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ORIGINAL ARTICLE

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# A fertile-aged woman with right lower abdominal pain but unelevated leukocyte count and C-reactive protein

## Acute appendicitis is very unlikely

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**Abstract** *Background and aims:* An uninflamed appendix at appendectomy represents a misdiagnosis. In fertile-aged women, the diagnostic accuracy in acute appendicitis is usually lower than 60%. We studied the role of preoperative leukocyte count and C-reactive protein (CRP) measurements in the diagnosis of acute appendicitis in fertile-aged women with a clinical suspicion of acute appendicitis. In particular, what is the clinical value of unelevated leukocyte count and CRP in excluding acute appendicitis in these patients? *Methods:* We calculated the mean leukocyte count and CRP values in (1) 100 consecutive fertile-aged women operated on for a clinical suspicion of acute appendicitis but with an uninflamed appendix found at appendectomy, and (2) 100 consecutive fertile-aged women operated on for a clinical suspicion of acute appendicitis and acute appendicitis found at appendectomy. The percentages of patients with (1) both values unelevated, (2) only leukocyte count elevated, (3) only CRP value elevated, or (4) both values elevated were calculated within the groups A (uninflamed appendix) and B (acute appendicitis). *Results:* The mean leukocyte value was significantly ($P<0.001$) higher in patients with acute appendicitis ($13.7\times10^9$/l) than in those with an uninflamed appendix ($10.6\times10^9$/l). Similarly, the mean CRP value was significantly ($P<0.05$) higher in patients with acute appendicitis (42 mg/l) than in those with an uninflamed appendix(29 mg/l). Taken together, 24 patients were operated on for a clinical suspicion of acute appendicitis, although preoperative leukocyte count and CRP values were unelevated. An uninflamed appendix was found in all these patients at appendectomy. *Conclusion:* Although clinical symptoms and signs indicated acute appendicitis, unelevated leukocyte count and CRP values excluded it, with a 100% predictive value in the current study of fertile-aged women. In our patients, 24% (24 of 100) of unnecessary appendectomies could have been avoided by trusting in this finding.

**Key words** Acute appendicitis · Appendectomy · CRP · Fertile-aged women · Leukocyte count

## Introduction

The most common diagnostic problem in clinical surgery is very probably a patient with right lower abdominal pain: appendectomy or not? The diagnosis is still difficult and – too often – incorrect. In females, the diagnostic accuracy in acute appendicitis is usually as low as 60–70% [1, 2, 3, 4] and, in fertile-aged women, the results are even less satisfactory with the diagnostic accuracy rate usually lower than 60% [1, 3], which is mainly due to gynecological disorders such as a rupture of an ovarian cyst or pelvic inflammatory disease, both of

which mimic acute appendicitis. In particular, the question still remains, how to avoid unnecessary appendectomies in fertile-aged women who have symptoms and signs suggesting acute appendicitis but, in fact, symptoms and signs are of origins other than appendiceal.

It seems to us, that, too often (if not always), an uninflamed appendix is found at appendectomy when leukocyte count and C-reactive protein (CRP) values were unelevated preoperatively. This feel for unnecessary appendectomies led us to study the preoperative leukocyte counts and CRP values in fertile-aged women who had been operated on for a clinical suspicion of acute appendicitis. In particular, the aim of the present work was to study the clinical value of unelevated leukocyte count and CRP in excluding acute appendicitis in fertile-aged women with right lower abdominal pain.

## Patients and Methods

All the patients were operated on between 1993 and 1997 in Turku University Central Hospital, which is a 1200-bed teaching hospital serving an area of 435,000 inhabitants in south-western Finland. Two groups of fertile-aged women (range 15–45 years) were included in the present retrospective study:

Group A.

One hundred consecutive fertile-aged women operated on for a clinical suspicion of acute appendicitis but an uninflamed appendix found at appendectomy. Most patients in this group suffered from non-specific abdominal pain, but a number of inflammatory and non-inflammatory diseases including rupture of an ovarian cyst, acute diverticulitis, urinary tract infection, and mesenteric lymphadenitis were also found (see *Discussion*). The mean age of the patients in this group was 28 years.

Group B.

One hundred consecutive fertile-aged women operated on for a clinical suspicion of acute appendicitis and acute appendicitis found at appendectomy. Eighty-five patients had an uncomplicated acute appendicitis and 15 suffered from a complicated disease (perforated appendix or periappendicular abscess). The mean age of the patients in this group was 29 years.

