

# Risk of Developing Perforations and Abscesses for Patients With Appendicitis, With Regards to Duration of Symptoms. A Retrospective Cohort Study.

Gunnar Andrésón (✉ [gua20hi@gmail.com](mailto:gua20hi@gmail.com))

National University Hospital of Iceland

Árný Kristínardóttir

National University Hospital of Iceland

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## Research Article

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# Abstract

## Objective

Some studies have supported delayed appendectomy citing that the risk of perforation does not increase until beyond 24-48 hours of hospitalization.

This retrospective cohort study looked at the relationship of duration of symptoms and the prevalence of perforated appendicitis. To evaluate if a delayed approach would be justifiable.

## Methods

Between 1<sup>st</sup> of January 2018 and 30<sup>th</sup> of March 2020, there were N=1274 patients, 40 years or younger, suspected of appendicitis at the National University Hospital of Iceland. n=658 had appendicitis and n=105 of them had a perforated appendix.

## Results

Relative risk for perforations depending on duration of symptoms were; 6.4, 14.7, 20.2 and 27.1 for 24-48, 48-72, 72-96, and over 96 hours, respectively, compared to 0-24 hours ( $p < 0.001$ ). There was also a significant correlation with increased duration of symptoms and prolonged hospital stay for patients with appendicitis ( $p < 0.0001$  and  $\rho = 0.36$ ).

## Conclusion

This indicates that perforations are dependent on the duration of the symptomatic period, and it is probably beneficial to react early and not postpone the workup or treatment past 24 hours.

## Key Points

**A prolonged symptomatic period for patients with appendicitis, increased the likelihood of perforations and formation of abscesses.**

## Introduction

Appendicitis is a common disease with a lifetime incidence of about 8% [1]. The evaluation of the patients can be difficult because its presentation is similar to many other diseases. Possibly one of the best clinical tools to help with the diagnosis of appendicitis is time. With a longer disease course, the symptoms evolve, like the maximal point of tenderness localizing to the right lower quadrant, increasing temperature and specific signs for appendicitis might become more evident, like Rovig's and psoas sign. While other differential diagnosis might have a different disease course, like gastroenteritis and ruptured ovarian cyst might improve spontaneously with time [2,3]. When considering that the treatment for appendicitis is surgery, which; carries a risk for morbidity, is time consuming and sometimes not readily

available. Then surgery is not a great option if the estimated risk of appendicitis is low. This might make the “wait and see” approach for suspected appendicitis an attractive choice. Ultrasound is the best initial imaging modality in young patients but sometimes it’s inconclusive [4]. In those incidences it could be tempting to attempt another ultrasound the following day.

One of the most common complications of appendicitis is perforation that can cause peritonitis, sepsis and abscess formation. When considering one of the mechanisms of appendicitis; luminal obstruction, the appendix continuous to excrete fluids, dilates, becomes inflamed, the pressure occludes veins causing necrosis and sometimes eventually perforating [1]. Then it makes sense that the process is time depended. Hence opting for the “wait and see” approach might come at the expense of increased risk for perforations and other complications.

It has recently been proposed in previous studies that it is acceptable to delay an appendectomy for up to 48 hours after a patient is hospitalized for suspected appendicitis and wait for up to 72 hours after the patients becomes symptomatic, and this is generally accepted by common guidelines on patients suspected of appendicitis [1,5,6,7,8]. While other articles have shown different results with benefit of an early appendectomy [9,10,11,12]. At our institution we have repeatedly observed that an inflamed appendix can perforate and cause an abscess to develop within 48-72 hours, so it seems reasonable that a timely approach to appendicitis might be beneficial despite the findings in previous articles. The aim of this article was assessing how duration of symptoms correlated to perforation, abscess development and length of hospital stay and if delayed imaging was justifiable.

## Material And Methods

This is a retrospective cohort study, where suspected appendicitis was the exposure and inflamed appendix and perforation were two different disease end points. Patients were included that were suspected of appendicitis from 1st of January 2018 to 30th March 2020, and were younger than 41-year-old.

