].

The COVID-19 fatality rate varies among countries and regions with an estimation of 0.5–8% [7-10]. Age is a main predictor of fatality. Individuals younger than 50 years old have a less than 0.5% risk of fatality while those older than 70 years old have a more than 8% risk of fatality [8-11]. As the absolute number of patients ultimately requiring mechanical ventilation was predicted to be high, preventative measures in the communities and in the healthcare systems were taken [12].

Currently, Israel's infectivity and fatality rates from COVID-19 pandemic have been low with 16,000 confirmed cases (1860 cases per 1 million population) and 227 deaths (26 cases per 1 million of population). The first documented patient in Israel was diagnosed on 27 February 2020. On 12 March 2020 all schools and non-essential work facilities were closed as part of the effort to control the outbreak. Starting on 22 March 2020 all medical institutions initiated a strict emergency protocol where all elective procedures, except certain oncological procedures, were postponed. During the study period, additional strict national preventative measures for social distancing were implemented [13].

Sheba Medical Center is a tertiary referral center in a university hospital setting that provides service to an area with more than 1.5 million citizens and is the largest hospital in Israel. Sheba was assigned to lead the national effort against COVID-19. A corona hospital was built with a dedicated ICU, step-down unit (70 beds), and a specialized COVID-19 unit (43 beds). Sheba also converted some of the internal medicine, pediatrics,

maternity, and psychiatry wards into departments capable of maintaining 400 COVID-19 patients with a capacity to ventilate more than 200 patients. The newly built COVID-19 units were located outside the main hospital building. These changes, in addition to strict isolation policy for patients and medical personnel, allowed the facility to maintain capability for emergency activities as well as urgent cardiac and oncological activities.

During the COVID-19 period, we noticed that the public seemed to avoid emergency department (ED) visits due to fears of exposure to infected patients. In addition, those who arrived appeared to be in worse physical condition. Our capacity to maintain core emergency surgical and trauma care during the outbreak allowed us to evaluate the patterns of utilization and care delivered to surgical patients with acute conditions during this time period. In this study we looked at the effects of the COVID-19 pandemic on surgical patients' acute admissions from the emergency department including acute trauma admissions and the characteristics and outcomes of urgent operations that were performed.

Our hypothesis was that as a result of the COVID-19 pandemic and prolonged national curfews, there would be fewer acute surgical and trauma admissions. Moreover, we hypothesized that patients who eventually arrived at the ED with an acute surgical condition would have presented later in their clinical course. To the best of our knowledge, no report previously studied the influence of COVID-19 on acute surgical care performance and service volumes during the COVID-19 outbreak in an area that was able to maintain all resources for emergency surgical care. We performed a prospective comparative study including patients admitted urgently to our surgical department during the COVID-19 pandemic and compared to acute admissions in the parallel time one year earlier.

PATIENTS AND METHODS

A prospective real-time registry identifying all patients admitted acutely from the ED to the surgical department during the COVID-19 pandemic between 15 March and 14 April 2020 in a single surgery referral center was performed (COVID-19 cohort). The COVID-19 cohort was compared to patients admitted in the parallel pre-COVID-19 time period 15 March to 14 April, 2019 (control cohort). The surgery and ED department teams were unaware of the data collection in order to prevent bias in decision making. The study was approved by the institutional review board.

Data collected included age, gender, co-morbidities, American Society of Anesthesiology (ASA) score [14], admission diagnosis, time interval between onset of symptoms and arrival at the ED, vital signs and lab results on presentation, non-surgical and surgical management if utilized, SARS-CoV-2 status by polymerase chain reaction (PCR), effect on length of ED and hospital stay, immediate outcomes, and postoperative complications.

Patient clinical and laboratory status in presentation to the emergency department were evaluated by heart rate, body temperature, white blood cell count (WBC), absolute neutrophil count, hemoglobin level, creatinine count and C-reactive protein level (CRP). Management approach was divided into three options: medical treatment (fluid, antibiotics, analgesics), invasive procedures (endoscopy, percutaneous trans-hepatic cholangiography, angiography), and surgical treatment, open or laparoscopy approach. Postoperative complications were measured by the Clavien-Dindo Classification score (CD) [15] ranged from 0 to 5. Data were recorded in a real time manner in an electronic spreadsheet.

