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Acute appendicitis in children: not only surgical treatment

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ABSTRACT

Purpose: An accurate diagnosis of acute appendicitis is important to avoid severe outcome or unnecessary surgery but management is controversial. The aim of study was to evaluate, in younger and older children, the efficacy of conservative management for uncomplicated appendicitis and the outcome of complicated forms underwent early surgery.
Methods: Children with acute appendicitis were investigated by clinical, laboratory variables and abdominal ultrasound and divided in two groups: complicated and uncomplicated. Complicated appendicitis underwent early surgery; uncomplicated appendicitis started conservative treatment with antibiotic. If in the next 24–48 h it was worsening, the conservative approach failed and patients underwent late surgery.
Results: A total of 362 pediatric patients were included. One hundred sixty-five underwent early appendectomy; 197 patients were at first treated conservatively: of these, 82 were operated within 24–48 h for failure. The total percentage of operated patients was 68.2%. An elevated association was found between surgery and ultrasound.
Conclusions: Conservative treatment for uncomplicated appendicitis had high percentage of success (58%). Complications in operated patients were infrequent. Our protocol was effective in order to decide which patients treat early surgically and which conservatively; specific red flags (age and onset) can identified patients at most risk of complications or conservative failure. Type of study: treatment study.
Level of evidence: II.

The incidence of acute abdominal pain in children visiting pediatric and emergency departments is about 5% and, among all acute causes, appendicitis has an incidence of 12.7% [1], representing the most common reason for abdominal surgery. Morbidity in children is high, with an overall frequency of appendix perforation of 12.5–30% [2]. An accurate and early diagnosis of acute appendicitis is important to avoid both severe outcome and unnecessary surgery. However, to date, the diagnosis remains challenging because clinical signs, symptoms and instrumental data can be nonspecific and unreliable especially in younger children [3,4]. In the recent years, even in children, acute appendicitis was no longer considered an invariably irreversible progressive disease and for this reason a conservative approach was considered safe and effective for uncomplicated and unperforated cases [5–8]. Conversely, the management of complicated cases, with early or interval appendectomy, is still a matter of debate because of high incidence of complications for both approaches [10–21]. There are no studies of acute appendicitis that analyze both therapeutic possibilities in different age groups. The aim of this study was to evaluate, in different ages (younger and older children) the efficacy of conservative management for early and uncomplicated appendicitis, and the outcome of complicated forms treated with early surgery.

1. Material and methods

1.1. Patients

A prospective analysis was conducted in our center from January 2013 to December 2015; pediatric patients (up to 14 years old) hospitalized with diagnosis of acute appendicitis were included in the study. We therefore excluded patients with other causes of abdominal pain as gastroenteritis, constipation, mesenteric lymphadenitis or other causes of acute abdomen.

1.2. Clinical and instrumental evaluation

On admission, a careful clinical history and proper physical examination were performed with the assignment of a rating using the Pediatric Appendicitis Score (PAS) [22–24]. All patients were investigated by laboratory variables as total leucocytes count (TLC) with neutrophils (N%), C-reactive protein (CRP) and abdominal ultrasound (US).

The age of patients (< or >6 years old) and the onset of symptoms (< or >48 h) were evaluated. A PAS score >4, TLC >12.000 cells/mm^3,

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N > 75%, CRP >3 mg/dL [25–28] were considered diagnostic of acute appendicitis.

As for ultrasound (US), we considered as diagnostic parameters of appendicitis: maximum diameter of appendix >6 mm, wall thickness >3 mm, hyperemia of appendiceal wall, free fluid or abscess in the periappendiceal region, increased echogenicity of the adjacent periappendiceal fat and enlarged mesenteric lymph nodes [29,30]. US was considered negative only if a normal appendix was visualized (patients excluded from study); patients with non-visualized appendix (non diagnostic ultrasound) were nonetheless included in this study in order to evaluate the outcome.

Based on clinical and radiologic variables and surgery (if performed), all cases were considered as uncomplicated and complicated appendicitis:

Uncomplicated appendicitis was defined as: unwell but not generally ill, localized tenderness in the right iliac region with no diffuse guarding, no palpable mass; ultrasonography criteria included: no signs of perforation, abscess, copious disseminated peritoneal fluid or extra luminal gas; no perforation on surgery.
Complicated appendicitis was defined as peritonitis or sepsis, complex mass (perforation or abscess) on ultrasound and surgery; the age and the onset of symptoms more than 48 h were not considered as absolute complicating factor.

All patients with complicated appendicitis underwent surgery within 12 h of assessment (EA, early appendectomy).

