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Treatment Strategies and Perforation Rate of Acute Appendicitis During the Early Phase of the COVID-19 Pandemic: A Swedish Cohort Study

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ABSTRACT

Introduction: It is unknown whether the COVID-19 pandemic has had an impact on emergency surgical care in Sweden. This study aimed to compare frequency, treatment strategies, severity, and complication rate of appendicitis during the initial phase of the COVID-19 pandemic with those of previous years.

Methods: In this single-center study, we identified all patients admitted with appendicitis between March 16 and June 16, 2020, at the Stockholm South General Hospital, and compared these with patients hospitalized with appendicitis during the same calendar period the three previous years. We used multivariate logistic regression to calculate Odds Ratios (OR) with 95% confidence intervals as measurement of the association between appendicitis treatment and perforation rate during the COVID-19 period compared to the nonCOVID-19 periods.

Results: In all, 892 patients hospitalized with appendicitis were identified, 241 (27%) in 2020 (Covid period group) and the remaining 651 (73%) during the same calendar periods 2017-2019 (nonCovid period group). Appendicitis during the COVID-19 period was associated with double the risk for undergoing conservative treatment (OR 2.15 [95% CI 1.44-3.21]), and a decreased risk for being diagnosed with perforated appendicitis (OR 0.68 [95% CI 0.48-0.98]).

Conclusions: Patients admitted with appendicitis during the early phase of the COVID-19 pandemic in Stockholm, Sweden, were more likely to receive conservative treatment and less likely to suffer from perforated appendicitis compared to patients hospitalized before

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the pandemic. Hypothetically, this difference could have been due to pandemic-associated resource reallocation, or it may simply reflect an increasing trend towards conservative management of appendicitis.

Introduction

Once the first patient was diagnosed with coronavirus disease (COVID-19) in December 2019 in Wuhan, China, the novel coronavirus spread rapidly throughout the world, and in March 2020, World Health Organization (WHO) declared a global pandemic.[1,2] To limit spread of the virus, public health services throughout the world imposed various restrictions.[3] During the same period, there were reports of decreasing numbers of patients seeking acute healthcare, and this was suggested to be a direct consequence of the restrictions or fear of exposure to the virus.[4-7] Previous studies have also reported longer patient-delay in seeking healthcare during the COVID-19 pandemic, including patients with serious conditions such as acute coronary syndrome,[4-7] stroke,[8] and acute surgical conditions.[9,10]

Acute appendicitis (AA) is the most common acute surgical condition globally, with a lifetime risk of approximately, 6% to 7%, and appendectomy is the most common emergent abdominal surgical procedure.[11,12] The severity of AA is commonly stratified as complicated and uncomplicated appendicitis, and the first-line treatment strategy is generally considered to be appendectomy.[13-15]

Reports from China, Israel, the United States, Spain, and Italy all indicate a general decrease in the frequency of AA during the COVID-19 pandemic compared to the pre-COVID-19 era. Furthermore, an increase in the proportion of complicated appendicitis, defined as gangrenous or perforated and/or appendicitis with abscess, was observed during the initial phase of the COVID-19 pandemic in those countries.[16-20] Likewise, two German studies observed a 12% decrease in the number of patients admitted with appendicitis between March and June 2020, and in the number of appendectomies performed. However, in contrast to the other reports, the German studies did not report an increased rate of perforated appendicitis.[21,22] In accordance with the German studies, a multicenter study from the United States reported that fewer patients presented with uncomplicated appendicitis during the pandemic, and that the number of patients with complicated appendicitis did not increase.[23]

The Swedish COVID-19 restriction strategy has differed from those of China and most western countries, in that lockdown measures have been relatively limited.[24] In Sweden, kindergartens and schools for children up to the age of 16, public spaces and restaurants remained opened. Sweden did not enforce quarantine for infected households, and working from home was encouraged if possible.[25]

So far, there are no reports from Sweden on how the pandemic has affected the frequency of AA, treatment strategy, severity of appendicitis, and complication rate. The aim of this study was thus to assess whether these four variables differed during the initial phase of the COVID-19 pandemic to those during the corresponding calendar periods 3 y prior to the pandemic.

Methods

Study design

A cohort study based on all patients admitted with AA at Stockholm South General hospital between 2017 and 2020.

