

Original Article

Risk of Complicated Appendicitis and Complications: Time to Hospital or Time to Surgery?

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Key Words

Appendicitis;

Time to surgery;

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Purpose. Acute appendicitis is a common cause of acute abdomen requiring surgery. However, it remains controversial whether patients may benefit from early appendectomy. The timing of appendectomy is determined by the time from the onset of symptoms to reaching the hospital (time to hospital) and the time from reaching the hospital to entering the operating room (time to surgery). We aimed to evaluate which period increases the risk for complicated appendicitis and postoperative complications.

Methods. We retrospectively reviewed patients who underwent appendectomy for acute appendicitis from December 2015 to December 2016. The demographic characteristics were collected. The patients were divided into two groups: abdominal pain duration (time to hospital) > 1 day and ≤ 1 day. From each group, the patients were further divided into two subgroups: time to surgery > 12 h and ≤ 12 h. The disease severity and surgical outcome were respectively compared.

Results. Among the 228 patients studied, 171 and 57 had abdominal pain for ≤ 1 and > 1 day, respectively. Abdominal pain duration (time to hospital) of > 1 day significantly increased the rates of complicated appendicitis (48.1% vs. 26.9%), operative time (78.8 vs. 61.4 min), post-operative hospital admission (5.1 vs. 3.4 days), overall hospital stay (5.8 vs. 4.1 days), and risk of intra-abdominal abscess (7% vs. 0.6%). Regardless of the time to hospital, operative time, disease severity, post-operative hospital admission, and complications were not significantly different between groups with time to surgery of > 12 and ≤ 12 h.

Conclusions. Prolonged abdominal pain duration (> 1 day) was associated with an increased risk of complicated appendicitis, longer operative time, post-operative hospital admission, overall hospital stay, and intra-abdominal abscess. Regardless of abdominal pain duration, the time to surgery did not significantly affect the disease progression or postoperative complication rates. Our results suggested that the time to hospital has a more important role than time to surgery in the treatment outcome of acute appendicitis.

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Acute appendicitis is a common disease that mostly requires surgery. It usually occurs in children and young people, occasionally in the elderly. Experts have proposed a grading system for acute appendicitis based on the disease severity.¹ In brief, simple appendicitis refers to an inflamed or suppurative appearance of the appendix. Complicated appendicitis refers to infection of the appendix with gangrenous change and perforation with or without intra-abdominal abscess. Compared with simple appendicitis, complicated appendicitis was believed to cause more postoperative complications, such as surgical site infection, intra-abdominal infection, and ileus. Delay in diagnosis and treatment may result in serious consequences.² The timing of appendectomy should be considered by the time from onset of symptoms to reaching the hospital (time to hospital) and the time from reaching the hospital to entering the operation room (time to surgery). Time to hospital was once proposed to be a predictor of complicated appendicitis;³ however, there was more debate about whether patients may benefit from shortening time to surgery. We aimed to evaluate which period has a more important role in the risk for complicated appendicitis and complications postoperatively.

Materials and Methods

From December 2015 to December 2016, data on patients diagnosed with acute appendicitis were retrospectively collected through the medical record database of National Taiwan University Hospital. Patients who initially received conservative treatment followed by interval appendectomy were excluded. In addition, patients who underwent appendectomy combined with other surgery also were excluded. Medical information, including age, sex, past history, body mass index (BMI), abdominal pain duration, blood test, and diagnostic imaging were collected. The exact time that patients reached the emergency room (ER), underwent diagnostic examination, and began the operation also were recorded for calculating the interval while waiting for surgery. The term “time to hospital” was defined as the interval between the onset of abdominal pain and reaching ER. Conversely, the term “time to

