ORIGINAL ARTICLE

Differences in the evolution and management of acute appendicitis in patients with COVID-19: a case–control study

Diferencias en la evolución y manejo de apendicitis aguda en pacientes con COVID-19: estudio de casos y controles

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Abstract

Background: *The COVID-19 pandemic has generated uncertainty about the management of appendicitis.* **Aim:** *The aim of this study was to evaluate differences in the evolution and treatment of acute appendicitis in patients with COVID-19 infection compared to patients without the infection.* **Methods:** *A case–control study of adult patients hospitalized for acute appendicitis was performed, having as cases those who presented COVID-19. Data were extracted from the medical records. The logistic regression model was used to calculate crude (cOR) and adjusted odds ratios (aOR) with their respective 95% confidence intervals (95% CI).* **Results:** *We evaluated 38 cases and 76 controls, the mean age of the patients was 38.2 years (± 16.8), of whom 55.3% were women. Multivariate analysis showed, in cases, a lower probability of intraoperative findings (aOR: 0.21; 95% CI: 0.05-0.90) and a surgery time of more than 60 min (aOR: 0.21; 95% CI: 0.06-0.80), while there was a greater probability of management by open surgery (aOR: 3.83; 95% CI: 1.42-10.32) and a hospitalization time of more than 3 days after surgery (aOR: 3.33; 95% CI: 1.34-8.26).* **Conclusion:** *Significant differences were observed in terms of intraoperative findings, type of surgery, intraoperative time, and hospitalization time in patients with acute appendicitis and COVID-19.*

Keywords: *COVID-19. Appendicitis. General surgery. Laparoscopy. Peru (source: MeSH).*

Resumen

Antecedentes: *La pandemia de COVID-19 ha generado incertidumbre sobre el manejo de la apendicitis.* **Objetivo:** *Evaluar las diferencias en la evolución y el tratamiento de la apendicitis en pacientes con COVID-19 en comparación con los pacientes sin la infección.* **Métodos:** *Se realizó un estudio de casos y controles de pacientes adultos hospitalizados por apendicitis aguda, teniendo como casos aquellos que presentaron COVID-19. Los datos se extrajeron de las historias clínicas. Se utilizó el modelo de regresión logística para calcular las odds ratios (OR) crudas y ajustadas con sus respectivos intervalos de confianza del 95% (IC 95%).* **Resultados:** *Se evaluaron 38 casos y 76 controles, la edad media de los pacientes fue de 38.2 años (± 16.8), de los cuales el 55,3% eran mujeres. El análisis multivariante mostró, en los casos, una menor probabilidad de hallazgos intra operatorios (ORa: 0,21; IC 95%: 0.05-0.90) y un tiempo de cirugía superior a 60 min (ORa: 0.21; IC 95%: 0.06-0.80), mientras que hubo una mayor probabilidad de manejo mediante cirugía abierta (ORa: 3.83; IC 95%: 1.42-10.32) y un tiempo de hospitalización superior a tres días tras la cirugía (ORa: 3.33; IC 95%: 1.34-8.26).* **Conclusiones:** *Se obser-*

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Date of reception: 11-11-2021
Date of acceptance: 15-12-2021
DOI: 10.24875/CIRU.21000816

Cir Cir. 2022;90(6):742-748
Contents available at PubMed
www.cirugiaycirujanos.com

varon diferencias significativas en cuanto a los hallazgos intraoperatorios, el tipo de cirugía, el tiempo intraoperatorio y el tiempo de hospitalización en pacientes con apendicitis aguda y COVID-19.

Palabras clave: *COVID-19. Apendicitis. Cirugía general. Laparoscopia. Perú (Fuente: DeCS).*

Introduction

Acute appendicitis remains the most common acute surgical abdomen[1]. Its global incidence has been increasing in recent decades (11.4% increase from 1990 to 2019). In 2019, a total of 17.7 million cases and 33,400 deaths have been reported[2]. This identified a low mortality, ranging from 0.1% in uncomplicated cases and up to approximately 5% in cases with perforation or peritonitis[3].

