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“The ultimate criterion for the usefulness of a diagnostic test is whether it adds information beyond that otherwise available, and whether this information leads to a change in management that is ultimately beneficial to the patient.”

D.L. SACKETT IN 'CLINICAL EPIDEMIOLOGY, A BASIC SCIENCE FOR CLINICAL MEDICINE'
SECOND EDITION. BOSTON/TORONTO: LITTLE, BROWN AND COMPANY; 1991

Diagnosis of Acute Appendicitis - Historical Review

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Submitted

Introduction

Since Reginald H. Fitz first described appendicitis at the 1886 meeting of the Association of American Physicians¹, numerous studies have been published on the subject. A PubMed data search using appendicitis as keyword may result in 15776 hits, reflecting the widespread interest in the subject. In the Western world, appendicitis is the most frequent cause for acute abdominal pain requiring surgical intervention. Annually, appendectomy is the most common abdominal operation performed on an emergency basis.² The lifetime risk for developing acute appendicitis is 8.6% for men and 6.7% for women.³ The diagnosis of acute appendicitis remains a challenge to modern medicine.

Although a carefully detailed history, physical examination and laboratory tests (white blood cell count and CRP) can provide the physician a proper diagnosis, yet as many as 12-40% of patients still undergo an unnecessary appendectomy.^{2,4} While the combination of rebound tenderness, fever and leucocytosis is regarded as a strong discriminator for acute appendicitis⁵, this classic clinical triad may be absent in up to 50% of patients.⁶ In order to prevent a delay in diagnosis, which often results in advanced disease with perforation and a marked increase in complication rate, the current accepted negative appendectomy rate is 10-15% in men and even up to 40% in women of childbearing age.^{7,8,9}

However, this classical approach to the balance between the negative appendicitis rate and the perforation rate is being questioned. Recent studies suggest that spontaneous resolution of appendicitis is common, that perforation seldom can be prevented, that risk of perforation has been exaggerated, and that in-hospital delay is safe.^{10,11} This could motivate a shift in focus from the prevention of perforation to the early detection and treatment of advanced appendicitis. Delay or error in diagnosis of acute appendicitis is now one of the most frequent allegations of medical malpractice that are levelled against general surgeons, emergency medicine physicians, and primary care physicians.¹²

Although clinical assessment remains the most essential and critical part of the initial evaluation of patients with suspected acute appendicitis, the clinical scoring systems, US, CT, MRI and diagnostic laparoscopy have been suggested for elucidating the cause for acute abdominal pain when acute appendicitis is suspected.

Clinical Scoring Systems

The initial management of patients with suspected appendicitis needs to be based on the disease history, physical signs, and basic laboratory tests reflecting the inflammatory response. This involves a subjective synthesis by a surgeon of a large amount of complex

information, relying on his knowledge and previous experience with similar patients. All clinical and laboratory variables are weak discriminators individually, yet when combined they achieve a high discriminatory power.¹³ To improve the process of combining these factors, clinical scoring systems have been developed of which the Alvarado score and the Ohmann score are the most well-known.^{14,15} However, evaluation of these scores in several prospective studies failed to show better outcomes than unaided clinical diagnosis or even showed unforeseen clinical effects.¹⁶⁻¹⁸ Recently, Andersson et al. presented the Appendicitis Inflammatory Response score (AIR) that is constructed from eight variables with independent diagnostic value.¹⁹ This AIR score could correctly classify the majority of patients having suspected appendicitis. However, this AIR score has not yet been validated in other studies. In general, the value of scoring systems in acute appendicitis is limited in every day clinical practice because a performance of these scores in other than study conditions is often optimistically biased.

Furthermore, combining clinical signs and symptoms with laboratory results have also led to the development of computer aided algorithms.²⁰ Although these algorithms have shown to be cost beneficial and can reduce the number of unnecessary appendectomies, they have never been widely accepted because of the requirement of new, costly equipment and expertise.

Ultrasonography

The first report of an inflamed appendix on ultrasonography (US) was by Deutsch in 1981.²¹ The late introduction of US as a diagnostic modality for appendicitis was largely due to the interference of bowel gas and the lack of a transducer with enough spatial resolution to pick up small structures such as the appendix. In 1986, the graded compression technique was introduced by Puylaert (Fig. 1).²²

This technique involves applying gradual, moderate pressure over the right lower quadrant in an effort to collapse normal bowels and visualize the distended appendix. US decreases the distance between the transducer and the appendix and compresses overlying bowels which results in a better visualization of the appendix. In 1987, a landmark study was presented by Puylaert et al.,



Fig 1. J.B.C.M. Puylaert

reporting graded compression by US with a specificity of 100% and a lower sensitivity of 75%.²³