Study setting

Sweden, located in the north of Europe, is divided into 21 healthcare regions with autonomous organizations.[26] The Stockholm South General Hospital is centrally located in the Swedish capital, and is one of six hospitals providing emergency care to the 2.3 million inhabitants of Stockholm and its surroundings.[27] As well as providing acute abdominal surgery for adults, the Surgical Department at Stockholm South General Hospital has been the regional referral center for pediatric patients (between 10 and 14 y old) with appendicitis since 2017. Approximately 800 appendectomies are performed at Stockholm South General Hospital each year, around 200 (25%) of which are pediatric patients. A previous study between 2004 and 2014 at Stockholm South General Hospital reported perforation rates among patients undergoing appendectomy of between 26 and 28%.[28]

During the first phase of the pandemic, all hospitals in Stockholm including the South General Hospital, were subject to surgical care restrictions due to limited operative and postoperative anesthetic resources. The restrictions primarily limited elective surgery, not emergency surgery. During the study period, Stockholm South General Hospital accounted for 14% (9682 in-hospital days of a total of 68,675 in-hospital days) of all COVID-19 inpatient care in the Stockholm region (unpublished data from the Region of Stockholm).

Study period

The study period began when the World Health Organization (WHO) classified COVID-19 as a global pandemic, corresponding to when Stockholm authorities imposed restrictions including the recommendation to work at home and limit personal contacts,[2,29] and ended when there was a clear decrease in the number of COVID-19 patients admitted to Swedish hospitals (including Stockholm South General Hospital). An attempt to illustrate the decrease of admitted patient with COVID-19, marking the end of the study period is presented in Figure 2. However, a strict definition of when the first phase ended has, to our knowledge, not been established in Sweden.

Data sources and study population

Qlikview software, as used at the hospital and coupled to the Electronic Medical Record, was used to identify all patients hospitalized with appendicitis. Diagnoses are registered using International Classification of Disease (ICD) codes (10th revision since 1997), and surgeries are registered using surgical procedure codes. All study patients were identified based on registered ICD-10 codes for appendicitis (K35.2, K35.3, K35.8, K36.9, K37.9), and/or surgical procedure codes for appendectomy (JEA00, JEA01, JEA10) or percutaneous drainage (TJA40). The diagnoses of all study patients were validated against medical records by the main author (IE). For study patients undergoing surgery, the date of surgery was used as study inclusion (date of diagnosis). For patients receiving conservative treatment, the date of discharge from hospital was used as inclusion date as this corresponds with the date of ICD-code registration.

Covid period group

All patients diagnosed with AA between March 16 and June 16, 2020, were included in the Covid period group.

Non-covid period group

All patients hospitalized for appendicitis between March 16 and June 16 (corresponding to the covid study period), for the years 2017-2019. Previous studies have reported a possible seasonal difference in appendicitis rate,[30] which is the reason we chose the same calendar period for both Covid and non-Covid groups.

Additional data sources and covariates of interest

Data of all patients undergoing appendectomy at the Stockholm South Surgical Department are transferred from the operation planning software (Orbit 5) and the Electronic Medical Record to an appendicitis database. The database includes information on age, sex, length of hospital stay (in days), surgical approach, and information on perforation, 30-day complications, and reoperation rate. Among study patients not undergoing surgery, information on sex and age was extracted from Qlikview. We reviewed patients in the Covid period group for a positive SARS-CoV-2 polymerase chain reaction suggesting COVID-19 infection and registered as ICD-10 code U07.1.

Outcomes

All study patients—overall treatment strategies and perforation rate

Treatment strategies were divided into surgical and conservative treatment. Conservative treatment was defined no surgery but instead receiving either i) antibiotics only, or ii) percutaneous drainage with antibiotics. Perforation was defined as perforation diagnosed at surgery, or conservative treatment with percutaneous drainage.

