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Research Article

Assessment of negative appendectomy in acute appendicitis diagnoses

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ABSTRACT

Background: A negative appendectomy is a surgery performed due to a clinical suspicion of acute appendicitis, but no evidence of inflammation is identified upon examination. The main reason is the incorrect diagnosis of acute appendicitis, which remains a challenge, especially in developing countries, where the rates are different among populations. This study aims to explore the prevalence of negative appendectomies in a regional hospital and evaluate the diagnostic methods used in clinical practice.

Materials and methods: A retrospective analysis was conducted on patients who underwent emergency appendectomy between 2021 and 2022. Negative appendectomy was defined as the absence of histopathological evidence of acute appendicitis postoperatively.

Results: Out of 324 patients, 38 were found to have undergone a negative appendectomy, representing a two-year rate of 11.7%. Imaging was performed in 78% of cases, but no significant difference was observed in its use between patients with positive and negative appendectomies. Differential diagnoses showed pathologies such as cysts and intestinal lesions. The Alvarado score was found to be a useful tool when applied with a threshold score of 7. However, variability in clinical presentations such as nausea/vomiting, anorexia, right iliac fossa tenderness and fever highlighted the limitations of relying solely on this metric. The factors associated with negative appendectomy were previous abdominal surgery, Alvarado score <7, abdominal pain, rebound tenderness, leukocytosis and neutrophilia.

Conclusions: The prevalence of negative appendectomies at our institution was 11.7%. Despite the widespread use of diagnostic imaging and clinical scoring systems, improvements in diagnostic accuracy are necessary to reduce the rate of unnecessary surgeries.

Introduction

Acute appendicitis is currently one of the most common diagnoses in surgical emergencies, with a lifetime risk of 8.6% for men and 6.7% for women [1]. Despite the prevalence and understanding of this pathology, it continues to pose a diagnostic challenge. The dilemma lies in balancing early diagnosis and preventing more severe complications, such as tissue perforation, against the risk of unnecessary surgical intervention, as reflected in the phenomenon of negative appendectomies [2]. Negative appendectomies occur when surgery is undertaken based on a clinical suspicion of acute appendicitis, yet no pathological signs of inflammation are found. This is evidenced by the absence of mucosal or wall infiltration by inflammatory cells, including polymorphonuclear leukocytes, lymphocytes, or plasma cells [3]. Although this phenomenon might be perceived as a clinical shortcoming, it underscores the inherent complexity of medical practice and the challenges of decision-making in the face of uncertainty. Atypical presentations of appendicitis, false positives in diagnostic tests, and variability in symptomatology are key factors contributing to the occurrence of negative appendectomies.

The incidence of negative appendectomy was reported to range from 3% to 30%. However, advancements in diagnostic techniques, particularly the use of computed tomography (CT) of the abdomen, have significantly reduced this rate to between 5% and 10% in patients who

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underwent further investigation in developed and developing countries [4–6]. The characterization of negative appendectomy rates could highlight variations in diagnostic accuracy and procedural protocols between populations and decrease unnecessary hospital costs and the risk of complications related to anesthesia and postoperative recovery.

This study aims to assess the prevalence of negative appendectomies at a regional hospital and evaluate the effectiveness of different clinical, imaging and laboratory diagnostic tools, in accurately diagnosing acute appendicitis.

Methods

Study population

Data were retrospectively collected from 324 patients of all ages with a preoperative diagnosis of acute appendicitis who underwent emergency appendectomy from January 2021 to December 2022 in Colima Regional University Hospital. We include all participants who gave their consent (for the cases involving individuals under the age of 18, consent to participate was secured from their parents or legal guardians). Exclusion criteria consisted of individuals who had an appendectomy performed for reasons unrelated to a preoperative diagnosis of acute appendicitis, as well as those lacking pathological findings or incomplete files. Ethical permission for the study was obtained from the ethics committee of the Colima Regional University Hospital (approval number: CI/2023/02/SR/CIR/185).

