

Management of uncomplicated acute appendicitis during the COVID-19 pandemic: Appendectomy or non-surgical treatment?

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ABSTRACT

BACKGROUND: This study aims to compare medical treatment and appendectomy in patients diagnosed with uncomplicated acute appendicitis during the COVID-19 pandemic.

METHODS: Retrospectively analyzed were the data of 80 patients who received medical or surgical treatment for uncomplicated acute appendicitis between March 15, 2020, and August 31, 2020. The demographic characteristics of the patients, length of hospital stay, physical examination and radiology findings, laboratory results, and any complications were recorded. Patients were divided into two groups depending on the mode of treatment, as surgical and non-surgical.

RESULTS: Forty patients were given medical treatment and 40 patients were directly operated on for appendicitis. Of the 40 patients who received medical treatment, 8 (20%) ended up requiring an operation due to recurrence. The mean duration of hospitalization was 2 days (range: 1–3), and the mean follow-up duration was 285.35 ± 65.66 days (range: 101–379). The white blood cell count was significantly higher in the surgical group ($p=0.004$), and the length of hospital stay was longer in the non-surgical group ($p<0.001$). The prevalence of post-operative complications was similar for patients who underwent appendectomy directly on admission or after recurrence ($p=1.000$). Among the patients who received medical treatment, the most important predictors of requiring surgery were the red cell distribution width and increased appendix diameter in computed tomography ($p<0.05$).

CONCLUSION: Medical treatment is an effective alternative in patients with uncomplicated appendicitis. Even in the case of a recurrence in follow-up, surgery due to a potential recurrence is not associated with an increased rate of complication compared to direct surgery.

Keywords: Appendectomy; COVID-19; non-surgical treatment; red cell distribution width; uncomplicated appendicitis.

INTRODUCTION

Acute appendicitis is a common cause of acute abdominal pain that frequently requires emergency surgery.^[1] Diagnosis is based on patient history and physical examination findings and supported by radiography.^[2,3] Appendectomy, first described by McBurney in 1889, has been widely accepted as the standard treatment method for acute appendicitis.^[4,5] Recent studies have proposed that antibiotic therapy may be an alternative to appendectomy for the treatment of uncomplicated appendicitis.^[6] This concept was first described by

Coldrey in 1959, in a series of 471 cases.^[7] Subsequently, a number of studies have demonstrated the effectiveness of medical treatment in uncomplicated appendicitis.^[8]

The coronavirus epidemic first emerged in December 2019 in the Wuhan Province of Hubei, China. The disease, initially named novel coronavirus (2019-nCoV) infection, was named coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO) on February 11, 2020.^[9] Through direct contact and droplets, the virus rapidly spreads around the world and was declared a pandemic by the WHO on March

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11, 2020. Due to risk of infection, elective surgeries were delayed when possible, and emergency surgeries were performed while trying to minimize the time that each patient had to spend in the hospital.^[10]

Like most clinics around the world, patients who present to our general surgery clinic with acute appendicitis are treated surgically under normal conditions. However, after the onslaught of the COVID-19 pandemic, it was necessary to revise our treatment approach. Accordingly, all patients with uncomplicated appendicitis were offered the option of medical treatment. The patients were divided into two groups according to their preferred mode of treatment. The patients who accepted were provided with medical treatment, and the remainder underwent appendectomy.

This study aimed to compare medical treatment and appendectomy in patients diagnosed with uncomplicated acute appendicitis during the COVID-19 pandemic and to determine the more effective treatment method.

MATERIALS AND METHODS

Retrospectively analyzed were the data of patients who received medical or surgical treatment for uncomplicated acute appendicitis in the General Surgery Clinic between March 15, 2020, and August 31, 2020. Both methods of treatment were explained to each patient, and all of the patients were offered both surgical and non-surgical treatment, and were accordingly assigned to Group 1 (surgical) or Group 2 (non-surgical). Medical treatment consisted of ceftriaxone 1 g twice a day (bid) intravenously (IV) and metronidazole 500 mg 3 times a day (tid) IV in-hospital, and cefuroxime axetil 500 mg bid orally (PO) and metronidazole 500 mg tid PO on discharge. All appendectomy patients underwent open appendectomy due to the pandemic. In the power analysis, it was determined that the minimum number of samples required was 80. Therefore, patient recruitment was stopped when there were 40 patients in each group. The diagnosis of appendicitis was based on physical examination and supported by ultrasonography and/or computed tomography (CT). Demographic characteristics of the patients, length of hospital stay, physical examination findings, radiological findings, laboratory results, and complications were recorded. Patients under 18 years of age, who had complicated appendicitis, or a history of medical treatment were excluded from the study. This study was granted ethical approval by the Clinical Research Ethics Committee (date: December 09, 2020, number: 2020/187).