Study patients undergoing surgery—surgical approach, severity, and complications

Surgical procedures were either laparoscopic appendectomy or open appendectomy (OA). Conversion from laparoscopic appendectomy to OA was defined as OA. Among study patients undergoing appendectomy, the surgeon's macroscopic diagnosis during surgery, postoperative prolonged antibiotics, and histopathological diagnosis (when present) was used to classify the appendix as perforated. Proxy markers for disease severity among patients undergoing surgery included: i) duration of surgery (in minutes); ii) length of hospital stay (days); iii) 30-day complication (y/n); and iv) readmission within 30 d (y/n). When first line treatment was percutaneous drainage, patients were classified as having perforated appendicitis. Surgical complications were defined as: i) hematoma (requiring active treatment [additional hemoglobin testing, reoperation, radiology]); ii) small bowel obstruction (verified by radiology and requiring a gastrografin challenge and/or surgery); iii) postoperative paralytic ileus (postoperative course longer than expected with radiologic or clinical signs of paralytic ileus); iv) surgical site infection (requiring prolonged or additional antibiotics, or wound debridement); v) intra-abdominal abscess (verified by radiology but not necessarily amenable for drainage); or vi) other complications (determined on case-to-case basis [e.g., urinary tract infection, wound dehiscence]).[28]

Statistical analysis

The number of study patients admitted with appendicitis for the respective periods were presented as absolute numbers and stratified into treatment groups (surgical or conservative). For a descriptive overview, a figure of the numbers of patients admitted each week with appendicitis during the study periods is presented, superimposed by the number curve of patients admitted with COVID-19 during the 2020 period (Fig. 2).

Baseline demographic characteristics of patients in the Covid period and nonCovid period groups were compiled and tabulated. A logistic regression model was used to calculate odds ratio with 95% confidence intervals as measurement of the risk for receiving conservative treatment (with surgery as reference), and for perforation (*versus*. nonperforated as reference) during the COVID-19 period compared to the non-Covid period. The model was adjusted for age and sex. For the study patients receiving surgery, differences in appendicitis severity and complications between the Covid period and nonCovid period groups, were tested using Chi-square test for dichotomous, *t*-test for normally distributed continuous, and Mann–Whitney *U* test for ordinal or nonnormally distributed continuous variables. Two-tailed *P*-values <0.05 were considered statistically significant.

Analyses were performed with SAS software package version 9.4 (SAS Institute, Cary, North Carolina).

Ethical considerations

This study was approved by the Swedish ethical review authority (2019-05976 and 2021-067572-2). Due to the register-based data and retrospective nature of the study, the requirement for informed consent was waived.

Results

In all, 892 study patients were hospitalized with AA between March 16 and June 16, 2017-2020. During the COVID-19 pandemic period (2020), 241 study patients (27%) were admitted and comprised the Covid period study group. The remaining 651 study patients (215 [24.1%] in 2017, 215 [24.1%] in 2018, and 221 [24.8%] in 2019) were admitted during the nonCovid periods and made up the nonCovid period group (Fig. 1).

Age distribution and sex were similar between the Covid period and nonCovid period groups. There was a slightly higher proportion of pediatric patients during the Covid

