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# Is acute appendicitis still misdiagnosed?

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**Abstract:** Objective. The optimal diagnostics and treatment of acute appendicitis continues to be a challenge. A false positive diagnosis of appendicitis may lead to an unnecessary operation, which has been appropriately termed negative appendectomy. The aim of our study was to identify the effectiveness of preoperative investigations in preventing negative appendectomy. Methods. A retrospective study was performed on adult patients who underwent operation for suspected acute appendicitis from 2008 to 2013 at Vilnius University Hospital Santariskiu Klinikos. Patients were divided into two groups: group A underwent an operation, where appendix was found to be normal (non-inflamed); group B underwent an appendectomy for inflamed appendix. Groups were compared for preoperative data, investigations, treatment results and pathology findings. Results. 554 patients were included in the study. Preoperative laboratory tests results of hemoglobin, hematocrit concentrations and white blood cell count were significantly higher in group B ($p<0.001$). Ultrasonography was performed for 78 % of patients in group A and 74 % in group B and did not provide any statistically significant results. Comparing Alvarado score results, there were more patients with Alvarado score less than 7 in group A than in group B. In our large series we could find only four independent risk factors, and they could only account for 24 % of cases. Conclusions. In summary, acute appendicitis is still often misdiagnosed and the ratio of negative appendectomies remains rather high. Additional investigations such as observation and computed tomography should be used to prevent this.

**Keywords:** Acute appendicitis, Negative appendectomy, Delay appendectomy

## 1 Introduction

Acute appendicitis (AA) is the most frequent acute abdomen disease with the lifetime incidence of approximately 7%, which requires operative treatment due to its life threatening complications. Imitation of the symptoms makes appendicitis similar to other urgent abdomen pathologies and causes diagnostic difficulties, especially in early disease manifestation [1]. Clinical examination, laboratory and radiological tests are essentials to suspect and obtain correct diagnosis [2, 3]. Inaccurate diagnosis of appendicitis follows the unnecessary operation. A term negative appendectomy implies appendectomy for not inflamed appendicitis and reports its rates up to 40% [3, 4]. Despite the fact that surgical appendectomy is the gold standard of AA, there are studies of conservative antibiotic treatment with low morbidity and mortality rate, and a recurrence rate between 7-15 % [5]. On the other hand, delay of operative treatment can stimulate the development of complications [6-8]. Co-morbidity and negative appendectomy are strongly related with higher mortality, where co-morbidity, diagnostic failure, and the anesthetic or surgical trauma are the important factors [9]. Abdominal ultrasound and computed tomography (CT) imaging with the clinical manifestation should be the key to reduce negative appendectomy rate, but none of these completely prevents a negative operation. Moreover, the surgeon mostly relies on his clinical examination and experience, supplementing it with a scoring system [10].

The aim of our study was to identify factors associated with negative appendectomy and to propose solutions to decrease the negative appendectomy rate.

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## 2 Methods

A retrospective study was performed. All adult patients (18 years and older) who underwent operation for suspected AA from 2008 to 2013 at Vilnius University Hospital Santariskiu Klinikos were included in the study. Case histories of patients, who were treated for suspected AA, were retrospectively reviewed. Data on history, clinical examination, laboratory, imaging investigation and Alvarado score were collected retrospectively from patient charts.

The following parameters were included: demographics (age, gender, body mass index), hours from onset of symptoms to diagnosis, hours from diagnosis to operation, laboratory tests (hemoglobin (Hgb), C-reactive peptide (CRP) concentration, hematocrit (Hct), white blood cell (WBC) count), Alvarado score, abdominal ultrasound or CT findings, gynecological examination results, method of operation, postoperative and pathological diagnoses.

Patients were divided into two groups based on intraoperative findings: patients in group A underwent an operation, where appendix was found to be normal (non-inflamed); patients in group B underwent appendectomy for inflamed appendix. Groups were compared for preoperative data, investigations, treatment results and pathology findings.

