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Challenges in uncomplicated acute appendicitis

Fernando Resende^{1*}, Ana Beatriz Almeida^{1,2}, José Costa Maia¹, Renato Bessa Melo^{1,2}¹Department of General Surgery, Centro Hospitalar de São João, Porto, Portugal²Faculty of Medicine, University of Porto, Porto, Portugal

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ABSTRACT

Acute appendicitis is one of the most common abdominal emergencies requiring surgery. It still represents, however, a challenging diagnosis. In order to facilitate this process, several scoring systems were developed, namely, the Alvarado score, acute inflammatory response and Raja Isteri Pengiran Anak Saleha Appendicitis scores, which are the most used in clinical practice. This clinical condition encompasses a wide spectrum of clinical presentations, from the uncomplicated form to the one with diffuse peritonitis. Treatment of uncomplicated acute appendicitis remains a matter of discussion. Although appendectomy has been regarded as the gold-standard, conservative management with antibiotics is gaining more and more acceptance. The approach to appendectomy constitutes another controversial issue, namely, its performance through an open or a laparoscopic approach, which seems to be establishing itself, in some centers, as the standard of care. With this paper, we intend to give some insight on the aforementioned topics, through a review of the available literature on uncomplicated appendicitis.

1. Introduction

Acute appendicitis is one of the most common abdominal emergencies requiring surgery, with a lifetime prevalence of 7%^[1,2]. However, it may pose a diagnostic challenge as it may mimic other conditions in the early phases of disease. Acute appendicitis encompasses a wide spectrum of clinical presentations, from the uncomplicated form to the one with diffuse peritonitis. While diffuse peritonitis remains an undisputed indication for urgent surgery, discussion focusing on the management of appendicular abscess in uncomplicated appendicitis, revolves around the need for surgery and the surgical approach.

The diagnosis continues to be mainly clinical and the decision whether to operate, observe or perform further workup is not always clear. Most patients with pain in the right lower quadrant do not have acute appendicitis. Several scoring systems were developed to help the clinicians in the diagnosis with the Alvarado score, the Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) score and the acute inflammatory response (AIR) being the most used.

The decision whether to operate or not, is key in the management of acute appendicitis. Historically, appendectomy has been the gold-standard for the treatment of acute appendicitis, either via an open or a laparoscopic approach. However, this strategy has been challenged in recent years with the advent of antibiotic therapy and studies documenting less morbidity with this nonoperative strategy^[3].

Authors who advocate a non-surgical approach argue that recurrent appendicitis seems to be a rather infrequent event (ranging from 3% to 30%), usually milder in presentation^[4], and that those who require appendectomy did not experience significant complications^[5].

Having this in consideration, it is important to weigh the benefits and potential disadvantages of both treatment options, keeping in mind that appendectomy itself carries risks and even mortality^[6]. In this setting, it would be beneficial to develop instruments to select patients to either approach^[7].

With this study, we intend to provide some insight on the questions arising nowadays when dealing with non-complicated acute appendicitis.

2. Diagnosis

The diagnosis of acute appendicitis can be achieved by several clinic, radiologic and laboratory criteria.

*Corresponding author: Fernando Resende, Department of General Surgery,

Centro Hospitalar de São João, Porto, Portugal.

Tel: +351 225512100

Fax: +351 225096908

E-mail: fernandosilvaresende@gmail.com

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The typical presentation includes symptoms such as abdominal pain with migration to the right iliac fossa (RIF), anorexia, nausea and vomiting and signs such as rebound tenderness in the RIF and fever. However, it is important to acknowledge that these signs and symptoms are common to many abdominal conditions, making the diagnosis more challenging, particularly among the young, elderly and females at reproductive age^[2].

Several scoring systems have been developed in order to facilitate early diagnosis of acute appendicitis, with the Alvarado, the RIPASA and the AIR score being the most used in clinical practice (Table 1). They are also applicable for risk stratification, which is a key recommendation of emergency surgical care guidelines^[8,9].

Table 1

Clinical scores in acute appendicitis.