The COVID-19 pandemic has had a negative impact on the management of surgical diseases[4], since the prioritization of logistics and resources toward patients with COVID-19, added to the lack of initial evidence of SARS-CoV-2 transmission during surgery, led to the suspension of elective surgeries, hospitalizations, and non-urgent procedures, to cover the demand for care of patients with COVID-19[4,5].

During the pandemic, health-care centers reported a decrease in consultations for acute abdominal pain[6]. In addition, respect to acute appendicitis, there was a longer delay for emergency care, longer hospital stays, higher frequency of complicated conditions, and a higher number of post-operative complications[7,8]. Although the management of acute appendicitis during the pandemic has been a challenge for the use of surgical equipment[9], the differences in the clinical evolution and management of acute appendicitis in patients with a diagnosis of COVID-19 at hospital admission compared to those who did not present the infection have not been reported.

Therefore, the objective of the present investigation was to evaluate the differences in the evolution and management of acute appendicitis in patients with COVID-19 infection compared to patients without the infection in a public hospital in Cusco, Peru. In this way, it is intended to provide evidence of the differences that may occur in the evolution and management of appendicitis between patients with and without COVID-19.

Material and methods

Study design and study population

An observational and analytical case–control study was conducted. The study was conducted in a public hospital in Peru, in June 2021. Data were obtained retrospectively from medical records in the period from April 2020 to April 2021.

Patients and data collection

Cases were defined as patients over 18 years of age with a diagnosis of acute appendicitis (anatomopathological criteria or proven by intraoperative findings) who, during hospital admission (first 72 h), had a positive test for COVID-19 (IgM or molecular positive rapid test). Controls were defined as patients older than 18 years with appendicitis (anatomopathological criteria or proven by intraoperative findings) and without evidence of COVID-19 at hospital admission (no respiratory signs or symptoms, negative rapid or molecular test). In both groups, patients with incomplete or illegible medical records and patients with voluntary discharge were excluded from the study. In addition, the control group excluded those who developed COVID-19 infection within the hospital (with evidence of any positive test greater than the 3rd day of admission).

The sampling method for the case group was non-probabilistic consecutive type (inclusion of all cases meeting the selection criteria at the defined time). Meanwhile, in the control group, it was a random sampling from the list of patients operated on for appendicitis who did not record a history of COVID-19. The control group was matched with the case group with respect to the date of hospital admission (patients operated on in the same week as the cases), because the evidence for the management of appendicitis during the COVID-19 pandemic was dynamic.

Outcomes: clinical course and management of appendicitis

The following was considered as outcomes of interest: variables on the clinical course of appendicitis, including the time of illness before going to the hospital (cutoff point of 48 hours), time of observation in emergency (cutoff point of 12 hours), stage of appendicitis (without necrosis or perforation versus necrotic or perforated), other intraoperative findings (none versus yes

[presence of peritonitis, abscess or plastron]), and the presence of infection of the operative site (not versus yes). In addition, variables on the management of appendicitis were recorded, such as the type of surgery performed (laparoscopic versus open appendectomy), surgery time (cutoff point 60 minutes), and hospitalization time after surgery (cutoff point 72 hours).

Other variables

Other variables were evaluated such as sex (female, male), age (youth 18-29 years versus, adult 30-59 years or older adult ≥ 60 years), and origin (Cusco city, Cusco provinces).

Statistical analysis

The data collected in the collection forms were processed and cleaned in Microsoft Excel. All analyses were performed with R software, version 4.1.0 (R Foundation for Statistical Computing, Vienna, Austria). Quantitative variables were reported as mean with standard deviation or median with interquartile range, according to their distribution, while qualitative variables were reported as percentage. Independent t-test compared means to find association (in case of non-normality of variables, Mann–Whitney U-test was used). For bivariate analysis of categorical variables, the Chi-square test was used. Finally, for the evaluation of the difference in the clinical course and management of patients with acute appendicitis between patients with and without COVID-19, logistic regression was used. We include all those variables, into the multivariable logistic regression model, that we considered as plausible associated factors (epidemiological model), obtaining the adjusted Odds Ratio (aOR) with their respective 95% confidence intervals (95% CI). It was considered significant if $p < 0.05$.