All patients with uncomplicated appendicitis started the following nonoperative management (CT, conservative treatment):

- After the first clinical, laboratory and ultrasound evaluation all patients received intravenous antibiotics (cefotaxime 50–100 mg/kg 3 times daily); no oral intake was permitted for the following 12 h and intravenously fluids were given. After 6 and 12 h clinical revaluation was performed and after 24–48 h ultrasonography and laboratory were repeated. In the absence of ultrasonographic and laboratory worsening and if clinical conditions were favorable (less pain, fever <38C, patient able to mobilize, fluid oral intake tolerated), a normal diet was permitted, the intravenous antibiotic maintained at least for 72 h and patients were discharged with oral antibiotics for others 5 days and clinical control after 1 week (NO, not operated patients);
- If in the next 24–48 h clinical conditions were not improved and/or laboratory and ultrasonographic data worsened, the conservative approach was considered failed and patients underwent surgery (LA, late appendectomy) using either open or laparoscopic approach, according to surgeon's preference.

For patients with *non-diagnostic ultrasound* at first evaluation we adopted the same protocol, but the decision to perform early appendectomy or conservative treatment was based on clinical and laboratory data; non-operated patients repeated an ultrasonography after 24 h and, if the ultrasound was again non-diagnostic or diagnostic for simple appendicitis, patients remained in the group of "conservative treatment".

At admission in the hospital a written consensus from parents was obtained for all patients, for early surgery in complicated appendicitis and for conservative treatment in uncomplicated appendicitis specifying the possibility of late surgery within 24–48 h in case of no response.

The endpoints were:

- evaluation of differences among three groups: EA, LA and NO
- correlation between ultrasound and outcome
- evaluation of risk factors as age and onset of symptoms among surgical patients
- analysis of complications as infections of surgical site, abscesses, intestinal occlusion, reoperations and others
- number of not operated patients with readmission in hospital or late surgery after discharge

1.3. Statistical analysis

Statistical analysis of quantitative and qualitative data, including descriptive statistics, was performed for all items. Continuous data are expressed as mean ± SD. The intergroup differences were assessed by the chi-square test or Fisher exact test, as needed for categorical variables; the univariate analysis of variance (ANOVA) was performed for parametric variables, and post hoc analysis with the Tukey's test was used to determine whether there were pairwise differences. Data were analyzed by the Epi Info software (version 6.0, Centers for Disease Control and Prevention, Atlanta, GA, USA) and by IBM SPSS Software 22 version (IBM Corp., Armonk, NY, USA). All p-values were two-sided and $p \leq 0.05$ was considered statistically significant.

2. Results

A total of 362 pediatric patients were included in the study.

At admission 165 patients were defined as complicated appendicitis and underwent early appendectomy whereas 197 patients were defined as uncomplicated and at first treated with CT: of these, 82 were operated within 24–48 h for failure of conservative treatment (LA). The total percentage of operated patients was 68.2%.

Demographic characteristics for different groups of NO, EA and LA are reported in Table 1.

Median age of all patients was 112.2 months with differences in three groups: patients treated early were younger than patients treated later and not treated ($p = 0.001$ and $p = 0.030$ respectively). Age <6 years was correlated to complicated surgery (Table 2).

As for sex, 215 were males and more males were treated early ($p = 0.043$ vs not operated patients).

Regarding onset, in 203 patients symptoms lasted less than 48 h and a duration of symptoms longer than 48 h was correlated to complicated surgery (Table 2).

Median PAS at admission was 8.6 with statistical differences among groups: it was higher in EA group.

Laboratory analysis at admission showed statistical differences between three groups: all parameters were more altered in early treated patients.

In the conservative group:

- 115 patients (58%) were treated successfully with complete regression of symptoms at discharge; at 24–48 h mean PAS was 1.9, laboratory data showed an average TLC 8.2 cell/mm^3, neutrophils 63% and CRP 14 mg/dL and the discharge home after an average of 4.9 days; 22 patients (19%) had further admissions after discharge but only 10 (8.6%) needed antibiotic therapy for AA and 2 (1.7%) were operated later (after 8 and 16 months respectively);
- 82 patients (42%) were non responsive to conservative treatment and were treated with LA; of these patients, only 2 (2.5%) showed perforation at surgery (Table 2);

Only 25% of EA patients were uncomplicated (misdiagnosis). 30% of all operated patients (EA and LA) were younger than 6 years and of these, 75.6% had complicated surgery (Table 2).

The overall percentage of complications was 7.7%, 95% of which in EA patients; 37% of patients with complications were younger than 6 years and 16% had an onset lower than 48 h (Table 4).

Only 1 case of negative appendicitis at surgery was recorded, in a patient treated with late appendectomy.

The ultrasound was positive for appendicitis in 264 patients (73%): 159 (60%) diagnosed as uncomplicated and 105(40%) as complicated. The ultrasound showed a sensitivity and a specificity of 85.5% and 99.2% respectively for diagnosis of complicated appendicitis with a positive predictive value of 98.1% and a negative predictive value of 93.1%. The correlation between ultrasound and outcome was reported in Table 3. Regarding non-diagnostic ultrasound (27%), after 24–48 h the ultrasound became diagnostic for uncomplicated appendicitis in 10%