	Alvarado	AIR	RIPASA
Gender			
Female			0.5
Male			1
Age			
< 40 years			1
≥ 40 years			0.5
Symptoms			
Migration of pain	1		0.5
Anorexia	1		1
Nausea	1		
Vomiting		1	
Nausea and vomiting			1
RIF pain		1	0.5
Symptoms < 48 h			1
Symptoms ≥ 48 h			0.5
Signs			
Rebound pain	1		1
Tenderness in right lower quadrant	2		1
Rebound tenderness or muscular defense			
-Light		1	
-Medium		2	
-Strong		3	
Guarding			2
Rovsing's sign			2
Temperature			
≥ 37.3 °C	1		
≥ 38.5 °C		1	
37 °C–39 °C			1
Laboratory values			
Leukocytosis	2		1
White blood cell count			
10.0–14.9 × 10 ⁹ /L			1
≥ 15.0 × 10 ⁹ /L			2
Shift of white blood cell count to the left	1		
Polymorphonuclear leucocytes			
70%–84%		1	
≥ 85%		2	
C-reactive protein (CRP) concentration			
10–49 g/L		1	
≥ 50 g/L		2	
Negative urinalysis			1
Other			
Foreign national registration identity card			1

The Alvarado score is a ten-point scoring system consisting of the following items: migration of pain, anorexia, nausea, rebound pain, elevated temperature, shift of white blood cell count to the left, scoring 2 points each; in turn, tenderness in right lower quadrant and leukocytosis, scoring 1 point each^[10]. This score also encompasses a management strategy, with

proposing to discharge those patients with scores under five, to keep under vigilance those scoring five or six and to operate those with scores over six. Some authors suggest that this system can facilitate the diagnostic process particularly in low-resource countries where imaging modalities are not widely available^[11].

Studies show that Alvarado score is best used as a rule out (scores < 5) diagnostic tool, because even scores > 7 are not specific enough to proceed to surgery without further workup. It is also important to stress that this score's performance is affected by age and gender, for instance, apparently over-predicting acute appendicitis in females of reproductive age and with inconclusive results when it is applied to the pediatric age group (17 or less)^[12].

Another issue regarding the Alvarado score is its applicability to the oriental population where it seems to have less sensitivity and specificity. In this setting, a new scoring system, the RIPASA has been proposed^[13]. The RIPASA system includes several factors which are absent in the Alvarado score, namely, age, gender and duration of symptoms. A study conducted at the Raja Isteri Pengiran Anak Saleha Hospital in Brunei comparing the application of the two scores in a population of two hundred patients with RIF pain observed in the Emergency Department showed that the RIPASA score performed better than the Alvarado score in terms of sensitivity, negative predictive value and diagnostic accuracy^[13]. These authors state that RIPASA might reduce unnecessary testing with a beneficial effect in terms of healthcare costs. Similar results were obtained in another study conducted in India^[2].

The AIR score is based on the same principles of the Alvarado score, similarly stratifying patients in one of three categories: low, medium or high probability of acute appendicitis^[14]. Incorporation of CRP into the score is the most significant difference to the Alvarado score. Considering its performance, according to Kollar *et al.*, both scores are accurate in terms of ruling out appendicitis. However, in terms of specificity, AIR seems to be superior^[11]. Despite of these results, it is important to stress that more studies need to be conducted in order to assess applicability of the score systems mentioned in clinical practice. It is important to stress that these tools not only can be used for diagnostic purposes, but also for stratification, separating those patients who require further workup and those who can be assigned for a certain treatment strategy^[15,16].

Imaging is an important part in the diagnosis of acute appendicitis as well. CT scan is classically considered the best radiological modality for this condition^[1]. However, what radiation exposure and the possible delay might bring to the diagnosis are concerns associated with the widespread application of this diagnostic tool. Ultrasound imaging would obviate some of these concerns, but its operator-dependence weighs against it. Furthermore, it is less accurate than CT scan in making the diagnosis. It is worth mentioning that some studies showing the widespread use of CT scan, even in the absence of an expedited imaging protocol, was not associated with an increased risk of appendiceal perforation^[17]. Despite of the role of imaging tools in diagnosing acute appendicitis, clinical assessment remains the key in the decision-making process. Routine use of imaging techniques including CT in all patients with RIF pain seems not only unnecessary but also potentially prejudicial to the patient. Scoring systems like those

mentioned above may be useful by selecting those patients who benefit the most from imaging studies, for instance, those classified as medium risk by the AIR score^[11].