surgery” was defined as the interval between reaching the hospital and starting operation. The surgeon was consulted once acute appendicitis was highly suspected. Appendectomy was performed via either laparoscopy or laparotomy based on the surgeon’s expertise. If the patient was younger than 18, surgery was performed by a pediatric surgeon. Otherwise, surgery was performed by a general surgeon. All resected appendices were examined by qualified pathologists. The operative method, operation time, and operative findings were reviewed from the operation note. The severity of appendicitis was classified as simple (erythematous, suppurative change of the appendix, and clear ascites) or complicated (perforation, gangrenous change, and intra-abdominal abscess). Postoperative course and outpatient clinic records were reviewed in all patients. The overall hospital stay was defined as the total of days in the ER and post-operative hospital admission. The post-operative hospital admission, overall hospital stay, and postoperative complications, including surgical site infection, ileus, intra-abdominal abscess, and internal bleeding, were collected. A patient is considered to have developed ileus if nasogastric tube decompression is required for symptom relief. The intra-abdominal abscess was confirmed by CT findings. All patients were divided into two groups according to the variable abdominal pain duration before arriving to the hospital: abdominal pain duration (time to hospital) of > 1 day and ≤ 1 day. In our study, we used “abdominal pain” as a sign of inflammation of appendix. The onset of abdominal pain may refer to the beginning of the disease. One day was set as the cut point of abdominal pain duration because the ER record revealed that patients could barely recall the exact time of onset of symptom if it lasted for > 1 day. The demographic characteristics and surgical results between the two groups were compared. Each group was further divided into two subgroups: time to appendectomy of > 12 h and ≤ 12 h. The associations of time to hospital and time to surgery with surgical results, disease severity, and complications were evaluated using the independent *t*-test or Mann-Whitney U test for continuous variables and the Fisher’s exact test for categorical variables. For those factors that were associated with surgical results at $p < 0.05$ were

re-evaluated in multivariable logistic regression models for each outcome.

Results

From December 2015 to December 2016, 256 patients underwent appendectomy at the National Taiwan University Hospital (Fig. 1). A total of 28 patients were excluded: 10 whose procedures were combined with other surgeries, 16 who underwent interval appendectomy, and 2 with inadequate data. A total of 228 patients presented to the ER and then underwent appendectomy. All appendices were examined by pathologists, but none had evidence of neoplasm. There were 57 and 171 patients suffering from abdominal pain for > 1 day and ≤ 1 day before reaching the hospital, respectively. Among patients with time to hospital of > 1 day, 28 and 29 patients had time to surgery of > 12 h and ≤ 12 h, respectively, and among those with time to hospital of ≤ 1 day, 89 and 82 patients had time to surgery of > 12 h and ≤ 12 h, respectively.

Time to hospital more than versus less than 1 day

Comparing demographic characteristics, abdominal pain duration of > 1 day or ≤ 1 day did not show a

significant difference (Table 1). The mean age, BMI, sex distribution, and white blood cell count were similar. On average, the abdominal pain lasted 13.2 h and 3.4 days in the groups with abdominal pain duration of ≤ 1 day and > 1 day, respectively. All patients underwent diagnostic exams preoperatively [most computed tomography (CT) scans (99.1%)]. One patient underwent magnetic resonance imaging and one underwent an abdominal echogram due to pregnancy. Mean waiting time for the diagnostic exam was 4.0 h. Mean time to appendectomy was slightly shorter in patients with time to hospital of > 1 day than in those with time to hospital of ≤ 1 day (15.7 vs. 17.7 h) but this did not reach significant difference.

Comparison of surgical results with different preoperative abdominal pain durations is shown in Table 2. No difference was found in operative method between the two groups, while the operative time (78.8 vs. 61.4 min), post-operative hospital admission (5.1 vs. 3.4 days), and overall hospital stay (5.8 vs. 4.1 days) were significantly longer in patients with time to hospital of > 1 day. Furthermore, there was a higher proportion of complicated cases (49.1% vs. 26.9%; $p = 0.003$). As for postoperative complications, the incidence of intra-abdominal abscess was higher in patients with time to hospital of > 1 day. There was no significant difference in the rates of surgical site infection, ileus, and internal bleeding between two groups.