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows 21.0 (IBM Corp., Armonk, NY, USA). Conformity of the data to normal distribution was evaluated using the Shapiro–Wilk test. Non-normally distributed numerical data were presented as the median and minimum-maximum, while normally

distributed numerical data were presented as the mean and standard deviation, and categorical data as numbers and percentages. Intergroup comparison was performed using the Mann–Whitney U and Student's t-tests for the non-normally and normally distributed numerical data, respectively, and the Chi-square test for the categorical data. Logistic regression analysis was performed to determine the factors that predicted surgical intervention following medical treatment. $P < 0.05$ was considered statistically significant.

RESULTS

The study included a total of 80 patients (40 with direct appendectomy and 40 with medical treatment). Of the 40 patients who received medical treatment, 8 (20%) presented with a recurrence and ended up requiring an operation. None of the patients presented to the clinic within the first 30 days after discharge. The median age of the patients was 27.5 (18–69) years, the median C-reactive protein (CRP) level was 4.95 (0.3–239.40), red cell distribution width (RDW) was 17.2 (11.4–17.3), length of hospital stay was 2 days (1–3), and the mean white blood cell (WBC) count was $13.75 \pm 4.09 \times 10^3/\mu\text{L}$. The mean follow-up time was 285.35 ± 65.66 (range: 101–379) days. Among the patients who initially received surgical treatment, 3 (7.5%) developed wound infection and 1 (2.5%) developed intra-abdominal abscess. Among the patients who developed recurrence after medical treatment and underwent surgery, 1 (12.5%) developed wound infection. Demographic characteristics, physical examination findings, and laboratory results of all of the patients are presented in Table 1.

The mean age was higher in the medical treatment group when compared to the surgical treatment group ($p = 0.033$). The WBC count was significantly higher in the surgical group ($p = 0.004$), and the length of hospital stay was longer in the non-surgical group ($p < 0.001$). The two groups were not statistically different in terms of the RDW, CRP level, or gender. Regarding the clinical findings, the surgical and non-surgical treatment groups were not significantly different in terms of tenderness, abdominal guarding, or rebound tenderness ($p > 0.05$) (Table 1).

The two groups were not statistically different in terms of the ultrasonography and tomography findings, namely, the appendix diameter, appendicolith, free fluid, and misty mesentery ($p > 0.05$) (Table 2).

The regression analysis revealed that the most important predictor of surgical treatment was the WBC count ($p < 0.05$). A one-unit increase in the WBC count increased the risk of surgery by 1.14-fold ($p = 0.044$). Other factors did not statistically predict surgical intervention ($p > 0.05$) (Table 3).

The prevalence of abdominal guarding and rebound tenderness was significantly higher among patients who underwent direct appendectomy ($p = 0.044$ and $p = 0.050$, respectively).

Table 1. Demographic and laboratory findings of the medical and surgical treatment groups

	Surgical (n=40)	Non-surgical (n=40)	p-value
Age (years)	24 (18–55)	33.5 (18–69)	0.033
White blood cell	14.68±3.74	12.81±4.24	0.004
Red cell distribution width	12.70 (11.40–15.40)	12.90 (4.70–17.30)	0.387
C-reactive protein	4.95 (0.30–239.40)	5.20 (0.70–159.00)	0.549
Length of hospital stay (days)	1 (1–3)	2 (1–3)	<0.001
Sex, n (%)			0.356
Female	15 (46.9)	17 (53.1)	
Male	25 (52.1)	23 (47.9)	
Right Lower Quadrant Pain, n (%)	39 (49.4)	40 (50.6)	0.394
Tenderness, n (%)	40 (53.3)	35 (46.7)	0.055
Abdominal guarding, n (%)	15 (68.2)	7 (31.8)	0.078
Rebound tenderness, n (%)	22 (61.1)	14 (38.9)	0.115

Results are presented as the mean±standard deviation, median (minimum–maximum). P<0.05 indicates a statistically significant difference.

The two groups were not significantly different in terms of other demographic and clinical findings ($p>0.05$) (Table 4).