Appendicitis during pregnancy carries a unique diagnostic and management challenge and can have a negative impact on outcomes for both mother and fetus. In pregnant women with suspicion of acute appendicitis and negative or inconclusive ultrasound, magnetic resonance imaging is a reasonable alternative to CT scan avoiding ionizing radiation exposure^[18,19].

In terms of laboratory markers, one beneficial approach seems to be combining several of these in order to enhance the diagnostic accuracy. Elevation of the white blood cell count with a left shift, elevation of the CRP, bilirubin and several novel markers such as granulocyte-colony stimulating factor and calprotectin are some of the markers warranting consideration^[1]. Accordingly, Al-Abed *et al.* propose that in patients presenting with RIF pain and elevated levels of white blood cell, CRP, and bilirubin, the likelihood of having appendicitis is 98%^[20].

3. Surgery vs. antibiotics

As stated above, appendectomy has been considered the gold-standard in the treatment of acute appendicitis for many years. McBurney emphasizes the importance of appendectomy in his 1891 article by stating that “If we wait long enough, say to the seventh, eighth or ninth day, many of these difficult questions will be solved, for one after another of our patients will have died, and one after another of our questions will have been answered”^[21].

This view may be based on the assumption that, in the absence of a surgical intervention, acute appendicitis will always lead to perforation. This traditional view has been recently challenged by evidence suggesting that perforated and non-perforated appendicitis may be distinct entities rather than sequential events^[22]. Additionally, one must consider surgical complications and the negative appendectomy rate (15%–30%) both rendering surgery a less appealing option^[6].

Another theory points to the similar pathologic aspects between acute appendicitis and diverticulitis, making nonoperative treatment a plausible approach to both conditions^[23].

There are several studies showing that, in cases of early uncomplicated acute appendicitis, medical treatment with antibiotics may lead to resolution in the majority of cases^[6,24,25]. Indeed, references to this approach can be found in literature as remote as the 1950's^[26]. The first randomized study was published in 1995 concluding that antibiotic treatment in patients with acute appendicitis was as effective as surgery^[27]. In 2008, Mason *et al.* concluded that up to 70% of patients could be spared from an appendectomy^[28]. In a more recent meta-analysis, antibiotics were associated with less morbidity and no increased risk of perforation, even when an appendectomy had been delayed by this initial approach, which is one of the main concerns associated with this strategy. These authors propose that antibiotic treatment associated with proper vigilance and supportive care can be employed in uncomplicated appendicitis, reducing the number of unnecessary surgeries and associated complications. Furthermore, hospital length of stay could be reduced as patients were able to maintain antibiotic treatment orally after discharge^[29].

Arguments against this nonoperative approach include the eventual need and subsequent delay in surgery, the possible recurrence of acute appendicitis and missing of other diagnosis.

Considering the rate of failure, the randomized clinical trials described the need for delayed appendectomy in up to 48% of patients treated initially with antibiotics^[5]. A recent study evaluating the rate of recurrence concluded that most patients randomized to antibiotic treatment did not require an appendectomy during the first year of follow-up and those who required surgery did not experience significant complications^[5].

Regarding the possibility of missing other lesions affecting the appendix or the adjacent colon that may have similar presentation to acute appendicitis, some authors propose that patients treated conservatively should undergo further endoscopic or radiologic study in order not to miss these lesions^[30].

In the last decades, many studies have been published on nonoperative treatment of acute appendicitis. However, conflicting results can be found. In a review published in 2011, Fitzmaurice *et al.* conducted a literature search using MEDLINE and the Cochrane Library including studies published between 1999 and 2009 evaluating those papers according to the Public Health Resource Unit (2006) appraisal tools. They concluded that several of the articles found had significant flaws in their design. Based on their research, they stated that more and better designed studies were needed in order to adequately assess the results of nonoperative treatment. This opinion was also shared by other authors concluding that existing data are not sufficient to undoubtedly support the conservative treatment strategies over the operative treatment, despite accepting a potential role in certain patient groups, such as those with high anesthetic risk and in remote locations in which surgical treatment is simply unavailable^[23,31].