Ethical issues

For the execution of the present investigation, approval and authorization was first requested from the office of the hospital, where the study was conducted (provided No. 055-2021-GORE-CUSCO-GERESA-HRC). It was also registered in the Peruvian Health Research Projects Platform (PRISA) with code EI00000002005. In addition, the authors did not record data that would allow the identification of the subjects evaluated and the confidentiality of the participants was assured.

Results

The patient selection flowchart is shown in figure 1. In the present study, a total of 114 patients with acute appendicitis are presented, 38 cases, of which 13.2% were asymptomatic COVID-19 patients, 65.8% were mild cases (with respiratory symptoms), and 21.1% were moderate cases (needing oxygen support) and 76 controls, individuals diagnosed with appendicitis during the same weeks, in which the cases were diagnosed.

The mean age of the patients was 38.2 years (16.8; standard deviation), of whom 55.3% (n = 63) were women and 51.8% (n = 59) were from the city of Cusco (Peru). The median duration before arriving at the hospital was 24 hours (24-48 hours; interquartile range) (Table 1).

In the case group, a higher proportion was observed compared to controls: of adult - older adults (68.4%, p = 0.223), of males (52.6%, p = 0.231), of pre-hospital clinical course time of appendicitis > 48 hours (50.0%, p = 0.227), of emergency observation time > 12 hours (39.5%, p = 0.680), of open surgery (31.6%, p = 0.019), and of post-surgery hospitalization time > 3 days (60.5%, p = 0.064). On the other hand, a lower proportion was observed with respect to controls of surgery time longer than 60 minutes (15.8%, p = 0.015), intraoperative finding of peritonitis, abscess or appendiceal plastron (42.1%, p = 0.023), and the proportion of surgical site infection (13.2%, p = 0.109) (Table 1).

In the multivariate regression analysis, a lower odds of peritonitis, abscess, or appendiceal plastron (aOR: 0.21; 95% CI: 0.05-0.90) and of surgery time exceeding 60 min (aOR: 0.21; 95% CI: 0.06-0.80), while there was a greater odds of management by open surgery (aOR: 3.83; 95% CI: 1.42-10.32) and a hospitalization time of more than 3 days after surgery (aOR: 3.33; 95% CI: 1.34-8.26). Respect to sociodemographic characteristics, patients with COVID-19 and appendicitis were more odds to be male (aOR: 3.34; 95% CI: 1.30-8.57) (Table 2).

Discussion

The present study demonstrates the differences in the clinical course and management of patients presenting to the emergency room with acute appendicitis and COVID-19, finding a greater probability of the cases being male and a lower probability of developing peritonitis, abscess, or appendiceal plastron. On the other hand, regarding management, there was a