STATISTICAL ANALYSES

Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 25 (SPSS, IBM Corp, Armonk, NY, USA). $P < 0.05$ indicated statistical significance. Descriptive statistics were presented using prevalence and percentage values for categorical variables, while continuous variables are presented with averages and standard deviation, non-continuous variables are presented by median and range. Cohort comparisons were performed using Student's *t*-test for continuous normally distributed variables, ANOVA for more than two groups normally distributed comparison, and the Mann-Whitney test for a-parametric comparison. Categorical comparisons used the chi-square test and Fisher's exact tests.

RESULTS

Overall, 606 patients were admitted to the department of surgery from the ED with a diagnosis of an acute surgical condition during the study periods. All 606 patients were included in the final analysis, of which, 259 in the COVID-19 cohort versus 347 in the control cohort. There were 25% less admissions during the COVID-19 period ($P < 0.0001$).

No significant differences in mean age (59.8 years in the COVID-19 cohort vs. 57.2 years in the control cohort, $P = 0.125$) or gender distribution (44.8% males within the COVID-19 cohort vs. 51% among the control cohort, $P = 0.13$) were noted. Patients in the COVID-19 cohort had a more advanced ASA score (median ASA score of 3 vs. 2, $P = 0.001$).

Patients in the COVID-19 cohort presented with higher heart rate (90.5 vs. 86.9 beats per minute, $P = 0.023$), more leukocyte disturbances (leukocytosis or leukopenia; 64.9 vs. 53.6% of patients respectively, $P = 0.005$), higher creatinine levels (1 vs. 0.9 mg/dl, $P = 0.03$), and higher CRP levels (78 vs. 53.5 mg/L, $P < 0.0001$) compared with the control cohort. No differences were noted in temperature, neutrophil, or hemoglobin counts. Patients' data is displayed in Table 1.

The mean time interval between the initiation of symptoms and arrival to the ED was 2.91 ± 4.2 days among the COVID-19 cohort compared to 1.58 ± 2.09 days in the control cohort

Table 1. Patients demographic and clinical data group comparison (n=606)

Variable Mean		COVID-19 group (2020) n=259	Control group (2019) n=347	
		Mean	*P* value*	
Age, mean ± SD		59.8 ± 21.2	57.2 ± 20.3	0.125
Gender, male/female (% males)		116/143 (44.8%)	177/170 (51%)	0.13
ASA score	**Median**	3 (1–5)	2 (1–4)	**0.001**
	1	43 (16.6%)	86 (24.9%)	
	2	65 (25.1%)	97 (28.1%)	
	3	101 (39%)	120 (34.8%)	
	4	45 (17.4%)	42 (12.2%)	
	5	5 (1.9%)	0	
Clinical	**Temperature, °C**	36.8 ± 0.6	36.8 ± 0.5	0.7
	Heart rate	90.5 ± 19.8	86.9 ± 16.7	**0.023**
	Symptoms days interval (home to ED)	2.91 ± 4.2	1.58 ±2.09	**< 0.0001**
Laboratory results	**WBC (109/L)**	11.9 ± 5.5	11.3 ± 6.9	0.25
	Leucocyte disturbance	168 (64.9%) patients	186 (53.6%) patients	**0.005**
	Neutrophil count (109/L)	9.2 ± 4.9	8.5 ± 4.4	0.079
	Hemoglobin (g/dl)	12.4 ± 2.8	12.7 ± 2.4	0.116
	CRE (mg/dl)	1 ± 0.7	0.9 ± 0.7	**0.03**
	CRP (mg/L)	78 ± 101.8	53.5 ± 68.2	**< 0.0001**

*Bold indicates significance
ASA = American Society of Anesthesiologists, CRE = creatinine level, CRP = C-reactive protein count, leukocyte disturbance = leukocytosis or leukopenia, symptoms days interval = from onset of symptoms until arrival at the emergency department, WB = white blood cell count

($P < 0.0001$). Specifically, significant differences in this time interval were found in patients presenting with either bowel obstruction (4.1 vs. 1.41 days, respectively, $P = 0.027$), enterocolitis (5.42 vs. 1.42 days, respectively, $P = 0.005$), hepato-biliary-pancreatic related diagnosis (3.39 vs. 1.73 days, respectively, $P = 0.021$), and perforated hollow viscus (3.4 $P = 0.7$ days, respectively, ($P = 0.018$).

