Clinical significance of C-reactive protein levels in the determination of pathological type of acute appendicitis

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Received July 2, 2015; Accepted July 17, 2015; Epub August 15, 2015; Published August 30, 2015

Abstract: Objective: To investigate the significance of C-reactive protein (CRP) in the discrimination of acute appendicitis pathology and its guiding role in the timing of surgery. Methods: 307 patients in our hospital from July 2012 to December 2013 were selected, who received appendectomy and simultaneous detections of WBC, neutrophil percentage and CRP; and Logistic regression analysis and Roc analysis of these indicators were conducted; Roc curve was drawn. Results: Logistic regression analysis showed that the proportion of neutrophils and CRP were the risk factors to determine gangrenous appendicitis, but the box chart and Roc curves showed that C-reactive protein was superior to neutrophil classification in determining gangrenous appendicitis (areas under the curve were 0.882 and 0.667 respectively), and the best diagnostic cutoff value was 44.42 mg/L (sensitivity 73.1%, specificity 89.5%). Conclusion: C-reactive protein levels can help distinguish pathological types of acute appendicitis, which can be used as a reference index for surgery determination.

Keywords: CRP, WBC count, neutrophil percentage, acute appendicitis, pathological type

Introduction

Acute appendicitis is the most common acute abdomen; the current treatment for appendicitis is still based on appendectomy; with the application of antibiotics and large numbers of clinical observations, some appendicitis can be treated with antibiotics, especially those simple appendicitis (inflammatory cell infiltration is limited to the mucosa and muscle layer) and cellulitis appendicitis (inflammatory cells infiltrate in the whole layer); and because of irreversible tissue necrosis, gangrenous appendicitis still needs surgery as soon as possible, but the pathological type of appendicitis cannot be determined before surgery; therefore determining or predicting the pathological type of acute appendicitis can not only help increase its diagnostic accuracy, but also help the surgeon to choose the right treatment and timing of surgery. This paper aims to investigate the role of C-reactive protein levels in determining the pathological type of acute appendicitis and surgery timing.

Materials and methods

General information

307 patients in our hospital from July 2012 to December 2013 were selected, who received appendectomy and simultaneous detections of WBC, neutrophil percentage and CRP, including 186 cases of male (60.6%) and 121 cases of female (39.4%). The age ranged between 1 and 79 years old, with an average age of 35.42±19.00 years. According to postoperative pathological observations, patients were divided into 33 cases of simple appendicitis (inflammatory cell infiltration was limited to the mucosa and muscle layer), 43 cases of cellulitis appendicitis (inflammatory cell infiltrated in the whole layer) and 25 cases of gangrenous appendicitis.

Research methods

WBC count and neutrophil percentage were tested using Sysmex XE5000 whole blood cell analyzer; CRP was detected using Omlipo auto-
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Table 1. Objective indicators of three pathological types of appendicitis

<table>
<thead>
<tr>
<th>Pathological types</th>
<th>Age (years)</th>
<th>Sex (Male/Female)</th>
<th>WBC count (10^9/L)</th>
<th>Neutrophil percentage (%)</th>
<th>CRP (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple appendicitis (n=107)</td>
<td>32.32±19.48</td>
<td>54/53</td>
<td>7.51±3.74</td>
<td>63.66±15.53</td>
<td>10.40±17.12</td>
</tr>
<tr>
<td>Cellulitis appendicitis (n=122)</td>
<td>34.84±17.80</td>
<td>81/41</td>
<td>12.23±4.21</td>
<td>81.70±11.65</td>
<td>20.99±28.03</td>
</tr>
<tr>
<td>Gangrenous appendicitis (n=78)</td>
<td>37.53±22.12</td>
<td>51/27</td>
<td>12.06±5.69</td>
<td>83.01±8.52</td>
<td>85.84±56.73</td>
</tr>
</tbody>
</table>

