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Original research

Diagnostic value of serum fibrinogen as a predictive factor for complicated appendicitis (perforated). A cross-sectional study

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HIGHLIGHTS

- AA is the most common indication for emergency abdominal surgery without a diagnostic method for complicated appendicitis.
- Serological methods to estimate the severity of acute appendicitis are currently of interest.
- The serum fibrinogen is a possible, easy, and accessible marker that can predict a complicated appendicitis.
- We demonstrate that serum fibrinogen has a high sensitivity and specificity for complicated appendicitis.

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ABSTRACT

Background: Acute appendicitis (AA) has a prevalence of 8% in the general population with a rate of complicated (perforated) appendicitis (CA) up to 40%. Serum fibrinogen may serve as an indicator for CA.
Patients and Methods: 115 patients were included from January 2012 to December 2012 using a positive pathology report for AA as a gold standard diagnostic method. We divided the patients into two groups accordingly to the pathology report: Complicated Appendicitis and Uncomplicated Appendicitis (UA). Our primary endpoint was to compare the levels of serum fibrinogen between the two groups and find if there is a relationship between fibrinogen level and CA.
Results: 68 patients were diagnosed with UA and 47 with CA. Using a fibrinogen value of 885 mg/dl we found to be the best cut-off for predicting complicated appendicitis with a sensitivity of 86.77% (76.87–93.71 IC 95%), a specificity of 91.49 (83.51–99.46 IC 95%), a positive predictive value of 93.65 (95% CI 86.81–99.64) and, a negative predictive value of 82.69 (95% CI 65.73–87.84).
Conclusion: In the setting of a patient with a clinical diagnosis of AA, this study demonstrates fibrinogen as a good predictor factor for appendiceal perforation.

1. Background

Acute appendicitis (AA) is the most common indication for an emergency abdominal surgery, with a reported prevalence of 8% in the general population [1]. Determination of the severity of appendicitis on clinical grounds is challenging for frontline surgeons, with some series reporting complicated appendicitis (CA) rates up to 40% [1–4]. There are tools to determine the severity of AA (abdominal ultrasound and computed tomography) [5–8]; nevertheless, this tools may be limited in some centers e.g. technicians that can not give a final report or lack of personnel to carry them out. Consequently, serological methods to estimate the severity of AA are currently of interest. Different authors have evaluated C-reactive protein, procalcitonin, total bilirubin, and leukocytes for predicting the severity of AA [3,5,9–14]. However,

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the use of fibrinogen as an indicator for CA has been described only by Li J et al. [15] and Mentes Ö et al. [16] (Table 6), therefore we hypothesized that the fibrinogen test could be used as a marker of severity in acute appendicitis with better sensitivity and specificity than the other serological markers.

2. Patients and Methods

Patients were included in the study if they presented to the adult emergency department with a diagnosis of acute appendicitis between January 2012 to December 2012. The initial diagnosis of acute appendicitis was carried out by performing the analysis of symptoms, physical exam and laboratory test, and we confirmed it with pathological criteria after surgery in all of them. We recorded the following variables: age (>16-year), gender, laboratory data (leukocytes, total neutrophil count, coagulation, fibrinogen) and pathology report. For the results and statistical analysis, we only included the patients older than 16-year with AA proven by the pathology analysis. We excluded all patients with a negative pathology report (no appendicitis), or histories of hemorrhagic, malignant neoplasm, thrombotic, hepatic, renal disease and having drug treatment that alter coagulation parameters.

Our primary endpoint was to compare the levels of serum fibrinogen between the patients with complicated appendicitis vs. uncomplicated appendicitis and find if there is a relationship between fibrinogen level and CA. To accomplish this, we divided the patients into two groups according to the pathological results. The patients with pathology report of an appendicitis stage I to III matched the uncomplicated appendicitis group; the patients with a stage IV of appendicitis were in the complicated group [7–10,14,17].

As reported elsewhere the stages of acute appendicitis were defined by the final pathology report as stage I edematous appendicitis, stage II suppurative appendicitis, stage III gangrenous appendicitis and stage IV perforated appendicitis [3,7,8].