Management and post-operative outcomes were compared as shown in Table 2.

In the COVID-19 cohort there were significantly more operative interventions (39 vs. 27.4%, $P = 0.03$), with no significant difference between the cohorts regarding the surgical approach (laparoscopic or open).

There were no significant differences in overall post-operative complication rate between the cohorts (22.7% within the COVID-19 cohort vs. 18.3% in the control cohort, $P = 0.347$), nor in the rates of severe complications (10.9 vs. 6.5% respectively, $P = 0.28$). The overall 30-days mortality rates were similar between the cohorts as well (4.2% in the COVID-19 cohort vs. 3.7% in the control cohort, $P = 0.76$). A total of 44 out of 249 patients (18.8%) in the COVID-19 cohort were tested for SARS-CoV-2, none were found to be positive.

Length of emergency department stay (ED-LOS) was 47 minutes longer during the COVID-19 pandemic (7:33 vs. 6:46 hours within the control period, $P = 0.003$). COVID-19 cohort patients who were tested for SARS-CoV-2 spent 10:58 hours in the ED compared to 7:02 when not tested ($P = 0.0001$). Patients that were not tested had a similar ED-LOS as the control cohort. LOS was shorter with a median of 3 days compared to 4 days in the control cohort ($P = 0.048$).

Main admission diagnoses were grouped and compared between the two study cohorts as shown in Table 3. In the COVID-19 period there were significantly more admissions due to appendicitis (16.2% vs. 8.9%, $P = 0.006$), and bowel obstruction (15.1% vs. 8.6%, $P = 0.014$), and fewer admissions due to breast-related problems (mastitis, abscess, mass) (0% vs. 2.3%, $P = 0.012$). Remaining admission diagnoses were without a significant difference between the two cohorts.

Admission diagnosis subgroup analyses was performed. Figure 1 displays a comparison of management approaches per diagnosis in the different groups. Overall, 73 patients were admitted for acute appendicitis; 59 were managed surgically. During the COVID-19 period, acute appendicitis pre-

Table 2. Management and postoperative outcomes

Variable		COVID-19 group (2020)	Control group (2019)	*P* value*
Management, n	**Conservative**	103 (39.8%)	184 (53%)	**0.003**
	Invasive procedure	55 (21.2%)	68 (19.6%)	
	Surgical	101 (39%)	95 (27.4%)	
Surgical approach	**Open**	46 (45.5%)	55 (57.9%)	0.08
	laparoscopic	55 (54.5%)	40 (42.1%)	
Complications	**Overall complications**	22.7%	18.3%	0.347
	Severe (CD-3)	11 (10.9%)	6 (6.5%)	0.28
	Death, n	11 (4.2%)	13 (3.7%)	0.76
ED-LOS, mean hours		7:33 ± 3:48	6:46 ± 3:16	**0.003**
Hospital-LOS, median (days)		3 (1–42)	4 (1–77)	**0.048**

*Bold indicates significance
Invasive procedure included endoscopy, percutaneous transhepatic cholangiography, angiography
CD = Clavien-Dindo classification severe CD score 3 or above, ED-LOS = length of stay in the emergency department before hospitalization in hours, Hospital-LOS = length of hospital stay in days