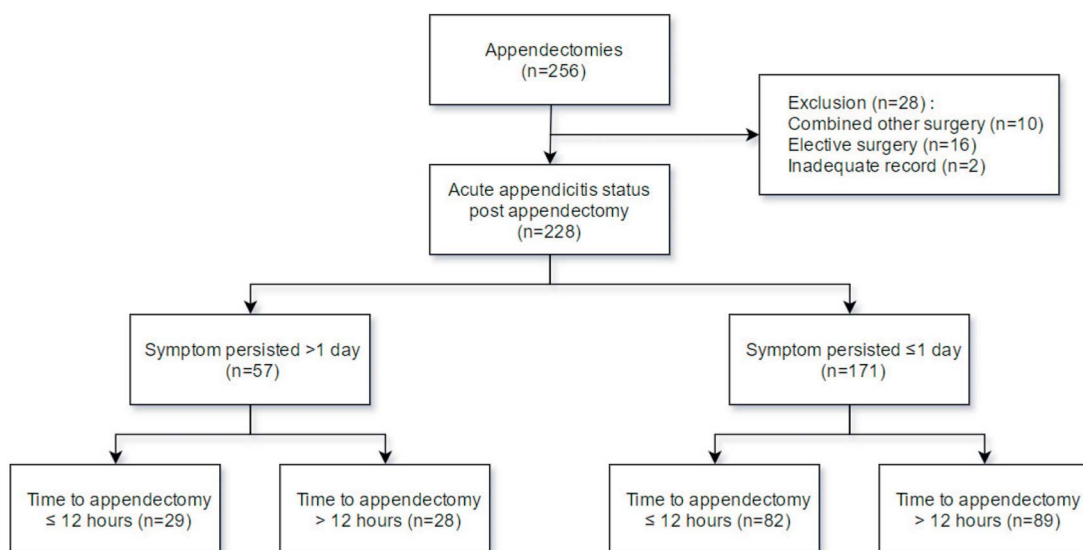


Fig. 1. Flow diagram of the study.

Table 1. Demographic characteristics of patients with variable time to hospital

Abdominal pain duration	Total (n = 228)	≤ 1 day (n = 171)	> 1 day (n = 57)	<i>p</i>
Age in years, mean	37.5	37.0	39.1	0.485
Sex, n (%)				1.000
Female	114 (50)	86 (50.3)	28 (49.1)	
Male	114 (50)	85 (49.7)	29 (50.9)	
BMI, mean	22.2	22.7	22.1	0.150
Abdominal pain duration, mean				
In days			3.4	
In hours		13.2		
Hours between ER triage and diagnosis exam, mean	4.0	4.1	3.6	0.329
Diagnosis exam, n (%)				0.068
CT	226 (99.1)	169 (98.8)	57 (100)	
Ultrasound	1 (0.4)	1 (0.6)	0 (0)	
MRI	1 (0.4)	1 (0.6)	0 (0)	
Hours between ER triage and operation, mean	17.2	17.7	15.7	0.341
Blood WBC count (K), mean	13.5	13.6	13.2	0.483

Table 2. Comparison of surgical results between time to hospital of > 1 day and ≤ 1 day

Abdominal pain duration	Total (n = 228)	≤ 1 day (n = 171)	> 1 day (n = 57)	<i>p</i>
Operative method, n (%)				0.101
Laparoscopy	223 (97.8)	169 (98.8)	54 (94.7)	
Open	5 (2.2)	2 (1.2)	3 (5.3)	
Operative time (min), mean	65.8	61.4	78.8	0.008*
Severity, n (%)				0.003*
Simple	154 (67.6)	125 (73.1)	29 (50.9)	
Complex	74 (32.4)	46 (26.9)	28 (49.1)	
Post-operative hospital admission in days	3.8	3.4	5.1	0.013*
Overall hospital stay in days	4.5	4.1	5.8	0.020*
Complication, n (%)				
Surgical site infection	18 (7.9)	14 (8.2)	4 (7.0)	1.000
Ileus	6 (2.6)	4 (4.1)	2 (3.5)	0.641
Intra-abdominal abscess	5 (2.2)	1 (0.6)	4 (7.0)	0.015*
Internal bleeding	1 (0.4)	0 (0)	1 (1.8)	0.250

* Multivariate analysis showed abdominal pain duration was associated with longer operative time ($p < 0.001$), complex severity ($p = 0.036$), longer post-operative hospital admission ($p < 0.001$) and overall hospital stay ($p = 0.001$), positive intra-abdominal abscess ($p = 0.004$).

