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Radiologic Diagnosis of Appendicitis in Children

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Stockholm 2004

*A minor operation is
one that is performed
on the other fellow.*

Russell Pettis Askue

To Sten and Ylva

ABSTRACT

Suspected appendicitis is the most common cause of emergency abdominal surgery in children. Because of the often atypical clinical findings, the diagnosis of appendicitis is difficult and may be delayed. Perforation has been reported to occur in 23-73% of children with acute appendicitis. The negative appendectomy rate has been reported to be 15-25%. Since the complication rate is not negligible, it is desirable to avoid unnecessary laparotomies.

The diagnostic accuracy of ultrasonography (US) and additional abdominal computed tomography (CT) was studied in a prospective study that included 600 children. It was found that US is a valuable and highly specific tool in the diagnosis of appendicitis in children. The sensitivity can be increased significantly by performing abdominal CT in addition to US. A negative appendectomy rate of 3.7% and a perforation rate of 21% were achieved.

The diagnostic accuracy of different CT techniques, namely non-enhanced helical CT limited to the lower part of the abdomen, CT of the entire abdomen after intravenously administered contrast medium, and the combination of both, were studied in a retrospective review of prospectively acquired data including 306 CT examinations. It was found that the limited non-enhanced CT had a significantly lower sensitivity than the contrast-enhanced CT, while the combination of both sequences did not further improve the diagnostic accuracy. Hence, the limited non-enhanced scan can be excluded, which results in a reduction of the radiation dose.

The negative appendectomy rate and the perforation rate were studied in a retrospective study including 600 children who underwent appendectomy because of suspected appendicitis during the past decade. A gradual and substantial decrease in the negative appendectomy rate was found during the years studied. The overall perforation rate remained stable, while the rate of perforations after admission appeared to decrease over time. Since nothing was changed in the management of suspected appendicitis apart from the increasing use of US and CT, it may be assumed that the findings result from the preoperative radiologic imaging.

The impact of radiologic imaging procedures, including US only or US and abdominal CT, on the surgeon's decision-making process in the management of suspected appendicitis was studied in a prospective study including 600 children. Radiologic imaging was found to provide valuable guidance as to whether a child with suspected appendicitis should be discharged, observed, or given surgical treatment. Following this guidance may lead to beneficial changes in the management plan. False negative imaging results are infrequent but may still occur and therefore, a close clinical re-examination and communication with the radiologist is of utmost importance for the appropriate final decision.

Key words: appendicitis, appendix, ultrasonography, computed tomography, appendectomy, perforation, diagnostic accuracy, decision analysis

LIST OF PUBLICATIONS

This thesis is based on the following four papers, which are referred to in the text by their Roman numerals:

I. **Kaiser S, Frenckner B, Jorulf HK.**
    Suspected appendicitis in children: US and CT – a prospective randomized study
    Radiology 2002; 223:633-638

II. **Kaiser S, Mesas-Burgos C, Söderman E, Frenckner B.**
    Appendicitis in children – impact of US and CT on the negative appendectomy rate
    European Journal of Pediatric Surgery 2004;14 (in press)

III. **Kaiser S, Finnbogason T, Jorulf HK, Söderman E, Frenckner B.**
    Suspected appendicitis in children: Diagnosis with contrast-enhanced versus nonenhanced helical CT
    Radiology 2004; 232 (in press).
    Published online before print March 18, 2004

IV. **Kaiser S, Jorulf H, Söderman E, Frenckner B.**
    Impact of radiologic imaging on surgical decision-making process in suspected appendicitis in children
    2004, Submitted.

ABBREVIATIONS

US	=	ultrasonography
CT	=	computed tomography
ROC	=	receiver operating characteristic
CRP	=	C-reactive protein
WBC	=	white blood cell count

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INTRODUCTION

Background

Appendicitis is one of the most common surgical diseases in western countries [1]. It accounts for 25% of hospital admissions due to abdominal pain [2] and for more than 40% of all emergency laparotomies. The lifetime cumulative risk of having appendicitis is approximately 7-9% in the US [3]. In Sweden, roughly 30,000 patients are admitted for observation in hospitals and 12,500 emergency laparotomies are performed annually because of suspected appendicitis [4]. There is a high peak in the second decade, and about 50% of patients with appendicitis are between 15 and 35 years of age [5]. In children, suspected appendicitis is the most common cause of emergency abdominal surgery [6].