Table 2. Two-dimensional Logistic regression analysis

<table>
<thead>
<tr>
<th>Objective indicators</th>
<th>Regression coefficient (B)</th>
<th>Standard error (SE)</th>
<th>Wald</th>
<th>p-value</th>
<th>OR-value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.014</td>
<td>0.010</td>
<td>1.901</td>
<td>0.168</td>
<td>1.014</td>
<td>0.994</td>
</tr>
<tr>
<td>Sex</td>
<td>-0.452</td>
<td>0.380</td>
<td>1.418</td>
<td>0.234</td>
<td>0.636</td>
<td>0.302</td>
</tr>
<tr>
<td>WBC count</td>
<td>0.033</td>
<td>0.046</td>
<td>0.508</td>
<td>0.476</td>
<td>1.034</td>
<td>0.944</td>
</tr>
<tr>
<td>Neutrophil percentage</td>
<td>0.041</td>
<td>0.021</td>
<td>3.944</td>
<td>0.047</td>
<td>1.042</td>
<td>1.001</td>
</tr>
<tr>
<td>CRP</td>
<td>0.041</td>
<td>0.005</td>
<td>59.60</td>
<td>0.000</td>
<td>1.042</td>
<td>1.031</td>
</tr>
<tr>
<td>Constant</td>
<td>-6.740</td>
<td>1.577</td>
<td>18.743</td>
<td>0.000</td>
<td>0.001</td>
<td></td>
</tr>
</tbody>
</table>

mantic specific protein analysis system. The preoperative WBC count, neutrophil percentage and CRP test results of 307 patients were used to draw box plot, showing the distribution of them in different pathologic types of appendicitis; the Logistic regression and Roc analysis of WBC count, neutrophil percentage and CRP levels were performed, and Roc curves were drawn to explore the effect of the three on discriminating gangrenous appendicitis and calculate the best diagnostic threshold.

Statistical methods

SPSS19.0 statistical software was used for statistical analysis and picture drawing. Measurement data were presented as X±s; Logistic regression analysis and Roc analysis of laboratory test data (WBC count, neutrophil percentage and CRP) of patients with different pathological types of appendicitis were performed. The best diagnostic thresholds were determined by the maximum Youden index method, Youden index = sensitivity + specificity - 1.

Results

Distribution of laboratory data for different pathological types of appendicitis

The results of WBC count, neutrophil percentage and CRP test of 307 appendicitis patients were shown in Table 1. Three kinds of test results showed an increasing trend in simple appendicitis, cellulitis appendicitis and gangrenous appendicitis. The box plots indicated that: the distribution of WBC count had no obvious boundaries in three different pathological types of appendicitis; the distribution of neutrophil percentage was mainly concentrated in cellulitis appendicitis and gangrenous appendicitis, which was significantly higher than that in simple appendicitis, but there was no significant difference between cellulitis appendicitis and gangrenous appendicitis; There were significantly differences in CRP levels among the three different pathological types of appendicitis; CRP levels in simple appendicitis and cellulitis appendicitis were mostly 50 mg/L or less, while which were more than 50 mg/L in about 70% gangrenous appendicitis.

Logistic regression analyses

The Logistic regression analysis of age, sex, WBC count, neutrophil percentage and CRP test results of 307 patients showed that the proportion of neutrophils and CRP were the risk factors to determine gangrenous appendicitis, which was shown in Table 2.

Roc analysis

The Roc analysis of WBC count, neutrophil percentage and CRP test results was conducted and Roc curve was drawn; it showed that the sensitivity of CRP was superior to WBC and neutrophils classification in judging gangrenous appendicitis, and the best diagnostic
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If a preliminary judgment was made according to the pathological type of acute appendicitis preoperatively, it will help surgeons make a reasonable treatment decision.

From the beginning of the 1990s, CT has been used for the diagnosis of appendicitis. Diagnostic accuracy and preliminary determination on preoperative pathological types of appendicitis has been greatly improved. But the application of CT in the diagnosis of acute appendicitis was restricted by various factors, such as higher cost, pregnant women contraindicated to x-rays, and so on. So the doctor’s subjective experience still played a key role in appendicitis diagnosis and surgical decision making [6-8]. Presentation of the disease and pain tolerance was different with different patients, and some deviations of subjective expression may also affect the doctors’ decisions. Therefore, this study attempted to explore the correlation between pathological types of acute appendicitis and white blood cell count, proportion of neutrophil and C-reactive protein level in order to find an objective indicators to guide physician for treatment decisions.