Categorical variables are expressed as frequencies and percentages and continuous variables as mean and standard deviation (±SD). The level of statistical significance was set at $p < 0.05$. All differences for which the probability value was less than 0.05 were considered to be significant in univariate analysis. All significant univariate risk factors were included in a multiple logistic regression model in order to identify independent predictive factors for AA. We conducted all statistical analyses using SPSS version 13.0 for Windows (SPSS Inc.).

The study was approved by regional ethics committee.

Informed consent has been obtained from all individuals included in this study

## 3 Results

Five hundred and fifty four patients were included in the study: one hundred twenty seven (22.9%) patients in group A and 427 (77.1%) patients in group B. Demographics, clinical characteristics, preoperative laboratory tests results and Alvarado score distribution frequencies are summarized in Table 1. The mean age of the study population was 31 years (range 18-88). The male/female ratio was 1.23/1 in both groups. Preoperative laboratory tests results of Hgb, Hct concentrations and WBC count were significantly higher in group B ($p < 0.001$). Comparing Alvarado score results, there were more patients with Alvarado score less than 7 in group A with significant difference. The patients' situations in group B were vice versa – there were more patients with Alvarado score 7 or higher. The three main Alvarado characteristics were migratory pain to right lower quadrant, tenderness in right lower quadrant and leukocytosis (Table 1).

Preoperative investigations are presented in Table 2. Abdominal or pelvic ultrasonography was performed for 75% of patients and abdominal CT was performed for only 3.4% of patients.

24% patients underwent laparoscopy, of the 6.5% were converted to open appendectomy, 0.9% – to midline laparotomy. 59.7% patients underwent open appendectomy, 1.3% patients were converted to midline laparotomy. Intraoperative findings are presented in Table 3. Two hundred eighty one (66%) patient of group B had phlegmonous appendicitis, 81 (19%) patient – gangrenous appendicitis, and 65 (15%) patients were with perforated gangrenous appendicitis.

Table 4 presents comparison of intra-operative findings with the pathological results. We identified 4 cases of phlegmonous appendicitis (1.4%), which were reported as non-inflamed appendix on pathologic examination. We also found 8 cases of macroscopically normally-appearing appendix, where pathology identified acute inflammation (15.4%).

All significant univariate risk factors were included in a multiple logistic regression model in order to identify independent risk factors (Table 5). Only four independent risk factors – gender, time in hours from the onset of symptoms to diagnosis, WBC count and neutrophilia were predictive of AA. R square coefficient for this model was only 0.24.

The outcomes in patients undergoing negative appendectomy or unnecessary operation did not differ from those, which had AA (Table 1) – the hospital stay was the same and there was no mortality.

## 4 Discussion

A retrospective study found the rate of negative appendectomy for 22.9%. A meta-analysis by Andersson has demonstrated that all clinical and laboratory variables are weak factors alone, but they can improve sensitivity in combination [11]. However, in our relatively large series we

could find only four independent risk factors, which, if all present, could account for only 24% of cases.

The key point of proper patient care lies in a balance between the perforated appendicitis and the negative appendectomy. Delayed diagnosis is one of the main causes of perforated appendicitis. Physicians should be cautious of delaying surgery of AA since after 36 hours of untreated symptoms, the risk of perforation is increased to 5% every 12 hour period [12]. In our study, the time from the patients' arrival to emergency room and diagnosis verification, transportation to operating theater differed twice between groups. Looking at this point, abdominal CT scan can reduce the time to diagnosis, which allows having correct diagnosis and decreases the chance of negative appendectomies [13].

Studies showed that abdominal CT scans are relatively accurate and increase correct AA diagnosis up to 95%. Moreover, there is a possibility to increase correct diagnosis to 98% when abdominal CT scan is combined with physical examination [14]. Stroman et al. reported the negative appendectomy rate close to 15% with only abdominal CT scan results and without taking into consideration the patient's clinical picture [13]. As we see, abdominal CT scan can improve correct diagnosis, but there is still a need of physical examination. However, in the present study abdominal CT scan was only used for a small number of patients due to its costs. The abdominal ultrasound was used in most cases – 75%. The results indicated that inflamed appendix was seen in 16.5% of patients in group A. In our opinion, this has increased the number of negative appendectomies.