The treatment of choice in the vast majority of patients is appendectomy, i.e. surgical removal of the inflamed appendix, although conservative treatment with antibiotics has also been used in adults [7]. However, appendicitis can mimic several other diseases and is a possible differential diagnosis in almost all patients with acute abdominal symptoms. In the youngest and in the oldest age groups, it is more likely that appendicitis will present with atypical history and clinical findings, and hence the diagnosis is often difficult and may be delayed. Therefore, the complication rates are highest in these populations [8]. In children, perforation has been reported in 23-73% [9].

The difficulties in differentiating the patients with appendicitis needing surgical intervention from the patients with non-surgical or spontaneously resolving abdominal pain, together with the aim to prevent complications, i.e. perforation of the appendix and peritonitis, has led to the traditional acceptance of a relatively high frequency of unnecessary surgery and removal of a healthy appendix (hereafter, negative appendectomy). In children, a negative appendectomy rate of 15-25% has been reported [9-11]. Since unnecessary surgery is a waste of medical resources, and the complication rate after negative appendectomy is not negligible [12-14], this practice is being increasingly questioned [15-17]. A more restrictive surgical approach is supported by the development of modern imaging techniques, in particular ultrasonography and computed tomography.

History of appendicitis

There are indications that appendicitis was present already in 3000 B.C., as adhesions in the right lower abdominal quadrant, strongly suggestive of

appendicitis, were detected in one Egyptian mummy [18, 19]. However, it is not clear whether the appendix was recognized by the Greek anatomists, since there are some uncertain descriptions by Soaranos from Ephesos around year 100 and Aretaios around year 200 [20].

From the late 15th century, the vermiform appendix has been described as an anatomical structure in autopsy reports, but the pathogenesis of appendicitis was not understood. In 1554, a French court physician to Catherine de Medici, Jean Fernel, provided the earliest documented description of appendicitis in a 7-year-old girl, who died of perforated appendicitis, although he called the disease "passion iliac" [21]. From the 18th century, there are several reports on both the appendix and appendicitis. The first known written description of the appendix in detail was done by Morgagni in 1719 [22]. During the following decades, several authors report cases of inflammation or gangrene of the appendix and pain in the right iliac fossa, but the connection was still not completely understood [19, 20]. The condition was believed to begin with an inflammation of the caecal mucosa, called stercoral typhlitis, which could be complicated by paratyphlitis (a retro-caecal abscess) or perityphlitis (an intra-abdominal abscess). In 1812, James William Keys Parkinson described a perforated appendix and recognized it as a cause of death in a 5-year old boy [19]. Several other reports followed, e.g. by Wegeler [20], Prescott [20] and Louyer-Villermay [23, 24], who seem to have understood the pathogenesis of appendicitis, although the typhlitis theory still predominated in contemporary reports by Melièr [20], Goldberg [25] and Dupuytren [19, 26].

The treatment of acute appendicitis was non-operative in almost all patients until the end of the 19th century and consisted of bed-rest, enemas, purgatives, venesectio, opium drops etc [20, 27]. The surgical treatment was limited to incision of abscesses [27]. In 1827, Melièr proposed a more radical treatment with early appendectomy before the complications occurred, but as this was prior to the aseptic and anaesthetic era, abdominal surgery was not possible [27]. In 1880, Robert Lawson Tait became the first to perform a successful appendectomy [28]. During the following years, appendectomy was performed by several surgeons in different countries with variable and not always successful results, e.g. Groves in Canada 1883 [20], Krönlein in Zürich 1884 [20, 27], Mikulicz-Radecki in Krakow 1884 [20, 24], and Barton Sands in New York 1888 [19, 24].

Charles McBurney, who had been an assistant to Barton Sands, delivered one of the better known early reports on appendectomy in 1889 [29], where he also described the point of maximal tenderness, now known as the point of McBurney. He was also the first to describe the classical muscle-splitting grid-iron incision [30], although this had already been used by others before McBurney's publication [19, 31].