The advantages of US are its widespread availability, lack of radiation exposure, non-invasiveness, safety, and relatively low costs. One of the major disadvantages of US is that making diagnostic images and their interpretation are highly dependent on operator clinical skills and technical skills. This is reflected in the wide range of diagnostic accuracy as published in numerous studies on graded compression ultrasound in acute appendicitis, with sensitivities and specificities in the 76% to 96% and 47% to 94% ranges, respectively.²⁴ The inability to visualize the appendix with the use of US is classically considered a major disadvantage, because it represents a serious limitation to confidently excluding appendicitis.²⁵ Due to this high false-negative rate, it is suggested that US should not be used to exclude appendicitis.^{26,27} On the contrary, single-center studies show sensitivities and specificities of US in acute appendicitis of 95%-98% and 94%-100%, respectively, concluding that US is a highly valuable tool in appendicitis.^{28,29} From this discrepancy between multicenter and single-center studies, it can be concluded that applying US for evaluation of appendicitis can only be optimally utilized when its facilities are concentrated in radiology departments having standardized methods and the availability of US-qualified doctors.

Computed Tomography (CT)

CT was invented in 1972 and its use was widely prevalent by the early 1980s. The first appendicitis viewed on CT was reported by Gale et al. in 1985.³⁰ A few years later, Balthazar (Fig. 2) et al. reported the first prospective study on the use of CT in patients with suspected appendicitis.³⁰

CT, performed with oral and IV contrast, showed a 98% sensitivity and a 83% specificity. Since then, numerous studies have reported accuracies of CT in acute appendicitis, showing sensitivities ranging from 70%-100% and specificities ranging from 83%-100%.^{24,32}

The benefit of CT relies in part on its ability to reveal an appendix more reliably and with greater consistency than US. In several studies, an enlarged appendix with periappendiceal fat stranding was observed in 93%-95% of patients with appendicitis.^{33,34} Another advantage of CT is that the interpretation of CT findings is less

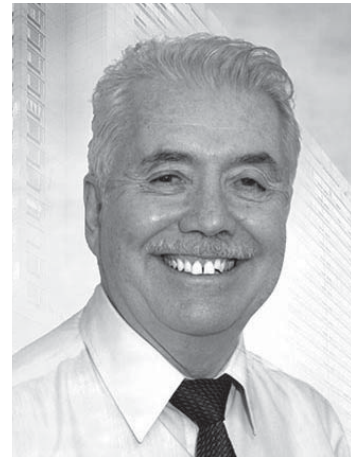


Fig 2. E. Balthazar

operator-dependent than US findings. However, recent studies suggest also an interobserver variability in CT scan interpretation for suspected appendicitis.^{35,36} High accuracy rates of CT might only be achieved in an academic environment and excellent diagnostic results of appendiceal CT might be difficult to reproduce in the daily clinical practice of a general community hospital.^{37,38}

A major disadvantage of CT is the exposure to radiation entailed in its use. A typical dose for an abdominal CT examination is about 10mSv, meaning that one CT examination carries about the same radiation dose as 500 chest radiographs.³⁹ An effective dose of 10mSv corresponds to an excess risk of radiation-induced cancer of 1 in 2000.⁴⁰ One can therefore make the assertion that in the case of a benign disease as appendicitis, the primary use of diagnostic CT examinations is to be avoided.

US and CT - Impact of imaging

Several studies have compared the diagnostic performance of US and CT in the same patient population.^{41,42} In most of these studies, CT was found to have a better test performance than US. One of the first reports on the impact of CT on the negative appendicitis rate was a landmark study in 1998 by Rao et al.⁴³ Routine appendiceal CT - as performed in all patients with suspected appendicitis - showed an improvement of patient care and reduction in the use of hospital resources. Over the years, numerous studies on the impact of CT on negative appendicitis and perforation rates have been published. Most of these studies show a significant reduction of the prevalence of negative appendicitis.⁴⁴⁻⁴⁷ Yet other significant studies cannot confirm these results leading to the conclusion that the liberal use of appendiceal CT may not contribute to reducing negative appendicitis rates.⁴⁸⁻⁵¹ It is suggested that these conflicting results are caused by the variety in patient population, research protocols and research-based settings. Additional large, randomized, and prospective studies, as well as the examination of appendiceal results of CT in individual institutions, are recommended to determine the true utility of CT in the evaluation of acute appendicitis.^{49,51} In a recent study by Cuschieri et al. on 3540 patients with suspected appendicitis, the variation in negative appendectomy between hospitals was closely linked to CT/US accuracy thereby suggesting that CT/US accuracy should be considered a measure of quality in the care of patients with presumed appendicitis.⁴⁴