In this group Logistic multivariate analysis were used and the result showed that the proportion of neutrophil and C-reactive protein were risk factors for the determination of gangrenous appendicitis. As can be seen from the box plot, the proportion of neutrophil was more concentrated in the distribution of cellulitis appendicitis and gangrenous appendicitis, both of which were higher than simple appendicitis. But the difference was not significant in the discriminant on cellulitis appendicitis and gangrenous appendicitis, both of which were higher than simple appendicitis. But the difference was not significant in the discriminant on cellulitis appendicitis and gangrenous appendicitis; C-reactive protein level was significantly different in the three different types of appendicitis in pathology. C-reactive protein level was less than 50 mg/L in most simple appendicitis and cellulitis appendicitis while it was more than 50 mg/L in more than about 70% of gangrenous appendicitis, we can also

### Table 3. Areas under the curve

<table>
<thead>
<tr>
<th>Test results</th>
<th>Area</th>
<th>SE</th>
<th>p-value</th>
<th>95% CI</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>The lower limit</td>
<td>The upper limit</td>
</tr>
<tr>
<td>WBC count</td>
<td>0.602</td>
<td>0.037</td>
<td>0.007</td>
<td>0.530</td>
<td>0.674</td>
</tr>
<tr>
<td>Neutrophil percentage</td>
<td>0.667</td>
<td>0.032</td>
<td>0.000</td>
<td>0.605</td>
<td>0.729</td>
</tr>
<tr>
<td>CRP</td>
<td>0.882</td>
<td>0.025</td>
<td>0.000</td>
<td>0.834</td>
<td>0.930</td>
</tr>
</tbody>
</table>

Discussion

Due to lacking of specific laboratory examination, selection on the diagnosis and treatment of acute appendicitis still haunted the emergency surgeons. Currently, most surgeons still advocated early appendectomy, but surgery was not the only treatment. Non-surgical treatment with antibiotics was also an important method for treatment of acute appendicitis [1, 2]. More and more evidence suggested that using a sufficient amount of antibiotic for the treatment of acute appendicitis was safe and effective. Although there was a certain recurrence rate, compared with postoperative complications after appendectomy, they were pros and cons [3-5]. However, the treatment effect of antibiotic and post-operative complications varied according to different pathological types of acute appendicitis. If a preliminary judgment was made according to the pathological type of acute appendicitis, it will help surgeons make a reasonable treatment decision.
find that diagnostic sensitivity of C-reactive protein for gangrenous appendicitis was better than the proportion of neutrophils and white blood cell count (Area under the curve were 0.882, 0.667 and 0.602, respectively). Best diagnostic value was 44.42 mg/L (sensitivity was 73.1% and specificity was 89.5%). In other words, if C-reactive protein level was greater than 45 mg/L, the higher the CRP values was, the stronger the specificity will be. Appendectomy should be considered as early as possible in order to avoid delaying treatment caused by antibiotic treatment and increasing complications caused by wound, intra-abdominal and other infections.

CRP was originally found in 1930 by Tillet and Fancis which was a non-specific acute phase proteins synthesized by hepatocytes. As a reaction product of non-disease-specific acute inflammation, CRP was not affected directly by commonly used anti-inflammatory or immunosuppressant, fever, increased erythrocyte sedimentation rate, leukocyte and other factors. Thus changes in serum levels of CRP may serve as an objective indicator for infection and efficacy [9]. However, CRP was not a specific marker for acute appendicitis. We should rule out the presence of infection such as diverticulitis, biliary tract infections, and urinary tract infections. We use C-reactive protein level to distinguish pathological type of acute appendicitis on the premise of acute appendicitis, and it can play a role in treatment decisions for us.

In summary, CRP had a guiding role in the choice of surgical treatment for patients with clinical diagnosis of acute appendicitis. When CRP level was greater than 45 mg/L, the higher the CRP value was, the greater specificity for gangrenous appendicitis will be. Surgical treatment should be taken as soon as possible. Treatment of acute appendicitis still needs to be considered. Course of acute appendicitis was an evolving process. For normal or low levels of CRP in patients with antibiotics treatment, CRP levels should be observed dynamically. Vital signs and abdominal signs should be observed closely. Accurately grasp the timing of surgery, and try to avoid the extra damage caused the delay of the treatment.

Disclosure of conflict of interest

None.

References