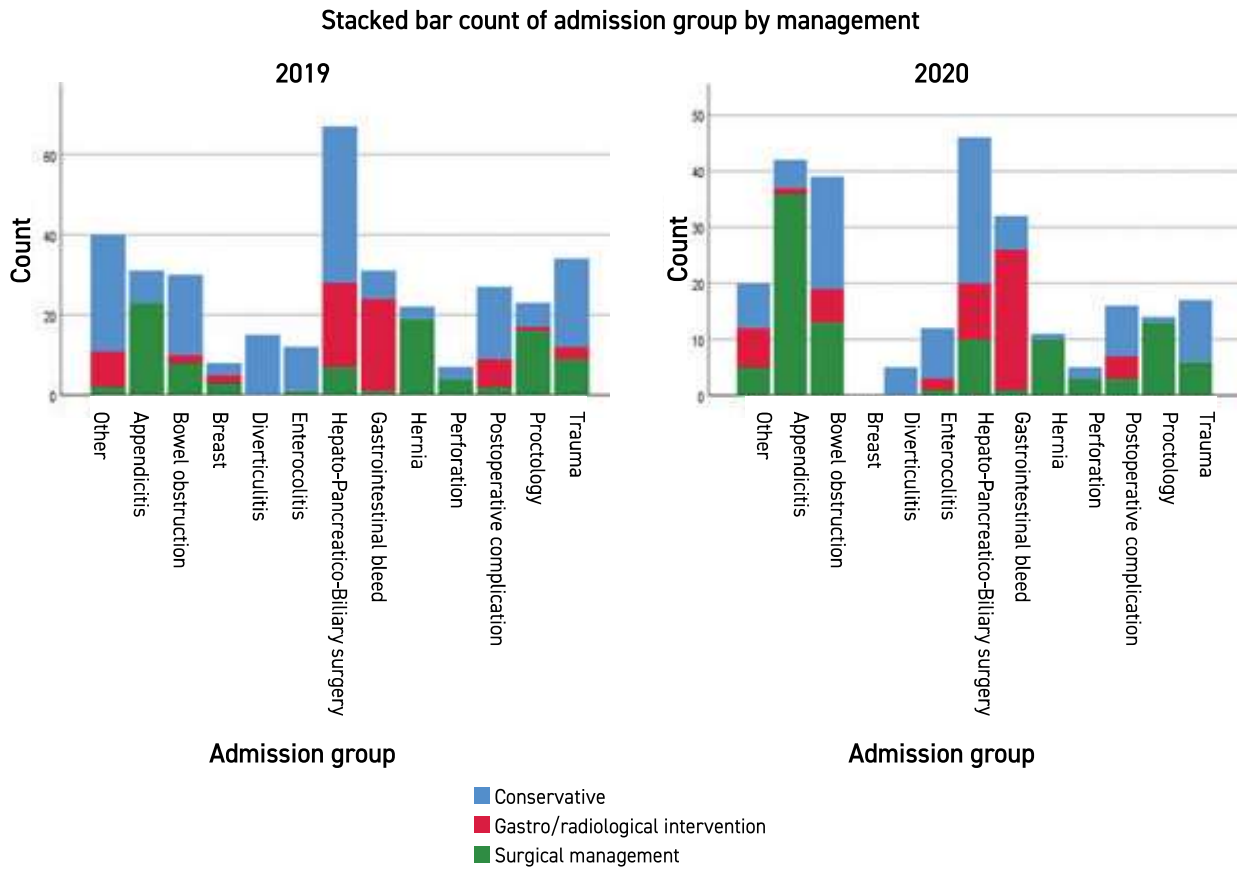
Table 3. Subgroup admission diagnosis analysis

Variable		COVID-19 group (2020)	Control group (2019)	*P* value*
Admissions	General			**0.004**
	Appendicitis	42 (16.2%)	31 (8.9%)	**0.006**
	Bowel obstruction	39 (15.1%)	30 (8.6%)	**0.014**
	Breast complaints	0	8 (2.3%)	**0.012**
	Diverticulitis	5 (1.9%)	15 (4.3%)	0.1
	Enterocolitis	12 (4.6%)	12 (3.5%)	0.46
	HBP	46 (17.8%)	67 (19.3%)	0.63
	Gastrointestinal bleeding	32 (12.4%)	31 (8.9%)	0.17
	Hernia	11 (4.2%)	22 (6.3%)	0.26
	Perforated viscus	5 (1.9%)	7 (2%)	0.94
	Post postoperative complication	16 (6.2%)	27 (7.8%)	0.45
	Proctology	14 (5.4%)	23 (6.6%)	0.53
	Trauma	17 (6.6%)	34 (9.8%)	0.16
	Other	20 (7.7%)	40 (11.5%)	0.121