All experimental protocols were approved, and the need for informed consent was waived, by the ethics committee of the National University Hospital of Iceland (Siðanefnd heilbrigðisrannsókna á Landspítala), and the methods were carried out in accordance with the relevant guidelines and regulations in the manuscript.

To find the participants, two different archives with medical records were queried. The imaging PACS archive for patients that had either computed tomography (CT) or ultrasound (US) of the abdomen and then the surgical archive for patients that had appendectomy or unspecified abdominal surgery. Patients from the imaging archive were included if the referring clinician asked about appendicitis, or the patients were thought to have appendicitis from a radiology stand point even though the clinician did not suspect appendicitis, but in that case only if the symptoms of that patient could be explained by an inflamed appendix and there was no better differential diagnosis. Then all the images were reevaluated by the researchers (GA) for signs of appendicitis and signs were chosen according to radiopaedia.com. The

signs of inflamed appendix for CT were: dilated appendix  $>6$  mm (and wall thickening  $\geq 3$  mm), adjacent inflammation and increased epithelial enhancement. To be regarded as inflamed it needed the first plus one of the other criteria. The criteria for inflamed appendix on US was; dilated appendix  $>6$  mm dilated, wall thickness  $\geq 3$  mm, increased color Doppler signal, non-compressible, free fluid and inflammation in the adjacent fat. To be viewed as inflamed it needed to fulfill two criteria.

It was common for the appendix not to be visualized during US and in those instances, it was decided by this study that the radiology report of the appendix was determined to be non-inflamed, unless there were other findings in the report indicating an inflamed appendix, in that case it was regarded as an inflamed appendix, but only if the report indicated that there was a substantial risk for appendicitis. These findings could be maximal point of tenderness over the right lower quadrant (RLQ), fatty inflammation near the caecum, abscess or free gas in the RLQ. Free fluid in the abdomen was not regarded as a sufficient sign for appendicitis. The images were first reevaluated and a decision from the reexamination was made, if the appendix was inflamed or not (or if it could not be visualized), and then the imaging report was read and the conclusion from the report was determined, and last the pathology report was access, which was the gold standard.

The final diagnosis of appendicitis or not appendicitis was based on pathology reports when there was an appendectomy, and reevaluation of the images, when there were no pathology reports available.

When it came to perforation then that depended mainly on the surgery reports because pathology and imaging reports underestimated the perforation rate, and was often inaccurate. Appendices that perforated during surgery were excluded. Microscopic abscesses found only on the pathology report were excluded if there was no mention of an abscess in the patients records or imaging studies.

The definition for days for duration of symptoms and hospital stay was for the first 24 hours, 1 day, between 24-48 hours 2 days and so on. The days of symptoms were from the start of the symptomatic period until the patient had imaging in the case patients that did not have surgery or went to the operating room for patients that had surgery.

Because presumably a perforation precedes an abscess formation, hence in future references, then a perforation is regarded as a broader category including both abscesses or perforations that have not developed into an abscess. If only referring to a perforation and not abscesses then it is mentioned as "perforation only".

For analyzes of categorical data with two variables Chi square test was done in excel, for statistically analyzes of numerical and categorical data then t test in R was performed. To compare two numerical sets of data, Pearson's correlation was utilized unless the numbers were not normal distributed in that case, Spearman's correlation in R, was chosen instead. This was done by the author GA.

## Results

In total there were N=1274 patients 40 years or younger that were suspected of having appendicitis. n=658 had appendicitis and n=616 did not have appendicitis. The mean age for patients with appendicitis was 21.8-years and ranged from 2-40, for patients just suspected of appendicitis but ultimately did not have appendicitis, the mean age was 24.9-years and ranged from 6 weeks to 40-years. Of those with appendicitis, there were n=40 patients that developed an abscess and n=65 patients that had a perforation without an abscess (figure 1).