Finally, multivariate analysis showed abdominal pain duration was associated with longer operative time ($p < 0.001$), complex severity ($p = 0.036$), longer post-operative hospital admission ($p < 0.001$) and overall hospital stay ($p = 0.001$), positive intra-abdominal abscess ($p = 0.004$).

Time to surgery more than versus less than 12 h (time to hospital less than 1 day)

Patients who suffered from abdominal pain for ≤ 1 day before going to the hospital were then divided into two subgroups according to time to appendectomy of >

12 h or ≤ 12 h. Comparison of disease severity and surgical results with time to appendectomy is shown in Table 3. There was no significant difference in operative time, disease severity, post-operative hospital admission, and complication rates except for overall hospital stay, which was significantly longer in patients with time to appendectomy of > 12 h (4.5 vs. 3.7 days).

Time to surgery more than versus less than 12 h (time to hospital more than 1 day)

Similarly, patients with abdominal pain duration >

Table 3. Comparison of surgical results between time to appendectomy of > 12 h and ≤ 12 h (time to hospital ≤ 1 day)

	Total (n = 171)	≤ 12h (n = 82)	> 12 h (n = 89)	<i>p</i>
Operative time (min), mean	61.4	63.3	59.1	0.290
Severity, n (%)				0.495
Simple	125 (73.1)	62 (75.6)	63 (71.8)	
Complex	46 (26.9)	20 (24.4)	26 (29.2)	
Post-operative hospital admission in days	3.4	3.3	3.5	0.749
Overall hospital stay in days	4.1	3.7	4.5	0.029*
Complication, n (%)				
Surgical site infection	14 (8.2)	4 (4.9)	10 (11.2)	0.167
Ileus	4 (4.1)	3 (3.7)	1 (1.1)	0.351
Intra-abdominal abscess	1 (0.6)	1 (1.2)	0 (0)	0.480

1 day were divided into two subgroups. Comparison of disease severity and surgical results with time to appendectomy is shown in Table 4. There was no significant difference in operative time, disease severity, post-operative hospital admission, overall hospital stay, and complication rates between the two subgroups.

Relation of demographic characteristics and time interval

Although demographic characteristics did not differ in patients with abdominal duration of > 1 day or ≤ 1 day, some characteristics seemed to affect the interval between arriving to the hospital and starting the operation (Table 5). Among all, patients younger than 18 years had a significantly shorter time to appendectomy (12.8 vs. 18.3 h). Furthermore, women took significantly more time waiting for the diagnostic exam since arriving to the hospital (time to exam) (4.6 vs. 3.3 h) but the time to appendectomy did not reach significance.

Discussion

Acute appendicitis is one of the most common causes of acute abdomen that requires surgical intervention, especially in young patients. In the past, the lack of patient education, physician experience, and diagnostic tools contributed to delay in diagnosis and treatment.^{2,3} Presently, almost every suspicious patient undergoes advanced technological procedures

Table 5. Relation of demographic characteristics with time to diagnostic exam and time to appendectomy

	Time to exam (h)	Time to surgery (h)
Age (n)		
≤ 18 years (45)	3.8	12.8
> 18 years (183)	4.0	18.3
	<i>p</i> = 0.676	<i>p</i> = 0.001
Sex (n)		
Female (114)	4.6	18.0
Male (114)	3.3	16.4
	<i>p</i> = 0.007	<i>p</i> = 0.374

Table 4. Comparison of surgical results between time to appendectomy of > 12 h and ≤ 12 h (time to hospital > 1 day)