Patients who underwent direct or post-treatment appendectomy were not statistically different in terms of their ultrasonography and tomography findings, namely, the appendix diameter, appendicolith, free fluid, and misty mesentery ($p>0.05$).

Patients who underwent direct or post-treatment appendectomy were not statistically different in terms of post-operative complications ($p=1.000$).

The regression analysis revealed that the most important predictors of surgery following medical treatment were the RDW and an increased appendix diameter on CT ($p<0.05$). A one-unit increase in RDW increased the risk of surgery by 1.9-fold ($p=0.026$), and a one-unit increase in appendix diameter on CT increased the risk of surgery by 1.14-fold ($p=0.002$) (Table 5).

DISCUSSION

During the COVID-19 pandemic, many guidelines and studies have recommended a conservative approach whenever possible in some emergency conditions,^[11,12] one of which is uncomplicated appendicitis.^[10] Coldrey first proposed that antibiotic treatment could be an alternative to appendectomy in uncomplicated acute appendicitis, and further studies were performed to investigate this approach.^[7]

In their study of 118 patients, Kırkıl et al.^[13] showed that antibiotic treatment was effective in uncomplicated appendicitis. In their 2020 acute appendicitis diagnosis and treatment guideline, Di Saverio et al.^[14] recommended antibiotic treatment in select patients with uncomplicated acute appendicitis. Curiously enough, surgical treatment is still the most commonly preferred treatment approach for acute appendicitis.^[5] Failure to embrace a more conservative approach in the management of appendicitis, a disease that has been managed surgically for over a century, may be more closely related

Table 2. Ultrasound and tomography findings of the medical and surgical treatment groups

	Surgical (n=40)		Non-surgical (n=40)		p-value	
	US	CT	US	CT	US	CT
Appendicolith, n (%)	12 (36.4)	34 (49.3)	21 (63.6)	35 (50.7)	0.069	0.737
Appendix diameter (mm), n (%)	3 (50)	7 (77.8)	3 (50)	2 (22.2)	0.643	0.080
Free fluid, n (%)	9 (7–11)	9.75 (7–12)	8 (7–11)	8.50 (6.50–12)	0.254	0.120
Misty mesentery, n (%)	2 (50)	6 (85.7)	2 (50)	1 (14.3)	0.610	0.055
	3 (37.5)	20 (52.6)	5 (62.5)	18 (47.4)	1.000	0.482

Results are presented as the median (minimum-maximum). P<0.05 indicates a statistically significant difference. US: Ultrasonography; CT: computed tomography.

Table 3. Predictors of surgical intervention

	B	S.E.	p	OR
Age	-0.048	0.025	0.054	0.953
Sex	-0.622	0.600	0.300	0.537
WBC	0.133	0.066	0.044	1.143
RDW	0.193	0.116	0.098	1.213
CRP	0.010	0.006	0.113	1.010
Length of hospital stay	-1.403	0.443	0.002	0.246
Duration of pain	-0.291	0.284	0.306	0.748
Tenderness	-20.966	15961.36	0.999	0.000
Rebound tenderness	0.127	0.747	0.865	1.135
Abdominal guarding	-1.195	0.663	0.072	0.303
US findings				
Appendicolith	0.693	0.408	0.090	2.000
Appendix diameter	-0.035	0.098	0.723	0.966
Free fluid	0.796	1.138	0.484	2.218
Misty mesentery	-0.091	0.965	0.925	0.913
CT findings				
Misty mesentery	-0.172	0.551	0.754	0.842
Appendicolith	1.253	0.802	0.118	3.500
Appendix diameter	-0.027	0.029	0.352	0.974
Free fluid	0.775	0.859	0.367	2.171

B: Regression coefficient; SE: Standard error; OR: Odds ratio, p<0.05 indicates statistical significance. US: Ultrasonography. CT: Computed tomography; CRP: C-reactive protein; RDW: Red cell distribution width; WBC: White blood cell.