With the potential benefits of nonoperative management in mind, it is relevant to identify factors that may be associated with failure of this approach. In 2006, Tsai *et al.* conducted a retrospective study including thirty-five patients with uncomplicated acute appendicitis managed conservatively. They concluded that past history of this condition and presence of a calcified appendicolith in CT scan predicted failure of medical treatment, deeming these patients good candidates for initial surgical treatment. Of note, they found no association between severity of leukocytosis, fever, gender, age, fluid accumulation and extent of abscess or phlegmon, with recurrence^[4].

In conclusion, more researches, both in quantity and in quality, are needed in order to establish that nonoperative treatment is at least as effective as appendectomy.

4. Open vs. laparoscopic appendectomy

Open appendectomy has been considered the standard treatment for acute appendicitis since its first description by McBurney in 1891 and is a well-established procedure counting years of experience attesting its efficacy and safety. However, since its introduction in 1980, laparoscopic appendectomy has been gaining more and more acceptance due to the advantages traditionally associated with this approach, namely, faster return to normal activity, less post-operative pain and less surgical wound infection rate. Furthermore, laparoscopy seems to be a better option for certain subsets of patients, namely, females of child-bearing age, allowing inspection of the pelvic organs and exclusion of other conditions with a similar presentation^[32]. However, there are some concerns associated with the laparoscopic approach, namely, longer operative times, higher costs and increased intra-abdominal abscess formation.

Conflicting results can be found in the literature regarding this subject: in 2010, Wei *et al.* randomly assigned 220 patients with signs and symptoms suggestive of acute appendicitis to undergo appendectomy either via a laparoscopic or an open approach concluding that the first is associated with a shorter hospital stay, earlier return to normal activity and less overall rate of complications (including intra-abdominal abscess and post-operative ileus). On the downside for the laparoscopic approach, these authors reported longer operative time and higher costs; however, these differences were not statistically significant^[33].

Concerning complications, there may be some confounding factors leading to the increased incidence of abscess formation found to be associated with laparoscopy in the literature, such as aggressive manipulation of the appendix or excessive use of irrigation fluid during surgery, thus facilitating bacterial spread and enhancing abscess formation^[34]. However, Xiao *et al.* reported a lower incidence of overall and surgical site infections, including intra-abdominal abscess formation rate^[35]. Similar results were obtained in a meta-analysis published in 2012 in which the authors state that the laparoscopic approach is becoming the procedure of choice for suspected acute appendicitis^[36]. Lastly, Minutolo *et al.* retrospectively analyzed two hundred and thirty patients, concluding that laparoscopy is associated with less post-operative complications (less wound infection with similar rate of intra-abdominal abscess formation), similar operative time and shorter hospital stay (approximately one day less)^[37]. This study points out the fact that the costs associated with laparoscopy are balanced by the savings associated with shorter hospital stays. Kocatas *et al.*, who performed a prospective randomized trial with ninety six patients undergoing open or laparoscopic appendectomy ($n = 46$ and $n = 50$, respectively) concluded that laparoscopic approach was not superior to the open procedure also stating that laparoscopic approach can be justified based on patient preference for minimally invasive surgery and surgical training for more demanding laparoscopic techniques^[32].

Finally, laparoscopic appendectomy can be performed either by a single or a three-port approach. A recent meta-analysis suggests that single-incision laparoscopic appendectomy is basically as feasible, effective and safe as three-port laparoscopic appendectomy in dealing with acute appendicitis, although, single-incision laparoscopic appendectomy seems to require longer operative time when compared with three-port laparoscopic appendectomy^[38].

5. Conclusions

In spite of being one of the most common surgical emergencies in clinical practice, diagnosis of acute appendicitis is far from straightforward. Several scores were proposed but they are not universally applicable. These scores are useful for risk stratification and for selection of patients requiring further imagiologic evaluation.

Antibiotics seem to be a safe and effective treatment in certain subsets of patients with uncomplicated acute appendicitis, possibly reducing the number of unnecessary surgeries and hence their associated morbidity. However, the present data are not sufficient to definitively recommend conservative management.

There are conflicting results in the literature regarding the best surgical approach to appendectomy. In fact, there is no

consensus regarding this topic despite an increasing trend towards laparoscopy. Several factors influence the procedure adopted, such as patient and surgeon preference, financial resources and surgical training and expertise.

Conflict of interest statement

The authors report no conflict of interest.

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