*Bold indicates significance
Breast related diagnoses included mastitis, abscess, and mass
HBP included hepatobiliary pancreatic related diagnosis
Proctology included perianal abscess, anal fissure, hemorrhoids

sented with more severe features demonstrated by significant difference in WBC count (10^9/L) 14.8 vs. 12.1 (P = 0.011), neutrophil level (10^9/L) 12.1 vs. 9.5 (P = 0.008), and serum creatinine (mg/L) 0.99 vs. 0.76 (P = 0.05). There were no significant differences in the other parameters (i.e., management and postoperative complications). Of 69 overall admissions for bowel obstruction, 8 were managed surgically in the control cohort vs. 13 in the COVID-19 cohort (P = 0.55). A significant creatinine elevation was noted in the COVID-19 cohort 1.12 vs. 0.81 mg/L (P = 0.017). Patients admitted for diverticulitis had higher body temperature, 37.44°C vs. 36.8°C in the control cohort (P = 0.012), and higher CRP levels of 144.2 vs. 73.6 mg/L in the control cohort (P = 0.026). Patients with gastrointestinal bleeding presented a non-significant trend of a lower hemoglobin count in the COVID-19 period 8.1 vs. 9.5 g/dl (P = 0.056).

Figure 1. Comparison of management approach per diagnosis in the different groups



DISCUSSION

Even as the COVID-19 pandemic rapidly spread worldwide and propagated fear, there was much uncertainty about the SARS-CoV-2 virus, its routes of transmission, most effective preventive measures, and fatality rates. This uncertainty, in addition to the estimated millions of casualties globally, led the WHO and world governments to swiftly react and impose strict emergency measures including closing schools and non-essential work facilities while enforcing prolonged national curfews that were accompanied by an aggressive stay-at-home call from governments to prevent the spread of the virus. Concern of exposure to infected patients, in addition to the consideration of the enormous burden imposed on hospitals and healthcare services during the COVID-19 pandemic, caused the public and practitioners to avoid or delay visits and referrals to EDs even when experiencing an acute illness, surgical or non-surgical. Acute illnesses, specifically acute surgical illnesses, often require prompt evaluation, diagnosis, and intervention to prevent further clinical deterioration and to achieve optimal prognosis and outcomes [16]. Hence, we hypothesized that the COVID-19 pandemic would indirectly affect the volumes of acute surgical admissions, their clinical presentation, and eventually their surgical outcomes.

We performed a prospective, comparative study comparing acute surgical admissions during a peak month of the COVID-19 pandemic with acute surgical admissions at a parallel month a year before. This comparison was performed in a tertiary, university-based, medical center that was caring for hundreds of COVID-19 patients while maintaining core resources to allow for emergency and essential care. We found a major decrease in acute surgical admissions during the COVID-19 period (25%, $P < 0.0001$). Patients who eventually arrived at the ED with an acute surgical problem had more co-morbidities and worse general status as demonstrated by a significant higher ASA score. Similarly, published reports from northern Italy indicated a decrease in acute coronary syndrome (ACS)-related hospitalization rates across several cardiovascular centers during the COVID-19 pandemic. The study raised the suspicion of increased mortality from ACS in patients who delayed or avoided seeking medical attention during the COVID-19 pandemic [17].

Likewise, our data also raise the question of whether some patients have died from an acute surgical condition without seeking medical attention during the COVID-19 period, or to a lesser extent whether some patients with surgical conditions have deteriorated while trying to delay or avoid surgical care during the pandemic. Patients during the COVID-19 period presented later in their clinical course, after a significantly longer time interval between onset of symptoms and admission to the ED, with markedly higher inflammatory markers: elevated heart rate, leukocyte disturbance (leukocytosis or leukopenia), higher CRP level, and decreased renal function.

Similar results were obtained when analyzing admission diagnosis by subgroups. Acute appendicitis and acute diverticulitis were presented with more severe inflammatory features. Bowel obstruction patients were admitted with a significant average creatinine elevation most likely secondary to dehydration. Cases with gastrointestinal bleeding presented with a non-significant trend of lower hematocrit levels at admission.