Data collection

Upon receiving approval from the ethics committee, medical records of emergency appendectomy were reviewed in the clinical archive to gather relevant information. Data collected were age, gender, Alvarado score, imaging study (abdominal ultrasonography, X-ray and CT) and histopathological findings during or after the surgical intervention. Alvarado score is divided into three categories: symptoms, signs, and laboratory findings. The symptoms include migratory pain to the right iliac fossa (RIF), nausea or vomiting, and anorexia, each assigned 1 point. The signs include tenderness in the RIF, positive rebound tenderness (severe pain in the RIF when pressure is abruptly released), and fever, with scores of 2, 1, and 1, respectively. Finally, the laboratory findings include leukocytosis and left shift of neutrophils, assigned 2 and 1 points, respectively [7].

Negative appendectomy was characterized by final pathological findings post-surgery, where the appendix was found to be normal, congested, showed signs of peri-appendicitis, or had a tumor, but without any evidence of inflammation.

Statistical analysis

Data analysis was conducted using SPSS software. Descriptive statistics were used to characterize the study population. Categorical variables are presented as absolute counts and percentages, while continuous variables are expressed as medians with interquartile ranges. The chi-square test was used to compare categorical variables between the positive and negative appendectomy groups, and the Mann-Whitney U test was applied for continuous variables. To assess the association between clinical factors and negative appendectomy, bivariate analysis was performed using binary logistic regression to estimate odds ratios (ORs) and 95% confidence intervals for each individual factor.

Results

Over the study period, a total of 324 patients were admitted between January 2021 and December 2022. Of these 324 patients, 38 (11.7%) were negative for appendicitis and the postoperative diagnoses for them are in Table 1. Baseline demographic, clinical data and comparison of positive and negative appendectomies are presented in Table 2. The average age was 23 years with no significant difference between negative and positive appendectomies. Gender distribution was similar across both groups. Statistical difference was found in patients with previous abdominal surgery ($p = 0.015$) with more prevalence in the group with negative appendectomies. As expected, Alvarado score was higher in the positive group ($p < 0.001$). For symptoms evaluated,

Table 1
Postoperative diagnosis for negative appendectomies.

Postoperative diagnosis	Cases (%)
Tubal or ovarian cyst	7 (18.5%)
Intestinal perforation	7 (18.5%)
Mesenteric adenitis	6 (15.8%)
Pelvic inflammatory disease	5 (13.2%)
Intestinal Obstruction	
• Sigmoid Volvulus	1 (2.6%)
• Ameboma	1 (2.6%)
• Bezoar	1 (2.6%)
Intestinal intussusception	1 (2.6%)
Retroperitoneal Cyst	1 (2.6%)
Hepatic cyst	1 (2.6%)
Incarcerated inguinal hernia	1 (2.6%)
Intestinal malrotation – volvulus	1 (2.6%)
No pathology identified	5 (13.2%)
Total	38 (100%)

Table 2
Demographic and clinical data of total patients with diagnosis of acute appendicitis who underwent emergency appendectomy.

	Total (n = 324)	Negative (n = 38)	Positive (n = 286)	p
Age in years, median (IR)	20 (11–32)	24 (13–34)	19 (11–31)	0.213[a]
Gender				
Male	184 (56.8%)	22 (57.9%)	162 (56.6%)	0.884[b]
Female	140 (43.2%)	16 (42.1%)	124 (43.4%)	
Previous abdominal surgery	38 (11.7%)	9 (23.7%)	29 (10.1%)	**0.015**[b]
Alvarado score, mean ± SD	7 ± 1.8	5 ± 2	7.6 ± 1.6	**<0.001**[b]
Symptoms				
Abdominal pain	223 (69%)	13 (34.2%)	210 (73.7%)	**<0.001**[b]
Nausea/vomiting	234 (72.2%)	23 (60.5%)	211 (73.8%)	0.087[b]
Anorexia	149 (46%)	12 (31.6%)	137 (47.9%)	0.058[b]
RIF tenderness	254 (78.4%)	26 (68.4%)	228 (79.7%)	0.112[b]
Rebound tenderness	272 (84%)	24 (63.2%)	248 (86.7%)	**<0.001**[b]
Fever	159 (49.1%)	13 (34.2%)	146 (51%)	0.051[b]
Leukocytosis	279 (86.1%)	25 (65.8%)	254 (88.8%)	**<0.001**[b]
Neutrophilia	278 (85.8%)	24 (63.2%)	254 (88.8%)	**<0.001**[b]
Imaging study				
None	71 (21.9%)	10 (26.3%)	61 (21.3%)	0.134[b]
X-ray	48 (14.8%)	7 (18.4%)	41 (14.3%)	
CT	48 (14.8%)	9 (23.7%)	39 (13.6%)	
Ultrasonography	157 (48.5%)	12 (31.6%)	145 (50.7%)	
Time of pain prior surgery in hours, median (IR)	24 (12–48)	22 (12–72)	24 (12–48)	0.235[a]

a Mann-Whitney test.
b Chi-square test.