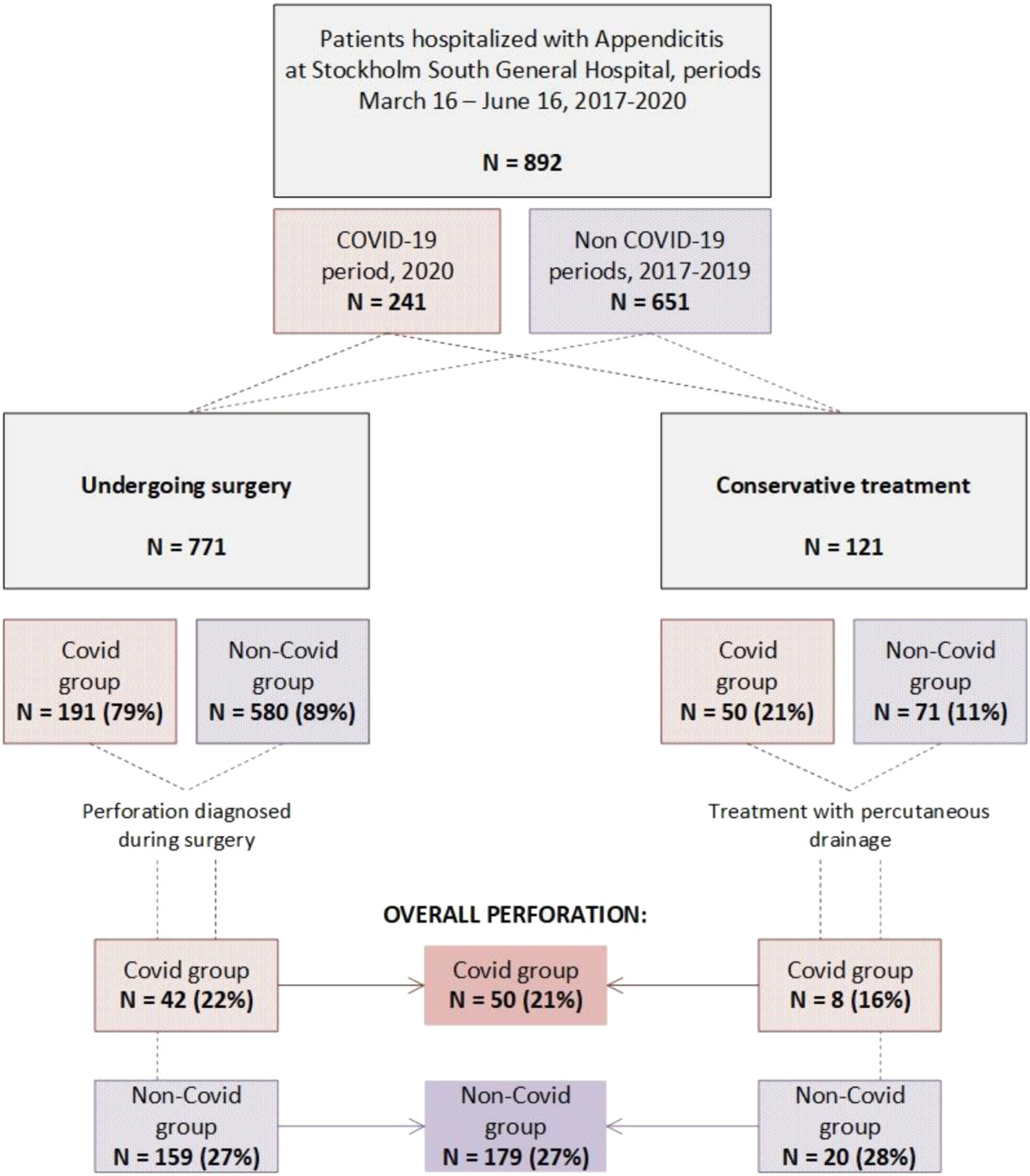

Fig. 1 – Overview of study population and outcome definitions.

Table 1 – Demographic and clinical baseline characteristics of all patients hospitalized with appendicitis during Covid period (COVID-19 pandemic) and non-Covid periods (2017-2019).

Characteristic	Covid period group appendicitis during COVID-19 period $n = 241$	Non-covid period group appendicitis during non-covid period $n = 651$	P-value
All patients			
Age, median (IQR)	29 (14-44)	29 (15-44)	0.5
Pediatric (<15 y), *n* (%)	68 (28.2)	160 (24.6)	0.3
Adult (≥15 y), *n* (%)	173 (71.8)	491 (75.4)	
15-40 y, *n* (%)	102 (42.5)	294 (45.4)	0.8
41-60 y, *n* (%)	49 (20.3)	138 (21.3)	
61-80 y, *n* (%)	20 (8.3)	49 (7.6)	
≥81 y, *n* (%)	1 (0.4)	7 (1.1)	
Sex, female *n* (%)	105 (43.6)	297 (46.0)*	0.5
Sex, male *n* (%)	136 (56.4)	349 (54.0)*	0.5
COVID-19 infection *n* (%)	7 (2.9)	n/a	

* Information on sex missing for five in non-Covid group.

period (28.2% Covid period *versus* 24.6% nonCovid), but this was not statistically significant. Among the patients admitted during the COVID-19 period, 3% had a registered ICD code indicating ongoing COVID-19 infection (Table 1).

Appendicitis frequency during the COVID-19 period versus *the non-Covid periods*

There was no difference in absolute numbers of patients admitted with appendicitis during the Covid period compared to the nonCovid periods. Weekly variations in number of patients admitted with appendicitis were observed during both Covid and nonCovid study periods (Fig. 2).