In Sweden, appendectomy was introduced as treatment for acute appendicitis by Karl Gustaf Lennander in Uppsala in 1889. The number of appendectomies performed in Sweden increased rapidly from 618 in 1901 to 10,449 in 1913 [32].
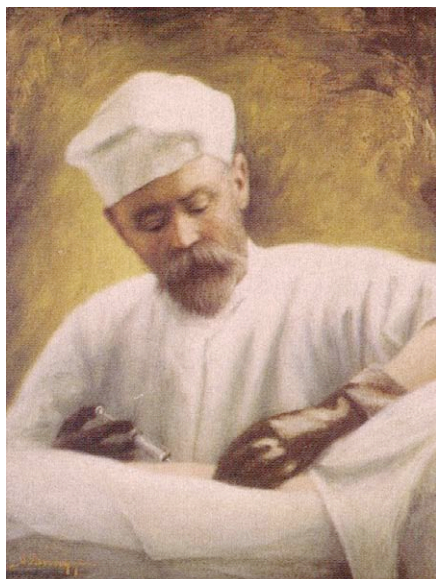
Karl Gustaf Lennander (1857-1908). Painting by J. A. Drougge (Museum of Medical History, Stockholm)

The indication for appendectomy, however, was still a subject of conflict. In 1895, the majority of appendicitis cases were thought to be self-limiting and spontaneously resolving [33]. There was a fear that the operative mortality would exceed that of conservative treatment and hence, surgery was avoided until signs of perforation or abscess were at hand [21]. McBurney and others proposed that an exploratory incision should be performed in all patients with suspected appendicitis [29, 34], but early surgery did not become common practice until the morbidity of unoperated perforated appendicitis greatly exceeded the morbidity of laparotomy. Due to modern anaesthetic techniques, treatment became predominantly surgical in less than 20 years. It became a principle to perform appendectomy early, on the slightest suspicion of appendicitis.

At this time, the cost of a negative laparotomy was felt to be low compared to the risk of a delayed operation [27]. A negative appendectomy was even regarded as a benefit, eliminating for the patient the risk of a serious and potentially life-threatening disease [35]. Interval appendectomies were also strongly recommended after an attack of appendicitis because of the risk for recurrence [36].
In Western Europe, the frequency of appendectomies reached a peak in mid-century and has steadily declined since then [37].

Embryology, anatomy and histopathology

The vermiform appendix and the caecum develop from the caecal bud, which arises from the antemesenteric border of the caudal limb of midgut loop around the beginning of the sixth gestational week [27]. It remains at the tip of the caecum until birth but reaches its final position on the posteriomedial wall below the ileocaecal valve [38] due to the lateral caecal wall growing faster than the medial. Both the anterior [38] and the retrocaecal position

[39] have been described as most frequent by different authors. Different degrees of malrotation may result in more ectopic locations of the appendix, e.g. subhepatic [40] and intracaecal [41].

The average appendix length is 9 cm (range 2-25 cm) [39]. The appendix has the same basic structures as the colon: serosa, muscularis propria, submucosa, muscularis mucosae, and large intestinal-type mucosa, and the mucosal features are similar to those of the colon [37]. However, development of lymphoid tissue resembling the arrangement in the distal small intestine occurs soon after birth and persists through childhood, until approximately the age of 25 years. The maximum transverse diameter is reported to be reached by 4 years of age and decreases gradually thereafter, due to the involution of the lymphoid tissue and increasing fibrosis [38, 42].

The commonly accepted view is that the appendix is a vestigial organ with no function. It has been suggested that there is a connection with food habits, since an appendix-like structure is found in other omnivores than man [43]. The appendix has also been proposed to play a role in the motility of the colon [44, 45] or for the immunological system, but these theories remain unproven.

The classical histopathological criterion of acute appendicitis is polymorphonuclear leucocytic infiltration of the muscularis [46, 47]. In more advanced stages of inflammation, necrosis of the muscular layer occurs and may be complicated by perforation, abscess formation or peritonitis. It has been proposed that simple appendicitis and advanced appendicitis are two different diseases with different etiologies [48, 49].