3. Blood sample collection and assays

The blood samples of all enrolled patients were collected within 2 h previous to the surgical procedure. Complete blood cell count and routine coagulation tests were done on blood samples as clinically indicated. The samples were analyzed using ACL Top 3G Instrumentation Laboratory® with software 4.2.0 with a commercial kit Hemosil IL®, PT-Fibrinogen HS® (Milan, Italy) to obtain the fibrinogen level, PT, and INR.

4. Statistical analyses

The variables were tested using Kolmogorov–Smirnov test for normality. The values were expressed as mean (SD) or percentages, as appropriate. We made a comparison of average fibrinogen levels between the two groups of patients using Student t-test for independent samples or one-way ANOVA. The comparison between proportions of both groups was performed using Chi-square test (or Fisher's exact test if required).

The diagnostic performance of serum levels of fibrinogen was evaluated analyzing the ROC curves. Frequencies of positivity of fibrinogen were obtained in the group with stage IV appendicitis, and through contingency table, positivity rates were compared. The calculation of the parameters of sensitivity, specificity and predictive values of the titles of these levels was determined using a Bayesian analysis. We evaluated the pathology stage of appendicitis and the preoperative value of the serum fibrinogen to investigate in the Bayesian analysis. The value of statistical significance was set at a $p \leq 0.05$. We analyzed all the information in SPSS version 21.0 (SPSS Inc, Chicago IL).

5. Ethics

The present research meets local requirements of ethics, informed consent, rights and regulations for the protection and privacy of patients. The study was performed by the principles of the Declaration of Helsinki. Approved by the Committee on Scientific Research of the Hospital Civil de Guadalajara "Dr. Juan I. Menchaca" under registration number: 1247-1213.

6. Results

The total numbers of patients screened during the study period were 150 consecutive patients with a preoperative diagnosis of AA who underwent an appendectomy. We excluded 35 (23.33%) (Table 1) leaving 115 for the statistical analyzes.

The patients were divided into two groups: UA (stage I–III) (n = 68) and CA (stage IV) (n = 47). The demographic data are shown in Tables 2 and 3. We found a trend in the prothrombin time (PT) and INR related to the severity of the disease, patients with CA showed significant difference compared with patients with UA (PT 13.51 ± 1.30 s vs. 12.12 ± 1.54 s, p = <0.001), (INR 1.18 ± 0.12 vs. 1.06 ± 0.15, p = <0.001 respectively). This result suggests that the extrinsic coagulation pathway is impaired in patients with AA, especially in CA as describe by Li J et al., 2011 [15]. Significant statistical differences in fibrinogen levels were observed in the UA group vs. the CA group (675.42 ± 213.48 vs. 1428.07 ± 514.83, p < 0.001) (Tables 2 and 4). The later demonstrates a relationship between fibrinogen level and the severity of the disease (see Graphic 1).

Graphic 2, illustrate the analysis of the ROC curve of fibrinogen level to identify patients with CA, finding an optimum sensitivity 85.9% (95% CI 76.87–93.71), and specificity 91.49% (95% CI 83.51–99.46) when calculated with a cutoff point of 885 mg/dL (AUC of 0.939, 95% CI 0.894–0.985). (Tables 4 and 5).

7. Discussion

Acute appendicitis remains a clinical diagnosis with laboratory and radiological test as an auxiliary diagnostic method. Been able to diagnose uncomplicated vs. complicated appendicitis allows the surgeon to choose the best surgical approach ranging from antibiotics and delayed appendectomy to laparotomy [20–23]. Since AA has a rate of been complicated of approximately 40% [1–4,24], different methods for predicting complications have been tested with inconsistent results. Radiological tests involving computed tomography, magnetic resonance imaging and ultrasonography prove to have an approximately 20% of false negative complicated

Table 1
Characteristic of screened patients.

Total of patients	147
Included	115
Pathology classification of included patients	
Stage I	22 (19.13%)
Stage II	28 (24.4%)
Stage III	18 (15.6%)
Stage IV	47 (40.9%)
Uncomplicated appendicitis	68 (59.13%)
Complicated appendicitis	47 (40.87%)
Excluded	32 (21.7%)
Reason for exclusion	
Pathology report different than acute appendicitis	22 (14.96%)
Coagulation of the blood sample	4 (2.7%)
Renal disease	2 (1.3%)
Oral anticoagulation therapy	3 (2.04%)
Liver insufficiency	1 (0.68%)