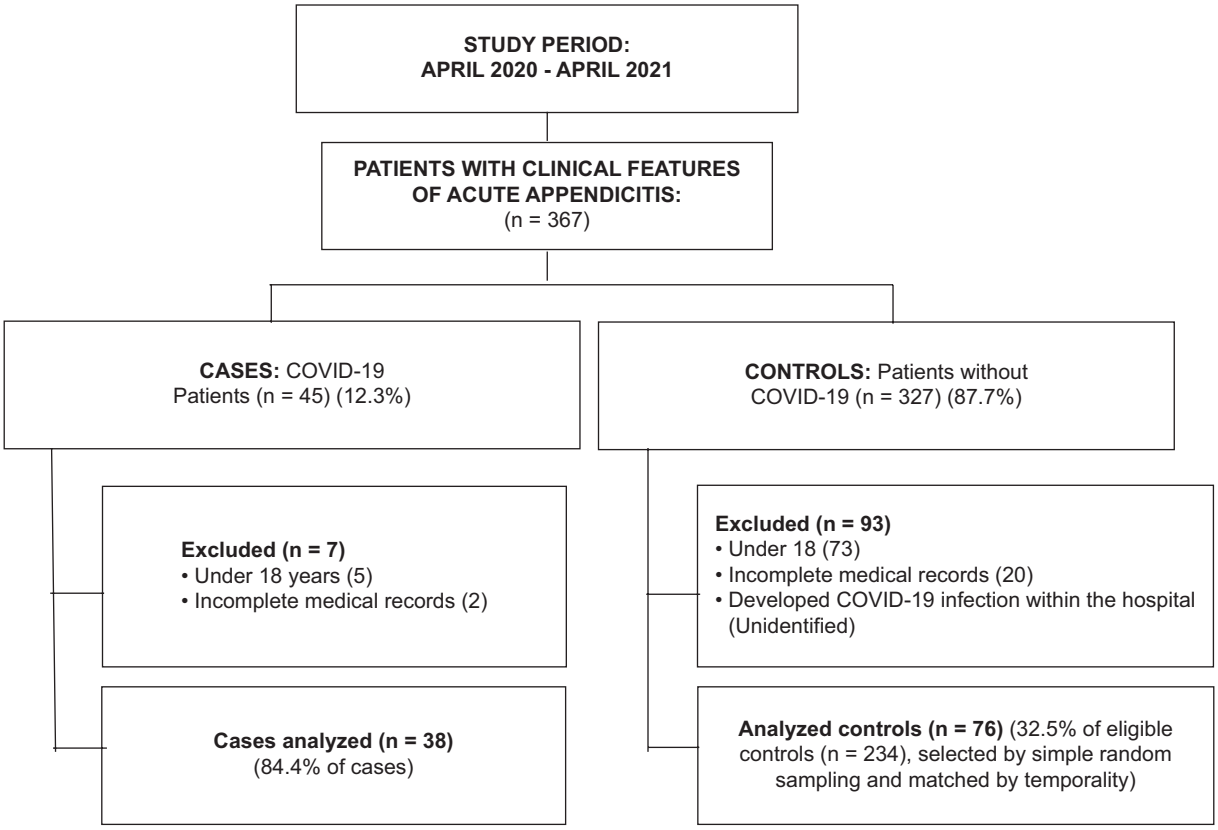

Figure 1. *Flowchart for sample selection.*

greater probability that the cases were managed by open surgery, that the surgery lasted less time, and that they had a longer hospitalization time after surgery compared to the controls.

The measures imposed for the prevention and control of COVID-19, together with the fear of being exposed to the virus, has led to a decrease in emergency department visits[2]. Consequently, an increase in the delay time before patients with appendicitis arrive at a health center (mean 37.9 hours) has been reported[10]. However, our findings indicate that there is no difference in the delay time to seek medical help between the 2 groups studied, with a median time > 36 hours. This constitutes a longer delay time for surgery and, therefore, a higher proportion of complications in both groups compared to previous years[11].

We observed a high proportion of patients with complicated appendicitis (around 60%), which is consistent with multiple reports[12-15]. However, in the case group, there is a lower probability of presenting other intraoperative findings (peritonitis, abscess, or plastron). This paradoxical finding, when considering that there is no difference between the pre-hospital and in-hospital delay time recorded in both groups until surgery, could be due to a beta-type error due to the low statistical power since the effect measure of the association (aOR: 0.21; 95% CI: 0.05-0.90) is very wide. Since the delay time before surgery is the best predictor of complications[3], it could also be due to inaccurate recording of pre-hospital evolution time in medical records.

Regarding the management of patients with appendicitis, it was found that all patients underwent surgery. Non-surgical management with antibiotics as recommended by the Jerusalem 2020 guidelines for patients without complications and absence of appendicolith was not found[3]. This could favor the standardization and homogeneity of the management given to both cases and controls.

A longer duration of appendectomies during the pandemic has been described in the literature (51.1 ± 9.4 minutes during the pandemic versus 45.3 ± 11.8 minutes before the pandemic)[16], coinciding with the mean time of surgeries performed in our study population (49.3 ± 15.4 minutes). However, we found that the surgery time among patients who also had a diagnosis

Table 1. Characteristics of the population studied according to COVID-19 diagnosis (n = 114)