Table 5. Predictors of surgical intervention following medical treatment

	B	S.E.	p	OR
Age	-0.083	0.043	0.051	0.920
Sex	0.973	1.019	0.339	2.647
Length of hospital stay	-0.571	1.052	0.587	0.565
Duration of pain	-0.405	0.402	0.313	0.667
WBC	-0.055	0.143	0.700	0.946
RDW	0.651	0.293	0.026	1.918
CRP	0.017	0.032	0.590	1.017
Rebound tenderness	-0.055	0.143	0.700	0.946
Abdominal guarding	-4.813	3.188	0.131	0.008
US findings				
Appendicolith	0.693	1.225	0.571	2.000
Appendix diameter	0.416	0.242	0.085	1.516
Free fluid	-19.582	23165.9	0.999	0.000
Misty mesentery	-4.307	2.503	0.085	0.013
CT findings				
Appendicolith	1.048	2.020	0.604	2.852
Appendix diameter	0.133	0.044	0.002	1.142
Free fluid	-0.140	1.332	0.916	0.869
Misty mesentery	-0.500	0.957	0.601	0.606

B: Regression coefficient; SE: Standard error; OR: Odds ratio, p<0.05 indicates statistical significance. US: Ultrasonography; CT: Computed tomography; CRP: C-reactive protein; RDW: Red cell distribution width; WBC: White blood cell.

to the old habits of the surgeons, rather than the available scientific evidence. Although there was a preference toward

using the surgical approach in treating acute appendicitis until the emergence of the COVID-19 pandemic, it became

Table 4. Demographic and laboratory findings of the patients who underwent direct surgery and those who underwent surgery following medical treatment

	Direct surgery (n=40)	Post-treatment surgery (n=8)	p-value
Age (years)	24 (18–55)	29 (18–59)	0.412
White blood cell	14.68±3.74	15.49±3.83	0.578
Red cell distribution width	12.70 (11.40–15.40)	12.65 (12.10–14.60)	0.792
C-reactive protein	4.95 (0.30–239.40)	3.70 (1.00–35.80)	0.658
Length of hospital stay (days)	1 (1–3)	1.5 (1–2)	0.596
Sex, n (%)			0.504
Male	15 (88.2)	2 (11.8)	
Female	25 (80.6)	6 (19.4)	
Right Lower Quadrant Pain, n (%)	40 (83)	8 (17)	–
Tenderness, n (%)	40 (83.3)	8 (16.7)	–
Abdominal guarding, n (%)	15 (100)	0 (0)	0.044
Rebound tenderness, n (%)	22 (95.7)	1 (4.3)	0.050

Results are presented as the mean±standard deviation, median (minimum–maximum), and number (percentage). P<0.05 indicates a statistically significant difference.

necessary to consider medical treatment as an option in select cases. During the pandemic and in light of the available guidelines, medical treatment was offered to every patient who presented to our clinic with uncomplicated appendicitis and their treatment was provided accordingly. Even more interestingly, appendectomy was also heartily embraced by our patients, who commonly preferred a surgical approach to medical treatment in the case of appendicitis. Hence, a significant number of patients preferred surgery despite having been offered and recommended medical treatment.

The literature has reported that some patients with uncomplicated appendicitis may develop recurrence after medical treatment. In a 5-year follow-up study, Salminen et al.^[15] reported a recurrence rate of 39.1% among 530 patients. A prospective study by Al Mulhim reported a recurrence rate of 12.2% after 1 year.^[16] In the study presented herein, the recurrence rate was 20%.

There are several available scoring systems for appendicitis, many of which utilize the WBC count as a parameter.^[14] Similarly, researchers have developed several systems to identify patients who may benefit from medical treatment. Hansson et al.^[17] stated that medical treatment had an 89% success rate for patients aged <60 years with a CRP level that was <60 g/L and WBC <12 ×10³/μL. In the present study, the WBC count was statistically higher in patients who underwent surgery. However, given that the mode of treatment was initially determined based on the choice of the patient, it was believed herein that this finding did not significantly steer the treatment or management of the condition, despite being statistically significant.

Recent studies have reported that the RDW is a marker of inflammation.^[18] It is also known that the RDW is increased in patients with acute appendicitis.^[19] It was found herein that, among the patients who initially received medical treatment, a one-unit increase in the RDW resulted in a 1.9-fold increase in the possibility of requiring surgery. Therefore, an elevated RDW on presenting with recurrent appendicitis may be useful and considered when deciding on surgery.

Loftus et al.^[20] reported that a smaller appendix diameter (<13 mm) was associated with a higher success rate for medical treatment. In their study of 164 patients, Tanaka et al.^[21] stated that appendicolith was associated with a poor success rate and higher risk of recurrence with medical treatment. The same study did not find a difference between patients who received medical and surgical treatment in terms of the length of hospital stay. In the present study, the presence of appendicolith(s) did not affect treatment success or recurrence. Among the patients who developed recurrence after medical treatment, a 1 mm increase in the appendix diameter was associated with a 1.14-fold increase in the risk of surgery. In this study, the length of hospital stay was significantly longer in the patients who received medical treatment. Howev-

er, this finding was ascribed not to the inefficacy of medical treatment, but to the painstaking approach of surgeons who are more used to managing appendicitis patients with a surgical approach. Considering that the patient will no longer need an invasive procedure such as surgery, it was believed herein that this difference in the length of stay can be afforded.