Appendicitis treatment strategies and overall perforation rates during the COVID-19 period versus *the non-Covid periods*

Table 2 shows the risk for receiving conservative treatment and for being diagnosed with perforated appendicitis during the Covid period as compared to the nonCovid periods. During the Covid period, 50/241 (20.8%) study patients received conservative treatment *versus* 71/651 (10.9%) patients during the nonCovid periods, corresponding to a doubled risk for conservative treatment during the Covid period compared to the nonCovid periods (OR 2.15 [95% CI 1.44-3.21]). The corresponding figures for perforated appendicitis were 50/241 (20.8%) during the Covid period *versus* 179/651 (27.5%) during the nonCovid periods, corresponding to significantly lower risk for being diagnosed with perforated appendicitis (OR 0.68 [0.48-0.98]) during the Covid period.

Surgical approach, severity, and complications during the COVID-19 period versus *the non-Covid periods*

In all, 771 patients (191 [79%] in the Covid group and 580 [89%] in the nonCovid group) received surgery and were included in the appendicitis database (Table 3). Open appendectomy was performed in 9/191 (4.7%) patients in the Covid group period versus 4/580 (0.7%) in the nonCovid group (P-value <0.001). The remaining patients were operated laparoscopically.

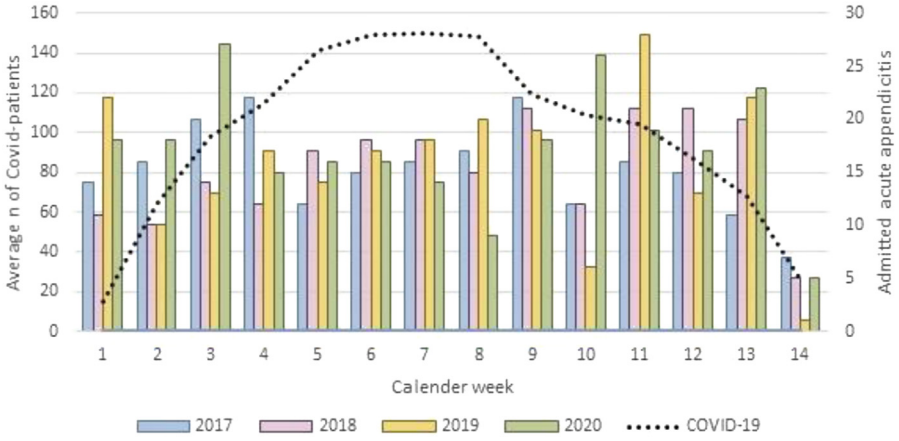

Fig. 2 – Weekly absolute number of patients admitted with acute appendicitis (colored bars) and number of patents admitted with COVID-19 from mid-March through mid-June (black dotted line).

Table 2 – The relative risk for appendicitis treated conservatively and perforated appendicitis during the COVID-19 period compared to the non-Covid period. Odds ratio (OR) with 95% confidence interval (CI). Appendicitis during COVID-19 period, $n = 241$. Appendicitis during non-Covid period, $n = 651$.

Time period	Conservative treatment*		Perforated appendicitis†	
	n (%)	OR (95% CI)‡	*n* (%)	OR (95% CI)‡
COVID-19 period	50 (20.8)	2.15 (01.44-3.21)	50 (20.8)	0.69 (0.48-0.98)
Non-covid periods	71 (10.9)	Ref. (1.0)	179 (27.5)	Ref. (1.0)

*Defined as not undergoing surgery but instead receiving i) antibiotics only or ii) percutaneous drainage with antibiotics as first line treatment.
†For patients undergoing appendectomy, the surgeon's macroscopic diagnosis was accepted as being perforation, patients not undergoing surgery who received first line treatment with percutaneous drainage were also classified as having perforated appendicitis.
‡Adjusted for age and sex.

Among the patients undergoing surgery, the frequency of perforation was slightly higher (159/580 [27.9%]) among patients hospitalized with appendicitis during the nonCovid periods compared to the Covid period (42/191 [22%]), this difference was not significant. A higher proportion of patients in the Covid group (166/191 [86.9%]) were discharged within 2 d than during the nonCovid periods (453/580 [78.7%]). A *post hoc* analysis adjusting for perforation showed this difference to be nonsignificant. The other proxy markers for AA severity showed no significant differences between the Covid and nonCovid periods.