Etiology

The etiology of appendicitis remains unknown. The most favoured theory today is that appendicitis starts with an obstruction, due to swelling of the mural lymphoid tissue during an acute infection, a faecolith or stenosis, with subsequent increase of the luminal pressure, leading to mucosal ischemia and secondary bacterial infection [27]. However, obstruction can only be demonstrated in approximately one third of surgically removed appendices [50, 51]. Still, it appears to be more frequent in advanced appendicitis compared to simple, phlegmonous appendicitis, which may indicate that obstruction is an aggravating factor when appendicitis is present [49].

Faecoliths or appendicoliths, regarded as possible causes of obstruction, are more frequently detected when using modern imaging techniques, especially CT [52, 53]. They appear more frequently associated with perforated appendicitis and may therefore represent a possible risk for perforation [52,

53]; faecoliths may also be an incidental finding when inflammation is absent [50, 54].

Several alternative causes of appendicitis have been suggested, i.e. primary infection of the appendix, either hematogenous or originating from a breach of the mucosal barrier [49, 55], or a consequence of a previous breakdown of the mucosal barrier with a subclinical infection, leading to a stricture [56]. A seasonal variance in incidence and cluster outbreaks of appendicitis, as well as the age distribution with an incidence peak in adolescence, resemble that of many infectious diseases, especially tonsillitis and influenza [57-59], but a causal relation has not been verified. There are series of specific infections of the appendix reported impossible to differ from common acute appendicitis. Although rare, they may be coincidental findings as well as predisposing factors: actinomyces [50], Helicobacter jejuni [60], pinworm [61-68], tuberculosis [50] and Yersinia enterocolica [50, 69, 70] among others. Other rare reported causes of appendicitis are foreign bodies [38, 71-73] and trauma [74-80].
Most probably, the etiology of appendicitis is multifactorial.

Epidemiology

The diagnosis of appendicitis is not always verified by histopathology and hence, a review of the epidemiology of appendicitis is difficult. It is generally assumed that the incidence of appendectomy reflects the incidence of appendicitis, but this assumption is disputable [27].

Appendectomy is more common in industrialized countries than in developing countries, and there are also regional differences within the industrialized countries [81-84]. The highest incidence is reported from Japan with an incidence of 750 per 100,000 inhabitants annually [85] and from France with 564 per 100,000 inhabitants [86]. In Sweden, incidences of 120-210 per 100,000 inhabitants have been reported [87-89]. The cause of regional variations in incidence is unclear. Hereditary as well as dietary factors have been suggested [90-95]. The relatively high incidence of appendectomy in Japan and France is thought to be related to the type of insurance systems, qualification regulations for surgeons and patient expectations [27].

Acute appendicitis occurs in all ages but there is a marked increase in the second decade [3, 21, 37]. About 10% of all patients are younger than 10 years and about 10% are older than 50 years [49]. Acute appendicitis occurs also in neonates [96-101], although the disease is rare under the age of two years.

Appendicitis is 15% to 48% more common in men and the gender difference is seen in all ages [3, 57, 87-89, 102]. From the United States, racial differences have been reported with a 50% lower incidence in blacks and Asians compared to Caucasians [3, 57]. A family history of appendicitis appears to be a significant risk factor [90, 91, 103, 104]. Synchronous appendicitis in first-degree relatives has been reported, indicating both a genetic susceptibility and an environmental cause [105-107]. Breastfeeding in infancy may have a protective effect since children who were breastfed for more than 7 months had a 40% lower risk of appendicitis than children who were never breastfed [108].

The lifetime risk of having appendicitis, based on data from the United States 1970-1984 [3] is approximately 9% for males and 7% for females. The lifetime risk of appendectomy is 12% for males and 23% for females [3].

CLINICAL MANAGEMENT

Epidemiological research during the last decades has demonstrated different incidence patterns of perforated and non-perforated appendicitis, and it has been suggested that these are two different entities [109]. There is a constant incidence of perforation in all age groups [102, 110], and there are indications that most perforations occur before admission to hospital [111, 112]. Since obstruction is more common in advanced appendicitis, it has been proposed that simple and complicated appendicitis have different etiology and pathogenesis [48, 49].
The overall incidence of perforation is 16%-39%, with a median of 20% [3, 12, 16, 27, 52, 111-114].