The potential post-operative complications of appendectomy include wound infection, intra-abdominal abscess, and ileus.^[22] In the present study, 32 (80%) patients who initially received medical treatment recovered without recurrence. Thus, these patients were able to avoid the potential complications of appendectomy. Among the patients who received medical treatment, 8 (20%) presented with recurrence and underwent surgery. The prevalence of surgical complications was similar for the patients who underwent direct appendectomy, and those who received medical treatment and went on to develop recurrence. Considering that 80% of the patients who received medical treatment recovered without undergoing a difficult invasive treatment, and that the risk of complications did not increase after a recurrence, it is recommended that medical treatment should be primarily considered in the management of uncomplicated appendicitis. Surprisingly, none of the patients who were initiated on medical treatment needed to be converted to surgical intervention during their hospitalization. That said, this may have been due to the small number of patients.

The limitations of this study included its retrospective design, the small number of patients, and the short follow-up time.

Conclusion

We conclude that patients with uncomplicated appendicitis can be initiated on medical treatment during and after the pandemic, which will be largely sufficient. Even in the case of a recurrence in follow-up, the complication rate is not higher for surgery during second admission.

Ethics Committee Approval: This study was approved by the Malatya Clinical Research Ethics Committee (Date: 09.12.2020, Decision No: 2020/187).

Peer-review: Internally peer-reviewed.

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Conflict of Interest: None declared.

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ORİJİNAL ÇALIŞMA - ÖZ

COVID-19 pandemi sürecinde unkomplike akut apandisit yönetimi: Appendektomi mi? nonoperatif tedavi mi?

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AMAÇ: COVID-19 pandemi döneminde, unkomplike akut apandisit tanılı hastalarda, tıbbi tedavi ve appendektomi tedavisi karşılaştırılarak, hangisinin daha etkin bir tedavi yöntemi olduğunun ortaya konması amaçlandı.

GEREÇ VE YÖNTEM: Çalışmada, 15.03.2020 ile 31.08.2020 tarihleri arasında, unkomplike akut apandisit nedeni ile cerrahi veya nonoperatif yöntem ile tedavi edilen 80 hastanın verileri geriye dönük olarak incelendi. Hastaların demografik özellikleri, hastanede yatış süresi, fizik muayene ve radyolojik bulgular, laboratuvar değerleri, ameliyat edilenlerde komplikasyonlar kaydedildi. Hastalar, ameliyat edilenler ve nonoperatif tedavi edilenler şeklinde iki gruba ayrılarak karşılaştırıldı.

BULGULAR: Kırk hastaya apandisit nedeni ile medikal tedavi verildi, 40 hasta ise direk olarak apandisit nedeni ile ameliyat edildi. Tıbbi tedavi verilen hastalardan sekizi (%20) ikinci başvuruda opere edildi. Hastaların yatış süresi iki (1–3) gün, ortalama takip süresi 285.35±65.66 gün (min: 101–maks: 379) idi. Yapılan incelemede WBC değerinin ameliyat olan grupta anlamlı olarak yüksek olduğu görülürken ($p=0.004$), yatış süresinin tıbbi tedavi grubunda ameliyat grubuna göre daha yüksek olduğu tespit edildi ($p<0.001$). Hemen ameliyat edilenler ile ikinci başvuruda ameliyat edilenler arasında, ameliyat sonrası komplikasyonlar açısından istatistiksel olarak fark izlenmedi ($p=1.000$). Tıbbi tedavi sonrası ikinci başvuruda ameliyat olmayı belirleyen en önemli faktörler RDW değeri ve bilgisayarlı tomografide apendiks çapında artış olduğu tespit edildi ($p<0.05$).

TARTIŞMA: Çalışmada, unkomplike apandisit tanılı hastalara medikal tedavi başlanabileceği, daha sonraki takiplerinde nüks olsa bile, ikinci başvuruda yapılan ameliyat ile komplikasyonların artmayacağı ortaya konmuştur.

Anahtar sözcükler: Appendektomi; COVID-19; eritrosit dağılım genişliği; nonoperable tedavi; unkomplike apandisit.

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