**Table 1.**: Demographics, clinical characteristics, preoperative laboratory tests results and Alvarado score distribution frequencies overall and between groups

| | Overall (n=554) | Group A (n=127) | Group B (n=427) | *p* value |
|---|---|---|---|---|
| Age, years | 31 (18-88) | 30 (18-88) | 32 (18-85) | >0.05 |
| Gender | | | | |
| male, n (%) | 306 (55) | 44 (35) | 262 (61) | <0.001 |
| female, n (%) | 248 (45) | 83 (65) | 165 (39) | <0.001 |
| BMI (kg/m$^2$) | 25.2 ± 4.44 | 24.2 ± 4.84 | 25.51 ± 4.27 | 0.016 |
| Hours | | | | |
| from onset of symptoms to diagnosis | 24 (3-336) | 24 (4-336) | 20 (3-336) | <0.0001 |
| from diagnosis to operation | 2:15 | 3:20 | 1:45 | >0.05 |
| Hospital stay, days | 3 (1-34) | 3 (1-34) | 3 (1-24) | >0.05 |
| Hgb (g/l) | 140.7 ± 16 | 136.6 ± 16.7 | 141.9 ± 15.6 | <0.001 |
| Hct (l/l) | 0.41 ± 0.043 | 0.40 ± 0.042 | 0.413 ± 0.042 | <0.001 |
| WBC (*10e9/l) | 13.35 ± 4.11 | 11.43 ± 3.78 | 13.91 ± 4.04 | <0.0001 |
| CRP (mg/l) | 27.6 (0.2-364) | 34.6 (0.2-251) | 26.8 (0.2-364) | >0.05 |
| Alvarado score < 7 (n, %) | 216 (39) | 75 (59) | 144 (33.7) | <0.0001 |
| Alvarado score ≥ 7 (n, %) | 338 (61) | 52 (41) | 283 (66.3) | <0.0001 |
| Mean of Alvarado score | 6.7 ± 1.9 | 5.8 ± 1.9 | 6.9 ± 1.8 | <0.0001 |
| Migration of pain to rlq* (n, %) | 537 (96.9) | 119 (93.7) | 418 (97.9) | 0.034 |
| Anorexia (n, %) | 327 (59) | 61 (48) | 267 (62.5) | 0.005 |
| Nausea and vomiting (n, %) | 332 (59.9) | 65 (51.2) | 269 (63) | 0.016 |
| Tenderness in rlq (n, %) | 527 (95.1) | 120 (94.5) | 410 (96) | >0.05 |
| Rebound tenderness (n, %) | 299 (54) | 59 (46.5) | 243 (56.9) | 0.047 |
| Elevated body temperature (n, %) | 60 (10.8) | 17 (13.4) | 44 (10.3) | >0.05 |
| Leukocytosis (n, %) | 447 (80.7) | 82 (64.6) | 365 (85.5) | <0.0001 |
| Neutrophilia (n, %) | 416 (75) | 76 (59.8) | 340 (79.6) | 0.001 |

* – right lower quadrant

**Table 2:** Percentages (%) of laboratory tests, investigations and methods of operation overall and between groups

| | Overall | Group A | Group B |
|---|---|---|---|
| Laboratory tests | | | |
| Hgb | 100 | 100 | 100 |
| Hct | 100 | 100 | 100 |
| WBC | 100 | 100 | 100 |
| CRP | 70.2 | 74.8 | 68.9 |
| Urine analysis | 52.3 | 49 | 53 |
| Ultrasonography | 75 | 78 | 74 |
| Visualized appendix | 26.7 | 17 | 29.5 |
| Visualized inflamed appendix | 24.9 | 16.5 | 27.4 |
| Infiltrated rlq* | 22.2 | 20 | 23 |
| Enlarged lymphnodes | 6.7 | 11 | 5.4 |
| Computed tomography | 3.4 | 5 | 3 |
| Gynecological examination | 83.5 | 83 | 84 |
| Method of operation | | | |
| Open app. | 59.7 | 32 | 68 |
| Laparoscopic app. | 24 | 24 | 24 |
| Diagnostic laparoscopy | 8.5 | 37 | 0 |
| Conversion** | 6.5 | 4 | 7 |
| Laparotomy | 1.3 | 2 | 1 |