By looking at the duration of symptoms, then most patients with appendicitis presented to the hospital during the first 48 hours of being symptomatic (72%). Perforation only and abscesses were rare during the first 24 hours, then “perforations only” started to become apparent on day 2 and abscesses on day 3. With increased duration of symptoms, the likelihood of perforations increased. On day 1, 2, 3, 4 and >4 days of being symptomatic the chance of perforations and abscesses were respectively 2.4%, 15.2%, 34.8%, 47.8% and 64.0% ( $p < 0.001$ ) and 0.8%, 2.3%, 10.9%, 34.8, 56.0% ( $p < 0.001$ ), when the appendix was inflamed (figure 2 and table 1).

When the cohort was divided based on the pediatric (0-18 years) and adult (19-40 years) population then a similar trend of when perforations and abscesses developed based on durations of symptoms could be seen as when they were regarded as a single group, but the rate of perforations and abscesses were about 3times higher in the pediatric population (table 2)

The average symptomatic period for patients, before they had imaging of the appendix or went to surgery was 1.8 days for uncomplicated appendicitis, 2.5 days for appendicitis with “perforation only”, and 5.3 days for appendicitis with abscess (table 3). The average hospital stay was calculated for each of these groups and was around 2.0 days for uncomplicated appendicitis, 5.6 days for appendicitis with “perforation only” and 8.9 days for appendicitis with abscesses. The hospital stay was longer for patients with perforations than those with uncomplicated appendicitis ( $p < 0.0001$ ).

The correlation between hospital stay and symptomatic duration was calculated. To make sure that the increased hospital stay was not due to exclusively observation period, then the groups were divided based on if the final diagnosis was appendicitis or not appendicitis. The result showed that for patients with appendicitis, and a longer symptomatic period then the hospital stay was more extensive ( $p < 0.0001$  and  $\rho 0.36$ ), but there was no such correlation between symptomatic duration and hospital stay when the patients were only suspected of having appendicitis, but ultimately did not have appendicitis ( $p = 0.15$  and  $\rho 0.06$ ) (table 4).

## Discussion

Appendicitis is a common disease with a high incidence in the young population. Some of the most feared complications of appendicitis are development of perforations and abscesses. It has been suggested that the mortality rate for appendicitis increases with the development of a perforations and abscesses from less than 0.1% to about 5% [1], highlighting the importance of preventing that complication. This high mortality rate was not seen in this relatively young and healthy cohort, with only

one fatality which was outside of the 30-day follow up and unrelated to appendicitis and one intensive care unit admission after drainage of an abscess. Perforation also increased the hospital stay ( $p < 0.0001$ ), which costs money and resources for the hospital and lost revenues for the patients. About 16% of patients with appendicitis developed perforation in our study. This article showed that the risk of perforations was correlated to the duration of symptoms, with few perforations occurring during the first 24 hours of being symptomatic (2.4%), and few abscesses before 48 hours (1.7%), but beyond that time window it rapidly increased (15% between 24-48 hours and 35% for 48-72 hours for perforations when there was appendicitis  $p = < 0.0006$ ). This is contrary to some other studies, that clinical guidelines are based on, which claim that the incidence of perforation or surgical site infections does not increase with delayed appendectomy until beyond 24-48 hours after presenting to the hospital, or up to 72 hours of being symptomatic [1,5,6,7,8]. While other articles support the notion of an early appendectomy rate [9,10,11,12]. The rate of perforations at 48 hours of being symptomatic has previously been estimated at 7% [1,6,7]. But the conclusion from this observation was that between 24-48 hours 15% perforated and between 48-72 hours 35% perforated so on average that would be around 25% that had perforated at 48 hours instead of 7%. A previous studies that looked at duration of symptoms did not include as many participants with appendicitis and looked at the average time for an appendix to perforate but not when they start to perforate. And for the study that looked at the delayed appendectomy rate did not specifically include perforations as an endpoint, rather it looked at different types of surgical site infection and sepsis.