Variables	n (%)	COVID-19 Diagnosis		
		No	Yes	p[b]
	114 (100%)	76 (66.7%)	38 (33.3%)	
Age (years)[a]	38.2 ± 16.8	38.7 ± 18.8	37.1 ± 12.2	
Young (18-29 years old)	45 (39.47)	33 (43.42)	12 (31.58)	0.633
Adult or older adult (> 30 years old)	69 (60.53)	43 (56.58)	26 (68.42)	0.223
Sex				
Female	63 (55.26)	45 (59.21)	18 (47.37)	0.231
Male	51 (44.74)	31 (40.79)	20 (52.63)	
Origin				
Cusco city	59 (51.75)	40 (52.63)	19 (50.00)	0.791
Other Provinces of Cusco	55 (48.25)	36 (47.37)	19 (50.00)	
Time before arriving at the hospital (hours)	24 (24-48)	35 (22.5 – 49.5)	39 (24-48)	
< 48 hours	66 (57.89)	47 (61.84)	19 (50.00)	0.304
> 48 hours	48 (42.11)	29 (38.16)	19 (50.00)	0.227
Emergency observation time (hours)[a]	12 (8-15)	11 (8-15.5)	12 (7-15)	
< 12 hours	72 (63.16)	49 (64.47)	23 (60.53)	0.964
> 12 hours	42 (36.84)	27 (35.53)	15 (39.47)	0.680
Type of surgery performed				
Laparoscopic	92 (80.70)	66 (86.84)	26 (68.42)	0.019
Open air	22 (19.30)	10 (13.16)	12 (31,58)	
Surgery time (minutes)[a]	49.3 ± 15.4	51.3 ± 15.8	45.4 ± 13.8	0.052
< 60 minutes	79 (69.30)	47 (61.84)	32 (84.21)	0.015
> 60 minutes	35 (30.70)	29 (38.16)	6 (15.79)	
Appendicitis phase				
No perforation or necrosis	29 (25.66)	19 (25.33)	10 (26.32)	0.910
With perforation or necrosis	84 (74.34)	56 (74.67)	28 (73.68)	
Other intraoperative findings				
None	49 (42.98)	27 (35.53)	22 (57.89)	0.023
Peritonitis, abscess, and plastron	65 (57.02)	49 (64.47)	16 (42.11)	
Time of hospitalization after surgery (days)[a]	3 (2-5)	3 (2-4)	4,5 (3-9)	
< 3 days	59 (51.75)	44 (57.89)	15 (39.47)	0.010
> 3 days	55 (48.25)	32 (42.11)	23 (60.53)	0.064
Operative site infection				
No	89 (78.07)	56 (73.68)	33 (86.84)	0.109
Yes	25 (21.93)	20 (26.32)	5 (13.16)	

[a]Mean ± standard deviation, median (Interquartile range). [b]Significant p < 0.05, found by Chi-square test, student's t-test or Mann–Whitney U-test.

of COVID-19 was shorter. Despite the fact that, as in the control group, surgeons should be cautious about the risk of exposure and take additional precautions to limit the transmission of COVID-19[4], possibly the surgeon's fear of spending more time in contact with fluids and possible aerosols generated during the surgical procedure favored a faster procedure in this group. Another factor that could have affected this point is that there was a greater probability of using laparoscopy in the control group, which implied a longer time compared to open techniques[17,18]. Furthermore, the fact that the use of laparoscopy was less frequent in the case group could be explained by the controversy over whether using the laparoscope would generate a large amount of aerosols, putting the safety of the workers at risk[19]. Therefore, some hospitals even decided to completely abandon this type of technique[16].

Regarding the use of laparoscopy, it should be noted that there is no conclusive scientific evidence to date as to whether the transmission of COVID-19 can occur due to the effects of laparoscopic surgery[20].