The diagnosis was confirmed in all cases by a histological examination of the appendix. Since some degree of superficial inflammation may follow drainage of exudate into the appendix from a more proximal lesion such as ileitis, the histological diagnosis of acute appendicitis required some involvement of the muscularis of the appendix. In all cases, at least two transverse sections from the proximal half of the appendix and one longitudinal section from the distal half of the appendix were studied.

Blood samples were obtained from the patients on admission to hospital. In those few cases in which patients underwent appendectomy only after a follow-up period, an additional blood sample taken after the follow-up period but before the operation was used for laboratory measurements. Leukocyte count was determined using an electronic cell counter (Coulter Counter T 890; Coulter Electronics, Hialeah, Fla.). The concentration of CRP was measured by means of immunoturbidimetry (Hitachi 717, Hitachi, Tokyo, Japan). The surgeon on duty was conscious of both laboratory results before he/she decided to operate. The upper limit of the reference interval for leukocyte count was $9\times10^9$/l and for CRP 10 mg/l.

Both patient groups (A and B) were divided into four subgroups according to the preoperative leukocyte counts and CRP values of the patients as follows:

Subgroup 1. Both leukocyte count and CRP values were unelevated
Subgroup 2. Only leukocyte count was elevated; CRP value was unelevated
Subgroup 3. Only CRP value was elevated; leukocyte count was unelevated
Subgroup 4. Both leukocyte count and CRP values were elevated

The number of patients in these four subgroups was calculated within both patient groups (A and B) and expressed as a percentage. Data are presented as means±SEM in groups A and B. The student's *t*-test (unpaired, two-sided) was used for comparison of laboratory values between the groups A and B.

## Results

Table 1 shows the mean±SEM values for leukocyte count and CRP in patient groups A (uninflamed appendix) and B (acute appendicitis). The mean leukocyte count was significantly ($P<0.001$) higher in patients with acute appendicitis (group B) than in those with an uninflamed appendix (group A). Similarly, the mean CRP value was significantly higher in patients with acute appendicitis (group B) than in those whose appendix proved to be uninflamed at appendectomy (group A), although the statistical difference ($P<0.05$) was less than that between the leukocyte counts.

Figure 1 shows the division of the patient groups A and B into four subgroups according to the preoperative leukocyte counts and CRP levels. All four subgroups are relatively equally represented within group A (uninflamed appendix). In group B (acute appendicitis), the vast majority of the patients belong to either subgroup 2 (only leukocyte count elevated) or subgroup 4 (both values elevated). The most conspicuous finding, however, is that group B (acute appendicitis, $n=100$) contains no patients with both values unelevated, whereas, in group A (uninflamed appendix, $n=100$), there are 24 patients with both values unelevated.

The sensitivity of leukocyte count in the diagnosis of acute appendicitis was 90% and the specificity 36%. The sensitivity of CRP in the diagnosis of acute appendicitis was 63% and the specificity 61%. Further, the sensitivity of leukocyte count and/or CRP in combination in the diagnosis of acute appendicitis was 100% and the specificity was 24%.

**Table 1** The mean±SEM leukocyte count and C-reactive protein (CRP) value in fertile-aged women who underwent appendectomy after a clinical suspicion of acute appendicitis. *Group A*, uninflamed appendix; *Group B*, acute appendicitis

| | Leukocyte count ($\times10^9$/l) | CRP (mg/l) |
|---|---|---|
| Group A ($n=100$) | 10.6±0.4 | 29±4 |
| Group B ($n=100$) | 13.7±0.4 | 42±4 |