* – right lower quadrant
** – conversion from laparoscopic to open appendectomy

**Table 3:** Intraoperative diagnoses and appendectomies performed

| Intraoperative diagnoses | n (% of all operations) | Appendectomies performed n (% of all operations) |
|---|---|---|
| Macroscopically inflamed appendix | | |
| Phlegmonous appendicitis | 281 (50.72) | 281 (100) |
| Gangrenous appendicitis | 81 (14.62) | 81 (100) |
| Perforated gangrenous appendicitis | 65 (11.73) | 65 (100) |
| Macroscopically normal appendix | 53 (9.57) | 52 (98.1) |
| Adenocarcinoma of the appendix | 1 (0.18) | 1 (1) |
| Mesenteric lymphadenitis | 26 (4.69) | 4 (15.4) |
| Acute enteritis | 9 (1.62) | 1 (11.1) |
| Pelvic inflammatory disease | 9 (1.62) | --- |
| Abdominal colic | 7 (1.26) | --- |
| Terminal ileitis | 2 (0.36) | --- |
| Acute colitis | 2 (0.36) | --- |
| Acute enterocolitis | 1 (0.18) | --- |
| Ovarian cyst | 1 (0.18) | --- |
| Acute pancreatitis | 1 (0.18) | --- |
| Menstruation | 1 (0.18) | --- |
| Rupture of ovary | 8 (1.44) | --- |
| Torsion and necrosis of part of the greater omentum | 4 (0.72) | --- |
| Abscess of the greater omentum | 1 (0.18) | --- |
| Torsion and necrosis of appendix epiploica | 1 (0.18) | --- |

**Table 4:** Intraoperative and pathological diagnoses of appendix

| Intraoperative diagnoses | Pathological diagnoses | | |
|---|---|---|---|
| | n (%) | Non-inflamed appendix, n (%*) | Inflamed appendix, n (%*) |
| Phlegmonous appendicitis | 281 (57.9) | 4 (1.4) | 277 (98.6) |
| Gangrenous appendicitis | 81 (16.7) | --- | 81 (100) |
| Perforated gangrenous appendicitis | 65 (13.4) | --- | 65 (100) |
| Macroscopically normal appendix | 52 (10.7) | 44 (84.6) | 8 (15.4) |
| Adenocarcinoma of the appendix | 1 (0.2) | 1 (100) | --- |
| Mesenteric lymphadenitis | 4 (0.8) | 4 (100) | --- |
| Acute enteritis | 1 (0.2) | 1 (100) | --- |

* – percentages (%) of intraoperative diagnosis

**Table 5:** Multivariate analysis of diagnostic criteria for acute appendicitis

| Variable | p value | Odds ratio | 95% CI |
|---|---|---|---|
| Gender | <0.001 | 0.256 | 0.147–0.446 |
| Hours* | 0.013 | 0.994 | 0.989–0.999 |
| WBC | 0.003 | 1.131 | 1.042–1.227 |
| Neutrophilia | 0.044 | 0.529 | 0.284–0.983 |

* – from onset of symptoms to diagnosis

The Alvarado score and clinical diagnosis of appendicitis have remained relevant concepts [15]. Patients, who scored 3-6 points, with reference to Alvarado score, were more likely to have negative appendectomy. Although Alvarado score of less than 7 has been suggested to exclude AA, in our study there were 66.3% patients with inflamed appendix, who had Alvarado score of up to 7 [16]. Therefore, we would advise additional tests prior to operation, such as abdominal CT scan.