Conservative treatment during the COVID-19 and non-Covid periods

During the Covid period, 8/50 [16%] of the patients with AA undergoing conservative treatment received percutaneous drainage compared to 20/71 (28%) patients during the nonCovid period ($P = 0.1$). The remaining 42/50 (84%) Covid period patients and 51/71 (72%) nonCovid period patients received no treatment or antibiotics only ($P = 0.1$).

Discussion

In this single-center study from Stockholm, Sweden, we found that the number of patients hospitalized for AA remained constant during the early phase of the COVID-19 pandemic compared to the same calendar periods the 3 y before. The risk for undergoing conservative treatment when hospitalized for AA during the Covid period was higher than during the non-Covid periods. Finally, despite conservative treatment being more common during the Covid period, the risk for being diagnosed with perforated appendicitis during the Covid period was lower than during the nonCovid periods.

Table 3 – Surgical approach, appendicitis severity, and complications among patients undergoing surgical treatment.

Characteristic	Covid period group appendicitis during COVID-19 period $n = 191$	Non-covid period group appendicitis during non-covid periods $n = 580$	*P*-value
ASA-classification			0.03
ASA-1 *n* (%)	130 (69.9)	346 (61.0)	
ASA-2 *n* (%)	51 (27.4)	197 (34.7)	
ASA-3 *n* (%)	5 (2.7)	24 (4.2)	
ASA 4–5 *n* (%)	0	0	
Pregnant *n* (%)	3 (1.6)	9 (2.2)	0.8
Laparoscopic appendectomy *n* (%)	180 (95.2)	554 (99.3)	<0.001
Open appendectomy *n* (%)	9 (4.7)	4 (0.7)	<0.001
Perforated *n* (%)	42 (22.0)	159 (27.9)	0.1
Length of surgery (min), Median (IQR)	50 (39-64)	50 (37-68)	0.8
Length of hospital stay, mean (d)			0.02
0-2 d *n* (%)	166 (86.9)	453 (78.7)	
3-5 d *n* (%)	16 (8.4)	98 (17.0)	
≥6 d *n* (%)	9 (4.7)	25 (4.3)	
30-day complication rate	17 (9.0)	51 (9.0)	1
Readmission within 30 d *n* (%)	4 (2.1)	17 (3.4)	0.5
Reoperation within 30 d *n* (%)	1 (0.5)	1 (0.17)	0.5
Time in emergency department before admission (h), median (IQR)	5 (3.4-7.4)	6.7 (4.6-8.7)	<0.001

ASA = "American Society of Anesthesiologist (ASA) Physical Status"-system; IQR = inter-quartile range.

Previous studies from the United States, Spain, Germany, Italy, Israel, and China have reported lower frequencies of patients admitted with AA during the initial phase of the COVID-19 pandemic when healthcare restrictions were imposed.[17-24] In contrast, the absolute number of patients admitted to the Stockholm South General Hospital with appendicitis during the Covid period remained the same as during the nonCovid periods. We cannot explain this difference, but it is possible that the Swedish strategy of refraining from total lockdown could have influenced the healthcare-seeking behavior of the population to a lesser extent than in the other countries. Different socio-cultural settings and heterogenous healthcare systems may also have contributed to the difference.

A clear increase in conservative treatment during the Covid period was observed, in particular in patients receiving only antibiotics. This study did not investigate the individual surgeons clinical decision process, but presumably conservatively treated are patients with milder symptoms and without perforation. To our knowledge, this has not been described previously. It is possible that the strained healthcare situation, with limited resources (*or* perceived limited resources), during the pandemic might have caused more surgeons to select conservative management for AA. However, there is nothing to indicate that resources for emergency surgery were reduced during the pandemic in Sweden. Furthermore, we did not observe a change in the number of patients hospitalized with AA during the Covid period, which indicates that the surgeons' stringency when selecting cases for surgery contributed to our results. Regarding reasons for surgeons' stringency when selecting surgical cases, we can only hypothesize that the overwhelming situation caused by the pandemic might have influenced since there was no official change of treatment strategy imposed at our clinic. A random variation in appendicitis clinical phenotypes over time is another potential explanation for our findings.