	Total (n = 57)	≤ 12 h (n = 29)	> 12 h (n = 28)	<i>p</i>
Operative time (min), mean	78.8	79.8	77.7	0.866
Severity, n (%)				0.594
Simple	29 (50.9)	13 (44.8)	16 (57.1)	
Complex	28 (49.1)	16 (55.2)	12 (42.9)	
Hospital stay in days	5.1	4.5	5.8	0.358
Overall hospital stay in days	5.8	4.9	6.7	0.183
Complication, n (%)				
Surgical site infection	4 (7.0)	1 (3.4)	3 (10.7)	0.352
Ileus	2 (3.5)	1 (3.4)	1 (3.6)	1.000
Intra-abdominal abscess	4 (7.0)	1 (3.4)	3 (10.7)	0.352
Internal bleeding	1 (1.8)	0 (0)	1 (3.6)	0.491

for differential diagnosis. Appendectomy often was postponed due to other urgent conditions, such as head trauma or cardiovascular disease. There was debate about how long patients with acute appendicitis could wait before disease progression or increasing complications occurred. Some reports suggested that appendectomy should be performed as soon as possible to prevent disease progression⁴⁻⁶ and postoperative complications.^{4,6,7} However, other reports claimed that delayed appendectomy did not significantly increase risk of perforation^{8-10,12} or surgical site infection.⁹⁻¹³ It is known that symptoms resulting from inflammation of the appendix started before the patient went to the hospital. Thus, other than the time from the ER to the operation room (time to surgery), the time from symptom onset to reaching the hospital (time to hospital) also may be an important factor to influence surgical outcome. Our study aimed to differentiate which period has a more important role in the disease progression.

Abdominal pain, nausea, vomiting, anorexia, and elevated temperature are common symptoms in acute appendicitis.¹⁴ Lewis et al.¹⁵ reported that nearly 99% patients experienced abdominal pain initially and duration of pain on admission to the hospital was related to the severity of disease. In our study, similarly, longer abdominal pain duration resulted in a higher rate of complicated appendicitis. In a multi-institutional analysis, Boomer¹³ also reported that longer duration of symptoms was associated with increased complicated appendicitis and surgical site infection rates. To our understanding, few reports focused on the relationship of abdominal pain duration and detailed surgical outcome. Our results suggested that time to hospital (abdominal pain duration) showed a strong relationship not only with disease severity, but also operative time, post-operative hospital admission, and overall hospital stay. However, regarding postoperative complications, only the rate of intra-abdominal abscess increased with longer abdominal pain duration. Several assumptions may contribute to similar surgical site infection rates regardless of longer abdominal pain duration. One is that the operative method did not differ between the time to hospital of > 1 day or ≤ 1 day. Most patients underwent laparoscopic rather than

open appendectomy, which may increase the wound infection rate.^{16,17} Another assumption was the routine postoperative use of oral or intravenous antibiotics for variable durations. The other was the surgical technique. In every laparoscopic appendectomy, a palm-sized bag made with a sterile surgical glove was inserted into the abdomen to place the resected appendix in the bag and pull it out with the trocar, to prevent contamination of the abdominal wound.

Time to surgery is determined by many factors, such as the size of the hospital, number of available wards and operation rooms, sufficiency of the employees in the hospital, and the frequency of use of diagnostic machines. Few reports discussed factors that may affect the time to surgery. In our study, most patients underwent CT as a diagnostic tool. Thus, women needed more time to wait for the result of the pregnancy test, resulting in a significant longer time to diagnostic exam. Nevertheless, the difference in time to surgery between men and women did not reach statistical significance. Age was another factor that caused difference in time to surgery. Patients younger than 18 years were more likely to undergo surgery earlier than those older than 18 years, probably because the surgery was performed by pediatric surgeons. The general surgeons often had to perform other surgeries, such as for hollow organ perforation or ischemic bowel disease, which were of higher priority than appendectomy, in the same day. Based on our record, age, BMI, or other factors did not cause a difference in the time to surgery. In our study, there was no difference in operative time, disease severity, hospital stay, and complication rate between patients with time to surgery of > 12 h and ≤ 12 h or in those with time to hospital of > 1 day or ≤ 1 day. Only in those with time to hospital of ≤ 1 day did the longer time to surgery result in a significantly longer overall hospital stay, probably due to prolonged waiting time to surgery. This result was compatible with results of other studies that questioned the importance of time to surgery. The reason that time to surgery did not affect the disease severity or surgical results probably was due to adequate treatment in the ER. At our hospital, once acute appendicitis was suspected, fasting, intravenous antibiotics, and fluid injection were administered before the