In recent studies, the primary use of CT in all patients with suspected acute appendicitis is criticized.^{24,42} Given the exposure to radiation using CT, their authors advocate US as primary imaging modality, especially for the young. Few studies have prospectively validated the

sequential use of graded compression US and CT for diagnosing patients with signs of acute appendicitis.^{52,53} US appeared to be valuable as a primary imaging modality in the diagnosis of appendicitis. In the event of negative or inconclusive US results, additional CT is needed to improve diagnostic accuracy. This approach has the distinct advantage of avoiding radiation exposure in all patients with suspected appendicitis. In a large retrospective study Wan et al. showed that this approach is also the most cost-effective method of imaging pediatric appendicitis.⁵⁴

Diagnostic Laparoscopy

Laparoscopic appendectomy was first reported in 1977 by de Kok, a Dutch surgeon^{Fig 3,55} but it was not until the early 1990s that this approach gained wide acceptance. Since that time, there have been multiple, prospective, randomized controlled trials, several meta-analyses, and nationwide database reviews that compare open appendectomy with laparoscopic appendectomy.⁵⁶⁻⁶¹ Despite the plethora of data, there is still controversy regarding laparoscopic vs. open appendectomy. Nonetheless, there appears to be an increasing trend in utilization of laparoscopic appendectomy.^{60,61} A major advantage of a laparoscopic approach compared to a split muscle incision is the possibility of inspecting the whole abdominal cavity in order to determine the true cause of patient's symptoms. However, a laparoscopic approach may be technically more challenging than an open approach and therefore diagnostic laparoscopy and laparoscopic appendectomy are only recommended in those clinical settings where surgical expertise and equipment are available and affordable.⁶¹

The impact of laparoscopic appendectomy on the clinical management of patients with suspected appendicitis has been described in several studies.⁶²⁻⁶⁴ As laparoscopy can be used as a diagnostic modality, it may lower the threshold to operate on patients with suspected appendicitis. It is suggested that patients with suspected appendicitis, especially women of child-bearing age, should undergo diagnostic laparoscopy, regardless of the certainty of the pre-operative diagnosis.⁵⁸ In a recent consensus statement, the European Association for Endoscopic Surgery advocates diagnostic laparoscopy in patients with suspected appendicitis after non-invasive diagnostic aids have been exhausted first.⁶⁵ As a

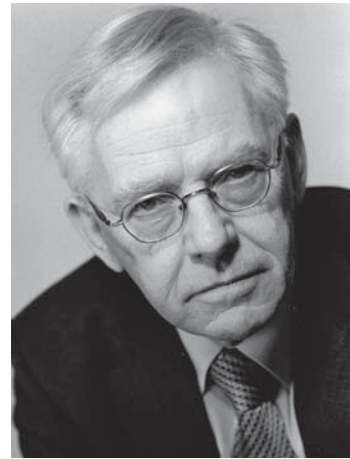


Fig 3. H.J.M. de Kok

pure diagnostic modality, laparoscopy is inferior to other imaging modalities, because of its invasive nature which can lead to secondary morbidity.^{66,67}

Magnetic Resonance Imaging (MRI)

During the past decade, MRI has become widely available in the Western world and technological developments have made ultrafast sequences possible, resulting in shorter examination times and fewer motion artifacts. MRI is also being investigated as a potential diagnostic modality for appendicitis. The first prospective study reporting the value of MRI in acute appendicitis was published by Incesu et al. in 1997.⁶⁸ In this study, the sensitivity of MRI for acute appendicitis was 97% and the specificity was 92%. Since then, detection of appendicitis with MRI has been published for a small group of pregnant and non-pregnant patients.^{69,70} MRI has not been shown to be superior to CT, but it has the explicit advantage of not involving radiation exposure, which is particularly important in pregnancy. However, the widespread use of MRI is limited by its high costs, the need for contrast material and especially a possible lack of scanner availability. In a recent prospective study of 138 patients with clinically suspected appendicitis, a simple MRI protocol was introduced, resulting in a sensitivity of 100% and a specificity of 99%.⁷¹ Besides that, the authors show that the overall effect of using MRI of patients suspected of appendicitis could result in a net saving of approximately 64.000 EURO of hospital resources. These authors suggest performing a MRI on pregnant patients or patients younger than 20 years of age for whom US has been equivocal for acute appendicitis. With this protocol, MRI is more user-friendly which may lead to its more frequent use.

Conclusion

The diagnosis of acute appendicitis remains challenging. Throughout the years different imaging modalities have been added to the clinical signs and symptoms to establish an accurate diagnosis. Nowadays no one single diagnostic strategy is acceptable for all patients with suspected appendicitis.

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