The perforation rate is higher in children (23-73%) [9, 114-118] and in elderly patients (55-70%) [54, 112, 113, 116], who are thought to have a lower resistance to perforation or a more rapidly progressive disease [119]. Patients who have a delayed diagnosis have a high perforation rate [120-123]. These patients often have concurrent diseases and unclear clinical symptoms [124].

In children, there is often a delay before being brought to medical attention [125]. Approximately one third of patients are regarded to have atypical clinical findings [9]. Furthermore, children may be difficult to examine and may be unable to communicate their complaints [126]. It has also been suggested, that the thinner appendiceal wall in children may result in a more rapid progression of appendicitis to perforation [127].

Negative appendectomies

An inverse relationship between the rate of perforations and the rate of negative laparotomies has been demonstrated [16, 128]. It has been argued that "a proportion of normal appendices should appropriately be removed to avoid perforations" [16]. The reported negative appendectomy rate ranges in various studies from 14 to 25% [9-11, 129, 130] and even higher rates have been reported in selected populations with diagnostic difficulties and a higher risk of perforation, i.e. in children, women and elderly patients [12, 131]. A negative appendectomy rate of approximately 20% generally has been considered acceptable [11, 54].

The necessity of the inverse relationship between the perforation rate and the negative appendectomy rate was questioned already during the seventies [132]. In a study from Germany 1971, the high rate of negative explorations was associated with increased mortality [83]. Studies performed during the last decades have shown that most perforations probably have occurred

before the patient's admission to hospital, and the rate of explorations has not been found to influence the incidence of perforation [110, 111, 133, 134].

Avoiding unnecessary laparotomies has become increasingly desirable, since the complication rate is not negligible and is even higher with negative laparotomy, compared to positive [12-14, 135]. The increased risk of developing small bowel obstruction after a negative appendectomy may be attributable to both the surgical technique [12, 13] and to patient-related factors, i.e. increased inflammatory response [136]. Economic aspects on the negative appendectomy rate have also become increasingly important, since unnecessary surgery is a waste of medical resources. The death and complication rates following perforated appendicitis have decreased over the years as a result of improved perioperative routines and postoperative care, including treatment with modern antibiotics [137, 138].
Since the introduction in recent years of modern imaging techniques in the evaluation of suspected acute appendicitis, namely ultrasonography 1986 [139] and computed tomography [9, 52, 140-143], several studies have demonstrated that the negative appendectomy rate can be reduced without an increase of the perforation rate [10, 144-146].

Clinical course

In typical cases, the disease begins with a visceral pain located to the epigastrium. After a variable time interval, but usually within 6-18 hours, the pain migrates to the right lower quadrant of the abdomen and a constant, distinct tenderness develops, due to the peritoneal engagement. Rebound tenderness, as well as voluntary and involuntary muscular contraction, may also be present. Associated symptoms may include anorexia, nausea, vomiting, constipation or, especially in children, diarrhoea.
Untreated appendicitis is thought to proceed to perforation in the vast majority of cases. Perforation may result in short-lasting pain relief, but is then followed by a gradual increase in severity of the symptoms [37]. Associated complications include peritonitis and septicaemia.

In approximately 2-3% of patients with acute appendicitis, perforation is followed by the development of a demarcated appendiceal abscess [33, 147]. The appendiceal abscess formation is also believed to occur without an obvious rupture of the appendiceal wall, since bacteria may readily permeate a damaged appendiceal wall [46].

The disease progression proceeds usually during 8-48 hours; if the diagnosis of appendicitis is not made within this time interval, the probability that it actually is appendicitis is progressively reduced [37]. A developed appendiceal

abscess may, however, have a history of less distinct symptoms during several weeks. As mentioned before, spontaneously resolving appendicitis has been reported [148-150]. Recurrent and chronic forms of appendicitis have also been recognized [151-154].

The typical presentation described above, however, occurs in only two thirds of the patients with appendicitis, and patients with other abdominal conditions may have similar symptoms [121, 155]. The variability in the precise anatomical location of the appendix affects the localized symptoms [155]. Children are more often believed to have an atypical presentation [9].