abdominal pain, rebound tenderness, leukocytosis, and neutrophilia were significantly more common in patients with confirmed appendicitis ($p < 0.001$).

There were no differences in time with pain before surgery between groups, however, patients with a longer period of pain have complications, such as perforated appendicitis or abscesses. The two-year negative appendectomy rate in patients diagnosed with acute appendicitis was 11.7 %, where no signs of appendiceal inflammation were observed. Additionally, 15.7% of the procedures were associated with early signs of inflammation, (Catarrhal appendicitis, Stage 1), 34% with fibrinopurulent appendicitis (Stage 2), 14.8% with gangrenous appendicitis (Stage 3), and 23.8% with perforated appendicitis (Stage 4).

Factors associated with negative appendectomy are shown in Table 3. Patients with a history of previous abdominal surgery had a higher risk for a negative appendectomy, as well as an Alvarado score of less than 7. Other significant risk factors included the absence of abdominal pain, rebound tenderness, leukocytosis, and neutrophilia. All patients who underwent emergency appendectomy showed improvement, with a 100% success rate. Additionally, 98.8% of the patients received antimicrobial treatment.

Discussion

Negative appendectomies rate is widely variant among populations with prevalence ranging from 3% to 30% [3–6,8]. Our study reports a negative appendectomies rate of 11.7%. This result aligns with existing literature in similar health systems with rates of 5.2 %, and 8.6 % and reflects the diagnostic accuracy achieved at the hospital in developing countries [6,9]. Nevertheless, it is essential to recognize that the prevalence of negative appendectomies still highlights the need for improvements in diagnostic strategies and patient selection for surgery.

All patients in this study were preoperatively diagnosed with acute appendicitis, however, intraoperative findings or postoperative evaluations revealed that the initial diagnoses were other pathologies being responsible for the clinical presentation mimicking acute appendicitis. It is essential to note that while these surgeries may appear unnecessary in hindsight, the postoperative diagnoses confirmed that surgical intervention was inevitable in conditions that often require surgical treatment as part of their management or as the definitive treatment. Furthermore, our results suggest that the improvement of our patients was also due to the administration of antibiotics since the majority received this treatment.

Several studies have demonstrated a strong association between gender and the rate of negative appendectomies. Specifically, gynecological conditions have been linked to higher rates of negative appendectomies in women [10]. Although we did not observe this gender difference in our report, ovarian cysts were among the most frequently diagnosed postoperative conditions, supporting the findings of previous research that suggest a higher incidence of negative appendectomies in women [6,11].

The factors associated with negative appendectomies identified in this study show the variability among populations. We observed that antecedents of abdominal surgery were more frequently in negative appendicectomies, and we also found it as a risk factor (OR, 95% CI: 2.75, 1.19–6.37, $p = 0.018$). A history of previous surgeries is a recognized risk factor for the development of abdominal adhesions and diverticulosis or diverticulitis, which can result in symptoms such as pain, abdominal distension, and nausea/vomiting, among others [12,13]. These symptoms can mimic acute appendicitis, but in our results, there were no reports of adhesions, diverticulosis or diverticulitis postoperative diagnosis in any patient. Previous abdominal surgery has been reported with a 7.9% prevalence in laparoscopic appendectomy for acute appendicitis but they did not report the prevalence in negative appendectomies [14].

The combination of symptoms (pain, anorexia, nausea/vomiting), signs (right iliac fossa tenderness, rebound tenderness, and fever), and laboratory findings (leukocytosis and neutrophilia) comprises the Alvarado score [15]. The total score divides patients into two groups: Alvarado score <7, representing the low and intermediate suspicion group, and Alvarado score ≥7, representing the high suspicion group [7]. While some recent studies continue to question the effectiveness of the score in diagnosing acute appendicitis [16,17], our findings indicate that a threshold of 7 in Alvarado score accurately differentiated between positive and negative appendectomies.