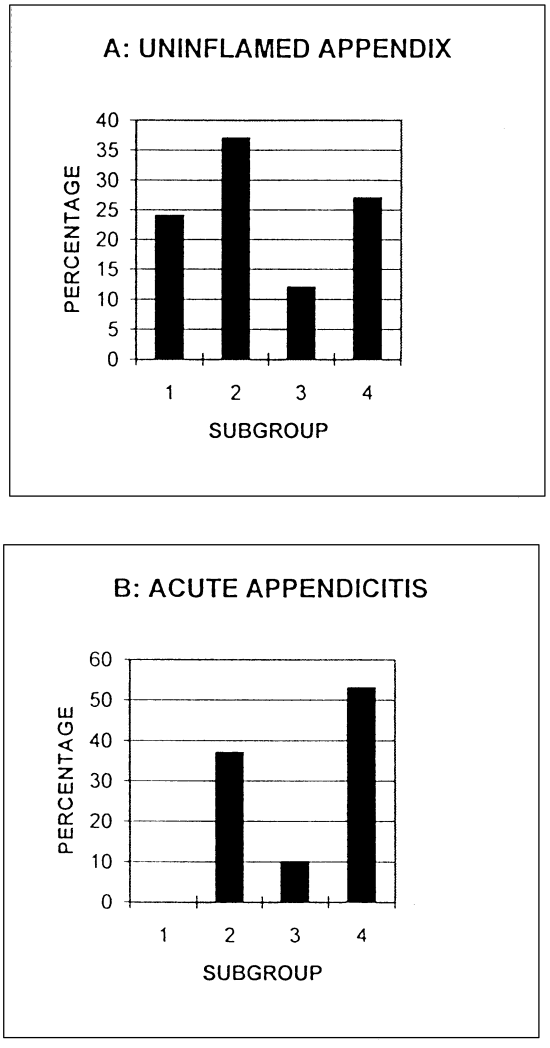


**Fig. 1** The division (percentages) of the study patients from groups A (uninflamed appendix, *n*=100) and B (acute appendicitis, *n*=100) into subgroups 1–4, according to the preoperative leukocyte counts and C-reactive protein (*CRP*) values. *Subgroup 1*, both values unelevated; *subgroup 2*, only leukocyte count elevated; *subgroup 3*, only CRP elevated; *subgroup 4*, both values elevated

## Discussion

The current results indicated that either leukocyte count or CRP value or both were elevated preoperatively in all fertile-aged women with acute appendicitis (*n*=100). However, in those with an uninflamed appendix at appendectomy (*n*=100), there were 24 women with both of these values unelevated preoperatively. Thus, all those patients who had been operated on for a clinical suspicion of acute appendicitis, despite the preoperative leukocyte count and CRP value being unelevated, presented an uninflamed appendix at appendectomy. In other words, in the present series of 100 consecutive fertile-aged women with acute appendicitis and 100 consecutive fertile-aged women with an uninflamed appendix at appendectomy, unelevated leukocyte count and CRP value excluded acute appendicitis with a 100% predictive value. In our patients, 24% (24 of 100) of unnecessary appendectomies could have been avoided by trusting in this finding. In this group of 24 patients with unnecessary appendectomies, there were 14 patients with non-specific abdominal pain, five with rupture of ovarian cyst, three with urinary tract infection, one with tiny omental fat necrosis and one with mesenteric lymphadenitis. None of these 24 patients had needed surgical intervention. Based on the present results, we do not recommend appendectomy to be performed in a fertile-aged woman with unelevated leukocyte count and CRP value, not even if clinical symptoms and signs indicate acute appendicitis. These patients should be treated by careful clinical follow-up and additional leukocyte count and CRP measurements during the follow-up period. If clinical symptoms and signs of acute appendicitis continue and leukocyte count and/or CRP value increase above the upper limit of the reference interval, the patient should undergo laparoscopy for a precise diagnosis. Otherwise, careful clinical follow-up should be continued and additional blood samples should be taken for leukocyte count and CRP measurements. We have changed our own treatment strategy accordingly and our initial experiences are most encouraging.

The measurement of the leukocyte count has been previously reported to be a more sensitive laboratory test than the measurement of the CRP value in diagnosing acute appendicitis [4]. The results of the present study support this view. Previous studies have indicated that, during the course of acute appendicitis, the increase in leukocyte count is a very early marker of appendiceal inflammation and, only later, during protracted inflammation, do acute-phase reactants such as CRP increase [5, 6, 7].

In fertile-aged women, the diagnostic accuracy in acute appendicitis is usually lower than 60% [1, 3]. Therefore, in a recent prospective randomized study aimed at reducing the rate of negative appendectomies, laparoscopy was recommended in a fertile woman with right lower abdominal pain [8]. We agree with this view. However, based on the current results, we believe that even laparoscopy may be unnecessary, if leukocyte count and CRP values are unelevated.

We conclude that although clinical symptoms and signs indicate acute appendicitis in a fertile-aged woman with right lower abdominal pain, it can be excluded if leukocyte count and CRP values are unelevated. In our patients, 24% (24 of 100) of unnecessary appendectomies could have been avoided by trusting in this finding. Accordingly, we do not recommend appendectomy to be performed in any fertile woman with right lower abdominal pain who has unelevated leukocyte count and CRP values.

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