With regards to operation type, the study results have showed that laparoscopic operation was chosen more often in group A (61.41% vs. 24%). However, there was no difference in operating time or rate of complications. As for demographic data, there was difference comparing age or body mass index. Nevertheless, negative appendectomies were performed for females more often than males (65% vs. 35%, respectively).

This review has demonstrated that elements of the disease history, clinical findings and results of laboratory tests are weak individual discriminators of appendicitis.

# 5 Conclusions

In summary, AA is still often misdiagnosed and the rate of negative appendectomies remains rather high. A high rate of negative appendectomy is caused by using solely clinical examinations to diagnose AA. Additional investigations such as observation and abdominal CT should be used to prevent this.

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# References

[1] Ohle R, O'Reilly F. O'Brien KK, Faheu T, Dimitrov BD. The Alvarado score for predicting acute appendicitis: a systematic review. BMC Med. 2011; 9:139
[2] Pisano M, Coccolini F, Poiasina E, Bertoli P, Capponi MG, Poletti E et al. Conservative treatment for uncomplicated acute appendicitis in adults. Emerg Med Health Care. 2013; 1:2
[3] Ruffolo C, Fiorot A, Pagura G, Antoniutti M, Massani M, Caratozzolo E et al. Acute appendicitis: What is the gold standard of treatment? World J Gastroenterol. 2013; 19(47): 8799-8807
[4] Zoarets I, Poluksht N, Halevy A. Does Selective Use of Computed Tomography Scan? Reduce the Rate of "White" (Negative) Appendectomy. Isr Med Assoc J. 2014; 16:335-337
[5] Hansson J, Korner U, Khorram-Manesh A, Solberg A, Lundholm K. Randomized clinical trial of antibiotic therapy versus appendicectomy as primary treatment of acute appendicitis in unselected patients. Br J Surg. 2009; 96(5):473-481
[6] Clyde C, Bax T, Merg A, MacFarlane M, Lin P, Beyersdorf S et al. Timing of intervention does not affect outcome in acute

appendicitis in a large community practice. Am J Surg. 2008; 195(5):590-593
[7] Eldar S, Nash E, Sabo E, Matter I, Kunin J, Mogilner JG et al. Delay of surgery in acute appendicitis. Am J Surg. 1997; 173:194-198
[8] Gupta A, Regmi S, Hazra NK, Panhani ML, Talwar OP. Clinically monitored delay-A valid option in cases with doubtful diagnosis of acute appendicitis. Indian J Surg. 2010; 72:215-219
[9] Andersson MN, Andersson RE. Causes of short-term mortality after appendectomy: a population-based case-controlled study. Ann Surg. 2011 Jul; 254(1):103-107
[10] Krajewski S, Brown J, Phang PT, Raval M, Brown CJ. Impact of computed tomography of the abdomen on clinical outcomes in patients with acute right lower quadrant pain: a meta-analysis. Can J Surg. 2011; 54(1): 43-53
[11] Andersson R.E. Meta-analysis of the clinical and laboratory diagnosis of appendicitis. Br J Surg. 2004; 91:28-37
[12] Wagner PL, Eachempati SR, Soe K, Pieracci FM, Shou J, Barie PS. Defining the current negative appendectomy rate: For whom is preoperative computed tomography making an impact? Surgery. 2008; 144(2):276-282
[13] Stroman DL, Bayouth CV, Kuhn JA, Westmoreland M, Jones RC, Fisher TL et al. The role of computed tomography in the diagnosis of acute appendicitis. Am J Surg. 1999; 178:485-489
[14] Jones K, Peña A, Dunn EL, Nadalo L, Mangram AJ. Are negative appendectomies still acceptable? Am J Surg. 2004; 188(6):748-754
[15] Hong JJ, Cohn SM, Ekeh AP, Newman M, Salama M, Leblang SD. A prospective randomized study of clinical assessment versus computed tomography for the dzagnosis of acute appendicitis. Surg Infect. 2003; 4(3):231-239
[16] Alvarado A. A practical score for the early diagnosis of acute appendicitis. Ann Emerg Med. 1986; 15:557-564