When analyzing the individual components of the Alvarado score, abdominal pain, rebound tenderness, leukocytosis, and neutrophilia were significant differentiators between groups. Not having these signs and symptoms is considered a risk factor for negative appendectomy (Table 3). In contrast, anorexia, nausea/vomiting, right iliac fossa tenderness, and fever were found to be statistically similar across groups. These results suggest that not all symptoms included in the score may be equally relevant across different populations, potentially leading to biases that contribute to reports of the score's ineffectiveness.

One of the primary concerns about the negative appendectomy rate is the need for a more accurate diagnostic process. Imaging techniques such as X-ray, CT, and ultrasonography have been proposed to improve the diagnosis of acute appendicitis [18]. However, our findings show that even though the majority of cases had imaging studies (78%), there was no significant difference in the use of these tools between the negative and positive appendectomy groups. This suggests that imaging alone is not always definitive in diagnosing acute appendicitis. It is crucial to consider the individual experience of medical centers, particularly regarding the modernization of imaging technologies, as well as the expertise of the operators and interpreters [11]. One possible explanation for the high false-negative rate in imaging studies could be related to operator dependency, especially in ultrasonography, which was the most used modality in our center. The availability of advanced imaging technology and the expertise of radiologists may also vary in developing countries. Additionally, in emergency settings, the need for rapid decision-making may lead to limited or inconclusive imaging interpretations.

Although our rate of negative appendectomy is higher than that reported in some previous reviews, it remains within the broader global range. This discrepancy may be attributed to variations in diagnostic protocols, availability of imaging modalities, and reliance on clinical judgment. Our hospital lacks 24/7 access to CT imaging, and ultrasonography, although widely used, is highly operator-dependent. Furthermore, clinical decision-making in urgent settings may favor early surgical intervention over extended observation to avoid complications associated with delayed treatment.

Even when there were no differences in time with pain before surgery between groups, the duration of pain before surgical intervention is a very important aspect in the management of acute appendicitis. Patients who experienced a longer period of pain before surgery tended to have complications, underscoring the importance of timely intervention.

Our limitations include a relatively small sample, and the lack of data in expedients as adhesions to deepen the analysis of risk factors.

Table 3
Risk factors for underwent to a negative appendectomy.

Variable	OR (95% CI)	*p*
Previous abdominal surgery	2.75 (1.19–6.37)	**0.018***
Alvarado score <7	8.52 (4.05–17.90)	**<0.001***
Not abdominal pain	5.38 (2.62–11.06)	**<0.001***
Not rebound tenderness	3.80 (1.81–8.00)	**<0.001***
Not leukocytosis	4.13 (1.92–8.86)	**<0.001***
Not neutrophilia	4.63 (2.18–9.85)	**<0.001***

*Logistic regression.

Conclusion

In conclusion, our study highlights the complexity of diagnosing acute appendicitis, with a negative appendectomy rate of 11.7%, aligning with reported rates in similar healthcare settings. The findings emphasize the need for ongoing refinement of diagnostic strategies, as imaging techniques and clinical scoring systems, such as the Alvarado score, may not always be reliable predictors. Factors such as previous abdominal surgeries and the variability in symptom presentation across different populations further complicate the diagnosis. Future research should focus on improving diagnostic accuracy to reduce the negative appendectomy rate and exploring the role of risk factors to optimize clinical decisions.

CRediT authorship contribution statement

Francisco Antonio Rodriguez-Garcia: Investigation, Conceptualization. **Carlos Enrique Rodríguez-Sánchez:** Supervision. **Julio Cesar Naranjo-Chávez:** Supervision. **Christian Jorge Torres-Ortiz-Ocampo:** Conceptualization. **Fabián Rojas-Larios:** Data curation. **Karen Covarrubias-Ramírez:** Resources, Project administration. **Eduardo Missael Evangelista-Ruiz:** Methodology, Investigation. **Quitzia Libertad Torres-Salazar:** Writing – review & editing, Writing – original draft, Formal analysis.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethics approval

Approval was obtained from the ethics committee of the Colima Regional University Hospital (approval number: CI/2023/02/SR/CIR/185). The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

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