By looking at the duration of symptoms, in our study the majority presented after 24 hours (61%) of being symptomatic, but previously it had been reported that over 75% of patients presented within the first 24 hours [1]. This means that the average duration of symptoms might be longer at presentation to the hospital and the 48-hour window to treat the patients might be an overestimation. Most perforations were diagnosed between 24-72 hours of being symptomatic (72% vs 33% beyond 3 days).

On day 3, 4 and >4 days of being symptomatic the chance of perforations and abscesses were respectively 34.8%, 47.8% and 64.0% ( $p < 0.001$ ) and 10.9%, 34.8, 56.0% ( $p < 0.001$ ), when the appendix was inflamed. The numbers after 3 days were probably an overestimation of how many would eventually perforate if not treated in a timely manner, because patients with appendicitis can get better without treatment and those who do not improve are probably more likely to seek medical treatment. Even when looking at data from places with rural health care and severe delayed time to presentation the proportion of perforation is not as high as reported beyond 3 days in this article [13].

For patients with appendicitis, and a longer symptomatic period then the hospital stay was more extensive ( $p < 0.0001$  and  $\rho 0.36$ ), but there was no such correlation between symptomatic duration and hospital stay when the patients were only suspected of having appendicitis, but ultimately did not have appendicitis ( $p = 0.15$  and  $\rho 0.06$ ) (table 4). This indicates that making a diagnosis in a timely manner is important for patients suspected of appendicitis only if the appendix is inflamed but might not be as necessary if the appendix is not inflamed, and that the prolonged hospital stay was probably not merely due to observation but rather because of the consequences of the prolonged symptomatic period.

A major drawback to this study is that the time is measured in days instead of hours, that is an interval of 24 hours at a time, which makes it difficult to pinpoint exactly when perforations and abscesses start to become significant. This study is also subject to reporter bias, because some patients might not remember exactly when the symptoms started.

It was not factored in if patients got antibiotics after being diagnosed with appendicitis because the duration of symptoms was defined as from when the symptoms first became apparent until the patient either had imaging or had an appendectomy, if patients was treated with antibiotics after getting the diagnosis, then that might theoretically influence the rate of perforation, which in turn could affect hospital stay [1,5,14].

The treatment approach does not change much for patients with a perforated appendicitis without abscess, from an uncomplicated one, they are both usually treated with an appendectomy but if there is contamination of the peritoneum, the patient is treated with a longer course of antibiotics, but for patients with abscesses then those are often treated with intraperitoneal drain placement and delayed appendectomy. So even though there are less benefits preventing a “perforation only” than an abscess, then patients with a perforation are often sicker than those with uncomplicated appendicitis, and it would also be preferable to prevent a perforation [5].

## Conclusion

By making a timely diagnosis and starting treatment early it should be possible to decrease the rate of perforation, abscess formation and hospital stay. It seems to be important to make a diagnosis and initiate treatment preferentially within 24 hours from when the patient becomes symptomatic, for beyond that time window the incidence of perforations increased ( $p < 0.0001$ ).