Table 1. *Diagnostic accuracy in acute appendicitis at Massachusetts General Hospital 1937-1959. Modified after Barnes et al. [156]*

Diagnosis	Incidence of diagnosis when appendicitis was diagnosed peroperatively (%)	Incidence of postoperative diagnosis when appendicitis was diagnosed preoperatively (%)
Mesenteric lymphadenitis	0.2	4.6
Ovarian cyst pathology	0.3	2.0
Pelvic inflammatory disease	0.2	1.3
Gastroenteritis		0.9
Small bowel pathology	0.3	0.5
Meckel's diverticulitis		0.4
Diverticulitis	0.1	0.3
Cholecystitis	0.2	0.3
Renal or urethral pathology		0.2
Regional ileitis		0.2
Endometriosis		0.2
Colon carcinoma	0.3	0.1
Pancreatitis		0.1

Diagnostic methods

History

Knowledge of the clinical course of appendicitis is mandatory for adequate history taking. In children, there are considerable difficulties involved; young children, especially, may be incapable of understanding and answering questions meaningfully [126], which may contribute to a delay before being brought to medical attention [125].

Physical examination

The basis for the diagnosis of appendicitis is the induction of abdominal tenderness in the right iliac fossa due to the local inflammation of the appendix. With further progress, the tenderness becomes more severe. A local muscle guarding develops as a response to peritoneal involvement. After a rupture and free peritonitis, the abdomen becomes distended with a general, pronounced tenderness and generalized muscular guarding [37].
Rectal examination may yield tenderness anteriorly or to the right. Some patients have a positive psoas stretch test; i.e., raising the right leg causes pain. Due to the dynamic character of the disease, repeated examinations are strongly recommended [157-160].

Laboratory findings

Appendicitis is often accompanied by a systemic inflammatory response, as seen by the presence of fever, leukocytosis, and an increase in the concentration of the C-reactive protein (CRP) [27]. The diagnostic efficacy of laboratory tests, however, depends on the stage of appendicitis [161].

The total white blood cell count (WBC) is usually increased to more than 9.0×10^9 per litre. Repeated measurements have shown that WBC may decrease and even be normalized despite the continuous process of inflammation [162].

CRP values exceeding 10 mg/l may be useful in clinical managements of acute infections, including appendicitis [8, 163-165]. In evaluating the CRP results, however, the duration of symptoms is important since patients with a short history of symptoms (less than 12 hours) may not have developed an increase of CRP values. Therefore, repeated measurement may be valuable [162]. In children, CRP values are less reliable in the evaluation of suspected appendicitis, than in adults [166].

Urinalysis

Bacteriuria can be detected in 15% of patients with appendicitis [167]. Haematuria and leukocyturia may occur, and are more frequent when the appendix is localized retrocaecally or in the pelvis [168]. A normal urine sample, however, does not rule out appendicitis.

Laparoscopy

Laparoscopy has been described as a cost-saving procedure in the diagnosis and treatment of abdominal pain in patients with unclear etiology [169, 170] and especially when appendicitis is suspected [171-174]. Still, laparoscopy is an invasive procedure requiring anaesthesia, and is associated with a risk for complications [175, 176].

Radiologic imaging

### PLAIN RADIOGRAPHS AND BARIUM ENEMA

Plain abdominal radiographs and barium enema are non-specific and of little value. Radiographs were reported to be normal or misleading in 75% of cases of pediatric appendicitis in one study [177], whereas other authors found radiographs helpful in only 6% of cases [178]. Filling of the appendix to the tip with contrast virtually excludes appendicitis, whereas non-filling of the appendix with mass effect on the caecum suggests appendicitis [179]. However, the appendix does not fill completely in 8% of normal cases [179]. Furthermore, determination of complete filling can be difficult because of the variation in the length of normal appendices and variation in the level of obstruction in appendicitis [180]. Other conditions than appendicitis can produce mass effect on the cecum [181]. Nowadays, plain radiographs and barium enema have been replaced by modern imaging techniques with higher sensitivity and specificity.
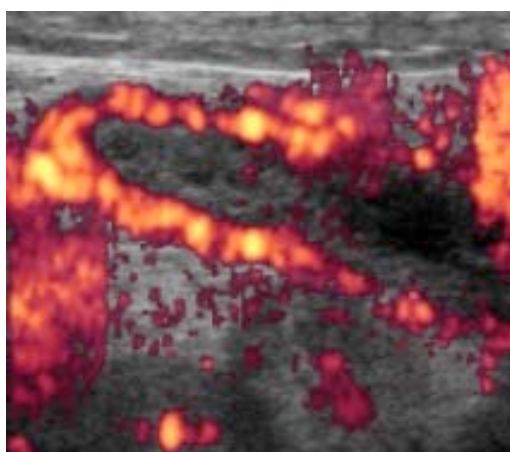
ULTRASONOGRAPHY (US)