During the first phase of the pandemic laparoscopic surgery was advised against due to fear of COVID-19 exposure for personnel in operating rooms, which presumably explained the higher rate of open appendectomy in the Covid-group.

Results from studies on appendicitis complications during the COVID-19 pandemic are inconsistent. Some studies, based on small populations, have reported higher rates of complicated appendicitis, defined as perforated with or without abscess,[17-21] whereas other studies could not show higher perforated appendicitis rates during the pandemic.[22-24] A German study used the same Covid/nonCovid periods as in the present study, showing a reduction in the number of patients admitted with AA, and a lower rate of patients operated for uncomplicated AA during the Covid period.[21] In contrast to previous studies, we found a lower perforation rate among patients hospitalized with AA during the COVID-19 period compared to the nonCovid periods. Interestingly, the perforation rate was lower during the COVID-19 period despite the lower numbers of surgically treated appendicitis. The result from our study, indicated lower rates of perforated appendicitis, is interesting in the light of Sweden's nonlock down policies during the pandemic. One could argue that the Swedish approach was beneficial regarding AA and maybe other acute surgical diagnosis since our study population neither show tendency of patient delay nor higher rates of perforation due to the pandemic and imposed restrictions. To investigate this in other surgical and nonsurgical emergency diagnoses would be of great interest to guide public health care services imposing restrictions in future pandemics.

The impact of prompt surgical management of AA to avoid perforation is subject of debate.[31,32] It is possible that widespread cancellation of elective surgery due to hospital restrictions during the early phase of the COVID-19 pandemic, in combination with more stringent selection of operative cases, may have led to less time waiting for emergency surgery. Timely emergency surgery during the COVID-19 pandemic might thus have resulted in a lower risk for perforation among patients at risk. In the present study, more patients in the Covid period group undergoing surgery were discharged within 2 days compared to those in the nonCovid group (86.9% *versus* 78.7%, $P < 0.02$), which reflects the lower number of patients with perforation. A *post hoc* analysis, however, did not confirm this difference to be significant when adjusting for perforation rate.

Our results should be interpreted in the light of some study limitations. Regardless of the retrospective nature of the study, the data were collected prospectively, precluding the risk of 'recall bias'. The study included patients admitted for appendicitis at one of six hospitals within the Stockholm region, and outpatient data were not included. It is possible that there were patients seeking outpatient care with uncomplicated appendicitis who were misdiagnosed and thus treated "conservatively". However, since the rate of hospitalization for appendicitis during the COVID-19 period was similar to the three previous years, there is nothing to suggest different inpatient-outpatient ratios during the study periods. During the initial phase of the pandemic, testing of patients admitted to the surgical department of Stockholm South General Hospital for COVID-19 was only done in cases where there was clinical suspicion, and the sensitivity of testing was unknown. Hence, the prevalence of COVID-19 among the patients in this study is uncertain. The proportion of pediatric appendicitis cases was higher during the Covid period, though this was not statistically significant. There might have been a difference in treatment strategy between pediatric and adult cases that could have been amplified during the pandemic and affected our results in either direction. The single-center approach makes it difficult to extrapolate our results to other settings due to differences in COVID-19 burden, surgical tradition, and pandemic-inflicted restrictions. However, within the region of Stockholm, all emergency hospitals were affected likewise during the initial pandemic phase, and there is no reason why the results should not be applicable to the other hospitals in Stockholm and other cities in Sweden.

Conclusions

The initial phase of the COVID-19 pandemic was not associated with an altered number of patients hospitalized for acute

appendicitis. Patients hospitalized with appendicitis during the pandemic were more likely to receive conservative treatment, and less likely to suffer from perforated appendicitis compared to the COVID-19-free years.

Author Contributions

Ivan Ernudd: design, collecting data, writing manuscript. Andreas Älgå: review and contribution to manuscript. Gabriel Sandblom: review and contribution to manuscript. Martin Dahlberg: design and planning of study, supervising main author, review and contribution to manuscript. Ängla Mantel: design and planning of study, supervising main author, review and contribution to manuscript, data analysis.

Disclosure

None declared.

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Funders had no role in the design or conduct of the study; collection, management or interpretation of the data; preparation, review, approval of the manuscript or decision of submission.

Ethical Considerations

This study was approved by the Swedish ethical review authority (2019-05976 and 2021-067572-2).

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