## Abbreviations

Perforation only = perforation without abscesses

Perforation = “perforation only” or abscesses

US = ultrasound

CT = computed tomography

## Declarations

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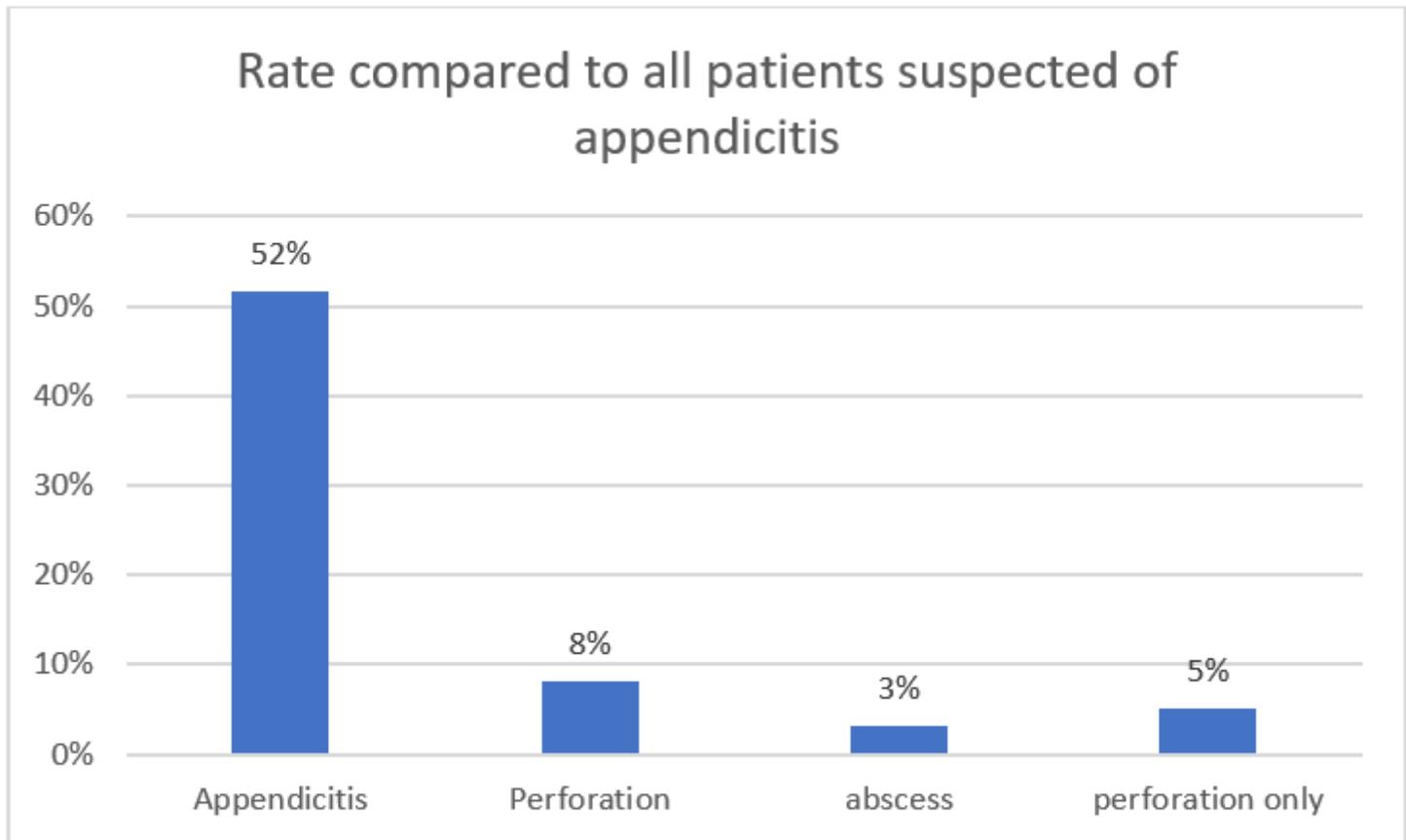
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## Tables

