Predictive value of C-reactive protein in children with appendicitis

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Few studies have addressed the predictive value of C-reactive protein at different cutoff values in appendicitis. We have determined the cutoff values for C-reactive protein levels at different periods during clinical evolution of appendicitis and established their use to support the diagnosis of appendicitis.

The analysis of C-reactive protein levels demonstrated a high sensitivity to differentiate patients with and without appendicitis. C-reactive protein levels can be used to support the clinical diagnosis of appendicitis, and depending on time from onset of symptoms to diagnosis, they also can be used to differentiate patients with and without appendicitis.

The determination of C-reactive protein levels in patients with suspected appendicitis will help to diagnose appendicitis earlier, avoiding perforation and consequently avoiding the economic and legal consequences associated with complications of appendicitis.

The classic clinical picture of appendicitis has been widely known for more than 110 years [1], and described mainly in adults. Some atypical symptoms that could lead to errors in the diagnosis of appendicitis have also been described in young adults and children [1, 2].

The problem with an erroneous diagnosis of appendicitis is that the removal of a normal appendix or, on the contrary, the delay in treatment of appendicitis associated to its major complications, such as phlegmon, abscess or peritonitis, has ethical, economical and legal implications [3, 4].

To avoid these problems and to improve the early and accurate diagnosis of appendicitis, technological approaches to diagnose appendicitis have been developed, including ultrasound, computed tomographic scan with intravenous contrast or immunological markers, magnetic resonance imaging, radiological contrasted techniques, and many different laboratory tests including C-reactive protein (CRP) [4-8].

The role of CRP levels in patients with appendicitis has been extensively studied in adults [9-14]. Some studies have addressed the predictive value of CRP at different cutoff levels in adults determined by ROC curve analysis and have found that CRP levels were useful for the diagnosis of appendicitis during the first 3 days after the onset of symptoms [14].

Appendicitis is the most common cause of abdominal surgery in children. Perforation rates as high as 50 % at the initial visit have been reported due to delays in diagnosis and late visits to the emergency department [15-17].

White blood cell (WBC) counts and CRP levels are commonly obtained in children with suspected appendicitis [1, 2]. White blood cell counts have been found to be insensitive and unspecific to diagnose appendicitis [2-4] and so has CRP.

However, some studies suggest that CRP may be more sensitive than WBC in detecting appendiceal perforation [8, 9, 17]. Few studies, mostly including only adult patients, have addressed the predictive value of CRP at different cutoff values in patients with appendicitis [14-16].

Some authors have attempted to determine the cutoff values for CRP levels at different periods from the time of the onset of symptoms to diagnosis in patients with histologically proven appendicitis [7, 8]; however, these and other similar studies have been performed in adult patients.

A recent retrospective report [9] analyzed the use of CRP levels in children with simple appendicitis (less than 48 hours of evolution) and children with advanced appendicitis (more than 48 hours of evolution) and concluded that a rise in CRP levels after 48 hours from the onset of symptoms was a strong indicator of appendiceal perforation.

We have determined cutoff values for CRP in children presenting at the hospital in different time slots after the onset of symptoms and we have established the sensitivity and specificity of CRP for the diagnosis of appendicitis in this population.

Establishing cutoffs

We established cutoff values based on pediatric patients (<15 years of age) having emergency surgery for suspected appendicitis. The diagnosis was established on clinical grounds. CRP levels were measured on admission.

All patients were divided into two groups according to histological diagnosis: patients with normal appendix and patients with appendicitis.

Patients in the two diagnostic groups were further divided into three more subgroups according to the time from the onset of symptoms to diagnosis: 0 to 12 hours, 13 to 24 hours, and 25 to 48 hours.

Groups were comparable in terms of gender, age and hours of evolution. For all of these groups, receiver operating characteristic (ROC) curves were constructed for CRP and the best cutoff points were used to calculate the sensitivity and specificity to discriminate patients with and without appendicitis.

The CRP levels were significantly higher in patients with appendicitis.

Variable	Normal Appendix	Appendicitis	p
Female/Male	11 (41 %)/16 (59 %)	85 (50 %)/86 (50 %)	0.534
Age (y)	10.7 ± 2.6 (5-14)	9.7 ± 3.2 (2-14)	0.068
Evolution (h)	23 ± 12 (2-52)	31.3 ± 3.3 (3-165)	0.104
CRP (mg/L)	7 ± 9 (1-48)	154 ± 210 (2-872)	0.001

TABLE I: Results of 198 patients operated for suspected appendicitis

Hours	Normal Appendix	Appendicitis	p
	Mean ± SD (n)	Mean ± SD (n)	
0-12	15 ± 21 (5)	79 ± 159 (47)	0.001
13-24	4 ± 1 (10)	210 ± 230 (68)	<0.0001
25-48	7 ± 5 (12)	172 ± 220 (46)	<0.0001

TABLE II: CRP levels (mg/L) in patients with normal appendix versus patients with appendicitis during the first 48 hours after the onset of symptoms

Hours	CRP (mg/L)	Sensitivity	Specificity
0-12	47	0.9	0.2
13-24	55	1.0	0.2
25-48	98	0.9	0.4

TABLE III: Cutoff points for CRP levels with the best sensitivity and specificity for the diagnosis of appendicitis

Patients with a normal appendix had similar CRP levels at all periods of time.

CRP levels were higher in patients with appendicitis compared with patients without appendicitis; CRP levels were significantly higher in patients diagnosed between 13 and 24 hours from the onset of symptoms compared with patients with symptoms for less than 12 hours.

CRP reaches its peak approximately at 40 hours [7]; consequently, the higher value encountered at 24 hours represents the rising of the CRP concentration. CRP levels increase with complications of appendicitis [6].

It has been reported that a CRP value higher than 100 mg/L was strongly related to appendiceal necrosis, and a CRP value higher than 170 mg/L was a strong predictor for the presence of infection [19]. These findings are supported by our findings.

CRP had a high sensitivity to differentiate patients with and without appendicitis; however, the specificity was very low.

Therefore, as CRP is an unspecific systemic inflammatory marker and as shown it has a high sensitivity to differentiate between patients with and without appendicitis, it can be used to support the clinical diagnosis of appendicitis.

Conclusions

CRP levels can be used to support the clinical diagnosis of appendicitis, and depending on time from onset of symptoms to diagnosis, CRP levels can also be used to differentiate patients with and without appendicitis.

The determination of CRP levels in patients with suspected appendicitis will help to diagnose appendicitis earlier, avoiding perforation and consequently avoiding the economic and legal consequences associated with complications of appendicitis.

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