The graded-compression ultrasonographic technique was originally introduced by Puylaert 1986 [139]. Since then, numerous studies have demonstrated the usefulness of US in the evaluation of suspected appendicitis [182-188]. The overall sensitivity of US varies in different studies, but usually lies within the range of 75-95% [183]; however, values as low as 44% have been reported [142]. The specificity of US is usually reported to lie within the range of 90-95% [183], although substantially lower values have been reported [189, 190]. The diagnosis of appendicitis is based on the detection of a blind-ending, non-compressible tubular structure with a maximal diameter exceeding 6 mm, with or without an appendicolith, and with no peristaltic activity. Color Doppler imaging may demonstrate hyperemia in the appendiceal wall which is regarded as a finding of high specificity [191]; however, detectable hyperemia may be absent in early and in advanced,

gangrenous appendicitis [9]. Currently, there are no reports on the use of contrast-enhanced ultrasonography in the evaluation of appendicitis.
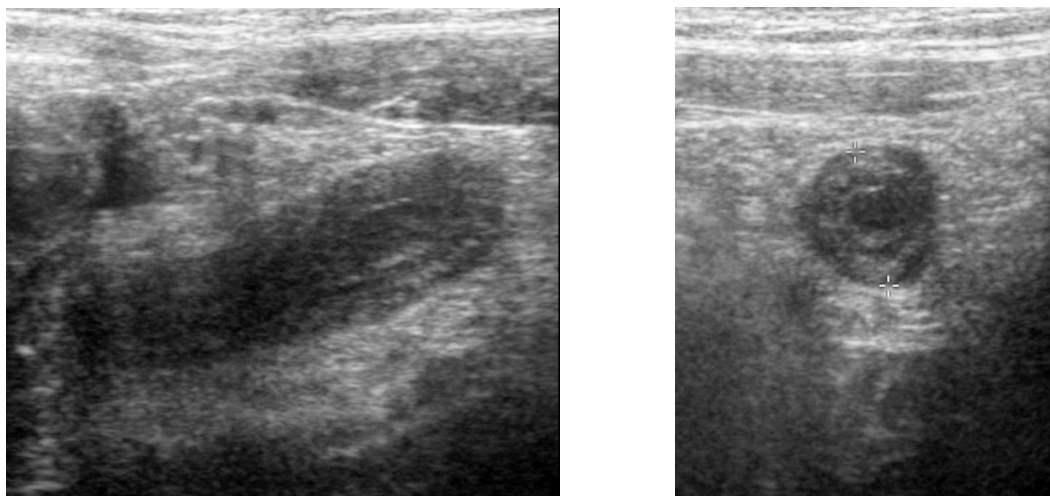
Ultrasonographic images of a phlegmonous appendicitis. Longitudinal (left) and transverse (right) image.

Phlegmonous appendicitis. Color Doppler ultrasonographic image demonstrating mural hyperemia.

The major limitation of US is its high operator dependency, as illustrated by the wide range of sensitivity and specificity values in different studies. The lowest values are generally achieved in studies when US is performed by sonographers with limited experience of imaging of the gastrointestinal tract [192], while substantially higher values are achieved when US is performed by a limited number of experienced specialists [187, 193]. A further limitation of US in diagnosing appendicitis is the fact that non-visualization of the appendix does not rule out appendicitis. Well-known difficulties in identifying the appendix may occur in patients with pain, obesity, overlying gas, or in perforated appendicitis. Several recent studies have demonstrated that a normal appendix can be visualized in a large number of patients with symptoms suggestive of appendicitis [182, 191, 193-196]; this finding is regarded as highly specific in excluding appendicitis [191]. In children, however, the smaller amount of intraabdominal fat compared to that in adults may affect the ability to identify the normal appendix and also to distinguish it from bowel loops.

Ultrasonographic longitudinal image of a gangrenous appendicitis.