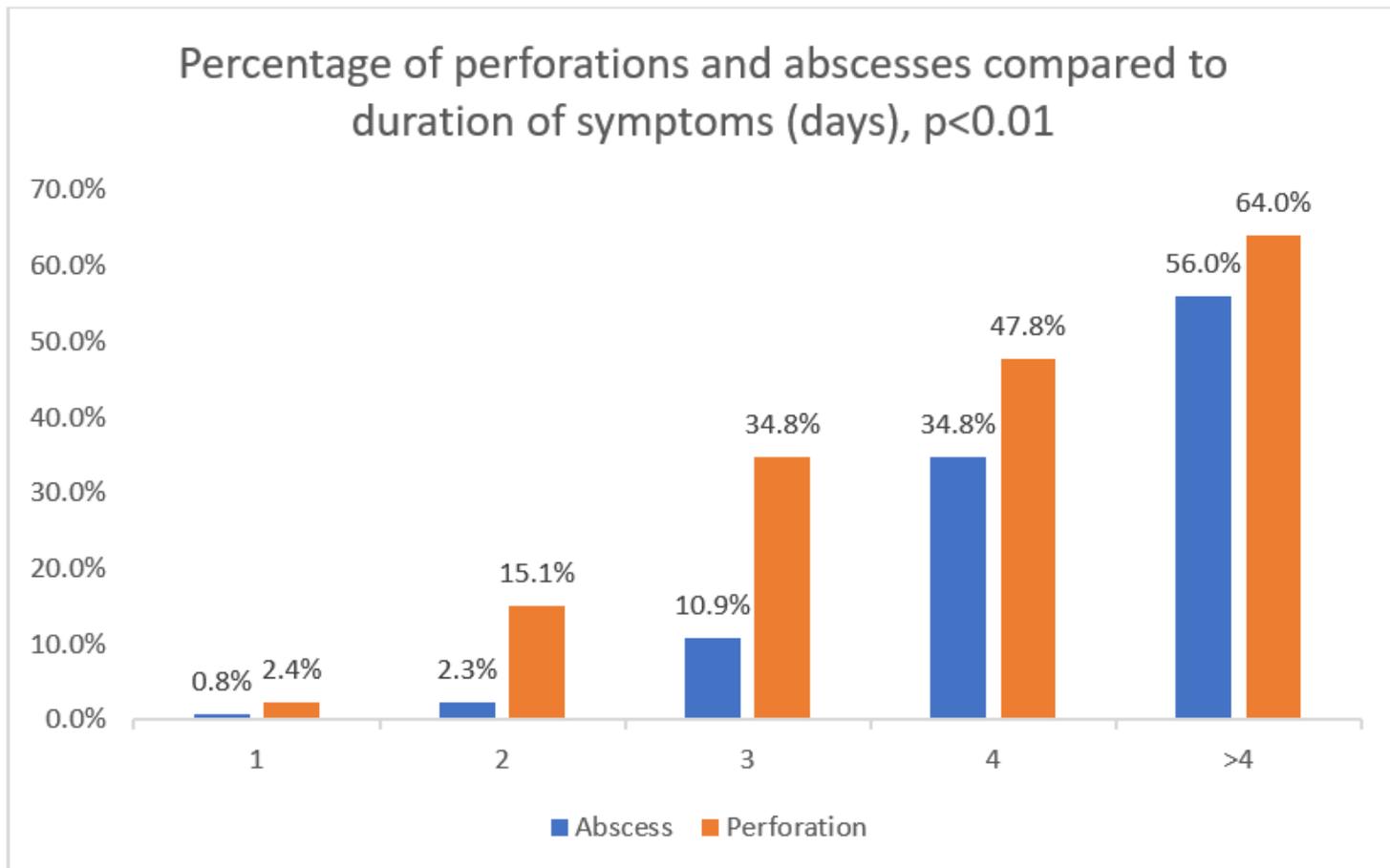
Due to technical limitations, table 1, 2, 3 and 4 is only available as a download in the Supplemental Files section.

## Figures



**Figure 1**

The rate of appendicitis and perforations was 51.7% and 8.2%, respectively. The perforation rate was 16.0% for patients with appendicitis, when patient suspected of appendicitis were excluded. perforations are regarded as either perforation with or without abscesses, while "perforation only" is just perforation without abscesses.



**Figure 2**

For patients with appendicitis during the first 24 hours, of being symptomatic, the chance of perforation was only 2.4% and abscess formation 0.8%, while between 48-72 hours the chance of perforations was 34.8% and abscesses 10.9%.

## Supplementary Files

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