This relatively advanced clinical presentation is most probably related to the fear of the public to be exposed to EDs crowded with sick people, some of whom were infected by COVID-19. Our observations can be explained either by the reluctance of patients to go to the ED or lack of accessibility to healthcare in the community. In many countries, including Israel, community healthcare is usually easily accessible and free of charge. At the time of the outbreak, many clinics ceased surgeries due to restrictions. Although we were not been able to analyze the patterns of referral to the ED, we believe that many of the delays occurred because medical consultations were either not available or were delivered remotely by telephone or video communication and missed essential conditions requiring acute surgical care. Many of the patients said that they were prescribed with medications and were ill-advised not to arrive at emergency facilities in large medical centers because of the risk of exposure.

Another significant observation was that more patients in the COVID-19 cohort were treated surgically. We believe that this result is due to a combination of these potential reasons: patients arrived late with worse physical status and have missed the option of conservative treatment, patients with mild surgical problems were resolved spontaneously at home or treated in the community and did not visit the ED, and elective surgeries were postponed, leaving the operation rooms relatively available. As such, cases that normally are operated in a delayed fashion (such as interval cholecystectomy) could be operated during the same admission.

Interestingly, the more severe clinical presentation of patients during the COVID-19 period has not been reflected in higher mortality rates nor in higher postoperative morbidity rates. This result might be related to the relatively small cohort of patients who eventually underwent surgery and the short follow-up time. This situation should be addressed by querying large national registries. The length of ED stay was longer during the COVID-19 period representing the time required for SARS-CoV-2 screening before hospitalization in some of the patients. There were some cases where urgent surgery was delayed until after the SARS-CoV-2 PCR results were available. PCR results were available. Interestingly enough, LOS was significantly shorter during the COVID-19 period. Most likely representing patient and healthcare fund fears of in-hospital exposure and infection with the virus and the desire of medical teams to decrease the number of in-house patients, thus shortening the length of hospital stay to the minimum. We can only speculate that such a policy could potentially put some of those patients at risk for being discharged from the hospital too soon. We anticipated that this trend towards earlier discharge would result in increased readmissions, but during our short study period, this observation was not witnessed.

Our study is unique because we were able to explore the influence of the COVID-19 pandemic from a different perspective in a prospective manner. To the best of our knowledge, this is the first study describing the effects of reluctance to seek surgical care and its consequences during the COVID-19 pandemic.

LIMITATIONS

First, we compared prospectively collected data during the current time period to retrospectively collected data of a parallel past time period. Although this is a potential pitfall, all the data collected was available in the electronic medical records and no missing data points were noted. Second, since the Sheba Medical Center was the first hospital in Israel to admit COVID-19 patients, the large numbers of patients admitted and the complexity of the care delivered received wide media exposure during the outbreak. Therefore, patients elected to approach other smaller medical centers and our observations may be a result of referral bias and not a true phenomenon. Further studies addressing regional or national registries may provide a more definite answer to the question of how COVID-19 has affected surgical hospitalizations and patient outcomes on a regional or a national level.

CONCLUSIONS

Our study examined the indirect effects of the COVID-19 pandemic and its social/governmental responses on the presentation and outcomes of patients with acute surgical conditions. Results showed that fewer patients presented to the ED and that those who did, often did so in a delayed fashion and in a worse clinical condition as demonstrated by derangement in clinical and laboratory properties. Likewise, a higher percentage of patients required surgical interventions compared to the control cohort. We speculate that some patients may have died or had worse surgical issues as a result of not seeking urgent surgical attention during the COVID-19 pandemic. Thus, we believe that during infectious pandemics such as this, healthcare systems must edu-

cate the general population and community healthcare providers about the importance of not delaying seeking required urgent medical or surgical attention in the ED. The experiences gained from SARS-CoV-2 management should serve as an example for the emerging need to improve the ability of healthcare systems to manage large number of patients with any infectious disease with hospital acquired infections and to reassure the public about hospital safety.