patients underwent surgery. Many studies reported that conservative treatment was safe and feasible for uncomplicated appendicitis.¹⁸⁻²¹ Even in complicated appendicitis, a meta-analysis showed that initial conservative treatment further decreased wound infection, abdominal abscess, ileus, and reoperation rates.²² In other words, the aid of initial medical treatment may protect the patients from disease progression; thus, the time interval between ER triage and entering the operation room could be well compensated.

Our study focused on the patients who underwent immediate appendectomy. Nevertheless, some patients received conservative treatment first, followed by elective appendectomy. The comparison of surgical outcome of immediate and delayed appendectomy needs further investigation. There were a few limitations in this study. First, this was a single institute retrospective study. Designing a prospective trial may result in ethical issues if we intentionally delay surgery. Second, the time of any procedure during patients' in-hospital course was accurate, since every moment was recorded by the computer. However, the onset of abdominal pain was described subjectively by the patients themselves and the quality of ER record was so various that we could hardly classify the pattern of abdominal pain. We could collect only the abdominal pain duration data according to the ER record and the past history from the admission note, which may be susceptible to information and recall bias. Furthermore, the case numbers of the study can be extended by a prolonging study period or seeking multi-institute cooperation to achieve stronger statistical significance.

Conclusions

Prolonged abdominal pain duration (> 1 day) was associated with increased risk of complicated appendicitis, longer operative time, post-operative hospital admission, overall hospital stay, and intra-abdominal abscess. Regardless of variable abdominal pain duration, the time to surgery did not significantly affect the disease progression or postoperative complication. Our results suggested that the time to hospital has a more important role than time to surgery in the treat-

ment outcome of acute appendicitis.

Author Disclosures

None reported.

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原 著

複雜性闌尾炎及術後併發症的危險因子： 到院時間或等待手術時間？

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目的 急性闌尾炎是最常見需要手術的腹部急症之一。然而，早期手術是否對病人有明顯幫助仍有爭議。闌尾炎手術時機由兩因素決定：出現症狀到抵達醫院的時間（到院時間），以及抵達醫院到開始動刀的時間（等待手術時間）。本篇論文旨在探討何種因素會增加複雜性闌尾炎及手術併發症的發生。

方法 本篇論文為回溯性研究，收錄自 2015/12 至 2016/12 於台大醫院接受闌尾炎手術之病患。本研究將病患先以『出現症狀到抵達醫院的時間大於或小於一天』分為兩個子群，子群中再以『抵達醫院到開始動刀的時間大於或小於 12 小時』各分做兩個次子群（共四群），接著比較其疾病嚴重度及手術預後是否有差異

結果 本研究共收錄 228 位病患，其中 171 位病患出現症狀到抵達醫院的時間小於一天，而 57 位病患則大於一天。研究結果發現出現症狀到抵達醫院的時間大於一天的病患的複雜性闌尾炎發生率 (48.1% vs. 26.9%)、手術時間 (78.8 vs. 61.4 min)、住院天數 (5.1 vs. 3.4 天)、待院天數 (5.8 vs. 4.1 天)、發生腹內膿瘍比率 (7% vs. 0.6%) 顯著增加。而抵達醫院到開始動刀的時間大於或小於 12 小時則沒有顯著差異。

結論 出現症狀到抵達醫院的時間與複雜性闌尾炎發生率、手術時間，住院天數、待院天數、腹內膿瘍發生率有明顯相關。因此根據本研究顯示，相較於等待手術時間，到院時間應為更重要的危險因子。

關鍵詞 闌尾炎、到院時間、等待手術時間、複雜性、併發症。