Table 2. Influence of COVID-19 on the management of acute appendicitis (n = 114)

Variables	Bivariate analysis	p[a]	Multivariate analysis	p[a]
	cOR (95% CI)		aOR (95% CI)	
Age (years)				
Young (18-29 years old)	Ref.	0.227	Ref.	0.413
Adult or older adult (> 30 years old)	1.66 (0.73-3.79)		1.50 (0.57-3.95)	
Sex				
Female	Ref.	0.234	Ref.	0.012
Male	1.61 (0.73-3.55)		3.34 (1.30-8.57)	
Origin				
Cusco city	Ref.	0.792	Ref.	0.352
Other provinces of cusco	1.11 (0.51-2.43)		0.64 (0.25-1.65)	
Time before arriving at the hospital (hours)				
< 48 hours	Ref.	0.231	Ref.	0.093
> 48 hours	1.62 (0.74-3.57)		1.62 (0.85-8.09)	
Emergency observation time (hours)	Ref.			
< 12 hours	1.18 (0.53-2.65)	0.682	Ref.	0.532
> 12 hours			1.39 (0.50-3.89)	
Type of surgery performed				
Laparoscopic	Ref.	0.023	Ref.	0.008
Open air	3.05 (1.17-7.94)		3.83 (1.42-10.32)	
Surgery time (minutes)				
< 60 minutes	Ref.	0.019	Ref.	0.022
> 60 minutes	0.30 (0.11-0.82)		0.21 (0.06-0.80)	
Appendicitis phase				
No perforation or necrosis	Ref.	0.91	Ref.	0.082
With perforation or necrosis	0.95 (0.39-2.32)		3.86 (0.84-17.66)	
Other intraoperative findings				
None	Ref.	0.025	Ref.	0.036
Peritonitis, abscess or plastron	0.40 (0.18-0.89)		0.21 (0.05-0.90)	
Hospitalization time after surgery (days)				
< 3 days	Ref.	0.067	Ref.	0.009
> 3 days	2.11 (0.95-4.68)		3.33 (1.34-8.26)	
Operative site infection				
No	Ref.	0.118	Ref.	0.166
Yes	0.42 (0.14-1.24)		0.37 (0.09-1.52)	

cOR: Crude Odds Ratio; aOR: Adjusted Odds Ratio; 95% CI: 95% confidence interval.
[a]Significant p < 0.05, found by logistic regression.

Therefore, its use should be performed more frequently and with the corresponding precautions, due to the fact that the benefits in comparison with open surgery (including a shorter hospital stay, less need for post-operative analgesia, early tolerance to food, earlier return to work, lower rate of wound infection, and among others) are quite ample[17].

With respect to post-operative length of stay, it has been seen that during the pandemic the mean time was longer than that found before the pandemic[16,21]. We found that there was a higher probability that the hospitalization time was longer than 72 hours in the case group. This could be due to the greater approach by open surgery among patients with COVID-19 and to the presence of COVID-19 itself, which generated respiratory symptoms and the need for oxygen in a greater proportion of cases, generating greater comorbidity among patients with appendicitis[21]. However, if the patient does not require oxygen and there are no surgical complications, home recovery should be allowed as soon as possible so that the health systems are not overwhelmed in their capacity.

There are some limitations in our study, among which we can highlight: first, the data were obtained indirectly from the medical records (retrospective), so the data could be imprecise. Second, since the medical records were physical and because the hospital restricted access to the work areas, only one person was able to extract the information from the medical records, which limited a pair-wise extraction. Third, it was not possible to verify whether all the indications for treatment and surgery conformed to the center's protocols; however, they did reflect standard clinical practice. Finally, we consider that due to the small number of patients who presented with the pre-operative diagnosis of acute appendicitis and COVID-19, statistical power as well as generalization of results should be taken with caution when reading this report. Thus, prospective studies with a larger sample size and multicenter studies are recommended to extrapolate the conclusions outside our setting.

Conclusion

Differences were evidenced in terms of intraoperative findings, type of surgery, intraoperative, and hospitalization time in patients with a diagnosis of acute appendicitis and COVID-19, at hospital admission compared to patients with appendicitis, but without COVID-19 infection. For all these reasons, it is necessary to inform the general population about the importance of timely visits to hospitals; as well as to recognize cases of acute appendicitis as early as possible at the first levels of care for prompt referral of patients. In addition, greater use of laparoscopy should be encouraged among surgeons to treat patients with acute appendicitis and COVID-19, taking into account general biosecurity measures since its use does not seem to increase the risk of virus transmission. Likewise, laparoscopy presents a great number of advantages for the patient and for the health systems, allowing a shorter hospitalization time and a prompt recovery.

Funding

No funding was received to carry out the research.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

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