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References

1. World Health Organization. Emergencies preparedness, response. Novel Coronavirus–China. 2020. [Available from https://www.who.int/csr/don/12-january-2020-novel-coronavirus-china/en/]. [Accessed 1 Feb 2020].
2. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020; 382: 727-33.
3. Chen Y, Liu Q, Guo D. Emerging coronaviruses: Genome structure, replication, and pathogenesis. *J Med Virol* 2020; 92 (4): 418-23.
4. Wuhan municipal health commission's briefing on the pneumonia epidemic situation (in Chinese). 2019; 12: 31. https://epaper.hubeidaily.net/pc/content/202001/01/content_15040. [Accessed 1 April 2020].
5. Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: the mystery and the miracle. *J Med Virol* 2020; 92 (4): 401-2.
6. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020 [Available from https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020]. [Accessed 1 April 2020].
7. World Health Organization. Coronavirus disease 2019 (COVID-19) Situation Report – 94. Data as reported by national authorities by 10:00 CET 23 April 2020. [Available from https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200423-sitrep-94-covid-19.pdf?sfvrsn=b8304bf0_4]. [Accessed 1 April 2020].
8. Cascella M, Rajnik M, Cuomo A, et al. Features, evaluation and treatment coronavirus (COVID-19) [Updated 10 August 2020]. [Available from: https://www.ncbi.nlm.nih.gov/books/NBK554776/]. [Accessed October 2020].
9. Kim DH, Choe YJ, Jeong JY. Understanding and interpretation of case fatality rate of coronavirus disease 2019. *J Korean Med Sci* 2020; 35 (12): e137.
10. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA* 2020; 323 (18): 1775-6.
11. Yuan M, Yin W, Tao Z, Tan W, Hu Y. Association of radiologic findings with mortality of patients infected with 2019 novel coronavirus in Wuhan, China. *PLoS One* 2020; 15 (3): e0230548.
12. White DB, Lo B. A framework for rationing ventilators and critical care beds during the COVID-19 pandemic. *JAMA* 2020; 323 (18): 1773-4.
13. State of Israel. Ministry of Health. COVID press releases. As of 17 March 2020. [Available from https://www.health.gov.il/English/Topics/Diseases/corona/Pages/press-release.aspx]. [Accessed October 2020].
14. Saklad M. Grading of patients for surgical procedures. *Anesthesiology* 1941; 2: 281-4.
15. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann* Surg 2004; 240 (2): 205-13.
16. Søreide K, Hallet J, Matthews JB, Schnitzbauer AA, et al. Immediate and long-term impact of the COVID-19 pandemic on delivery of surgical services. *Br J Surg* 2020; 10.1002/bjs.11670.
17. De Filippo O, D'Ascenzo F, Angelini F, et al. Reduced rate of hospital admissions for ACS during Covid-19 outbreak in Northern Italy. *N Engl J* Med 2020; 383 (1): 88-9.

I awoke this morning with devout thanksgiving for my friends, the old and the new.
Ralph Waldo Emerson (1803-1882), American essayist, lecturer and poet, and champion of individualism

Capsule

The genetics underlying severe COVID-19

The immune system is complex and involves many genes, including those that encode cytokines known as interferons (IFNs). Individuals who lack specific IFNs may be more susceptible to infectious diseases. Furthermore, the autoantibody system dampens IFN response to prevent damage from pathogen-induced inflammation. Two studies examined the likelihood that genetics affects the risk of severe coronavirus disease-2019 (COVID-19) through components of this. **Zhang** et al. used a candidate gene approach and identified patients with severe COVID-19 who have mutations in genes involved in the regulation of type I and III IFN immunity. They found enrichment of these genes in patients and conclude that genetics may determine the clinical course of the infection. **Bastard** and co-authors identified individuals with high titers of neutralizing autoantibodies against type I IFN-α2 and IFN-ω in about 10% of patients with severe COVID-19 pneumonia. These autoantibodies were not found either in infected people who were asymptomatic or those who had milder phenotype or in healthy individuals. Together, these studies identify a means by which individuals at highest risk of life-threatening COVID-19 can be identified.

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Eitan Israeli