The outer diameter of the appendix has been a subject of discussion. Rettenbacher et al [193] demonstrated a marked overlap of outer appendiceal diameter in normal and inflamed appendices, and concluded that an outer diameter of 6 mm or more as a sign of acute appendicitis provides high sensitivity but limited specificity. Hahn et al [187] reported lymphoid hyperplasia as a cause of a sonographically abnormal appendix. In children, the mucosa and submucosa are physiologically thicker [197], which might explain the relatively high number of false-positive US examinations reported by some authors [198]. Some cases regarded as false-positive in different studies may also represent spontaneously resolving appendicitis [148-150].

The great advantage of US as the primary imaging modality is the fact that it is relatively quick to perform and does not involve the use of ionizing radiation, which is of special importance in children [199].

COMPUTED TOMOGRAPHY (CT)

Helical computed tomography with use of a variety of techniques has been shown to be highly sensitive and specific for the diagnosis of appendicitis [10, 52, 54, 140-142, 144, 200-204]. The reported overall sensitivity lies usually within the range of 90-100%, and the specificity within 91-99% [142, 144, 178, 201, 202, 205, 206], although different techniques have been used in the various studies. Several institutions have now accepted CT as the method of first choice because of its advantages over US, including less operator dependence, more confident visualization of the appendix, and better delineation of the extent of phlegmon and abscess in complicated appendicitis [207]. The disadvantages of CT include higher cost, potential risks of contrast media, and ionizing radiation exposure, which is especially critical in children [199]. There is considerable controversy in the literature regarding the use of oral, rectal or intravenous contrast agents, as well as the question of whether the area scanned should be limited or not.
The diagnosis of appendicitis is based on the visualization of an enlarged appendix with a maximum diameter exceeding 6 mm, with contrast enhancement in the thickened appendiceal wall (in contrast enhanced CT

studies), and/or pericaecal inflammatory changes, or on the visualization of an abscess, with or without an appendicolith. The pericaecal inflammation may be absent, as reported by some authors [203, 204, 208], especially in patients with mild and incipient forms of appendicitis [52].

Transverse contrast-enhanced abdominal CT scan demonstrating an inflamed, curved appendix (arrows).
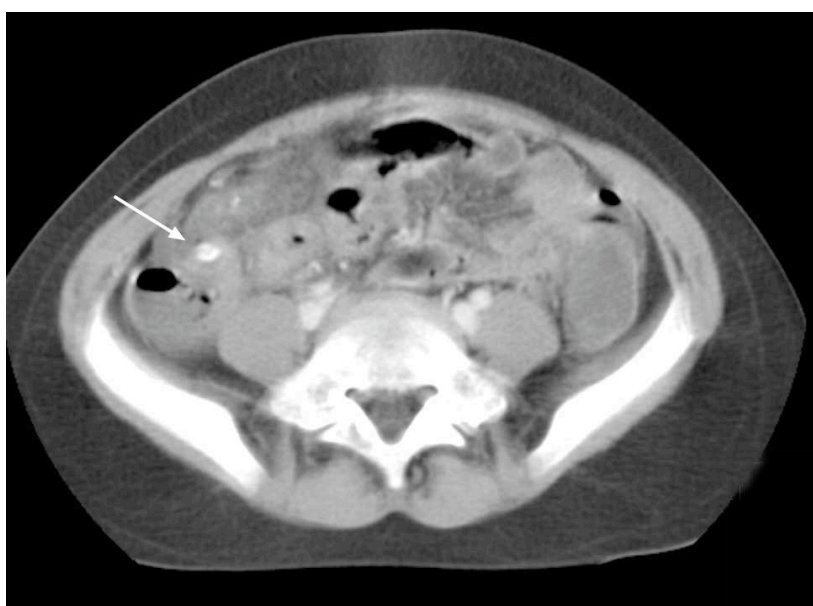
Transverse contrast-enhanced abdominal CT scan demonstrating a gangrenous appendicitis with an appendicolith (arrow) and pericaecal inflammation.

Accurate identification of the normal appendix in patients whose symptoms are caused by alternative conditions is of great value; however, the relatively small volume of intraperitoneal fat, which is generally seen in children, especially younger than 10 years, has been shown to decrease the rate of identification of a normal appendix [209].
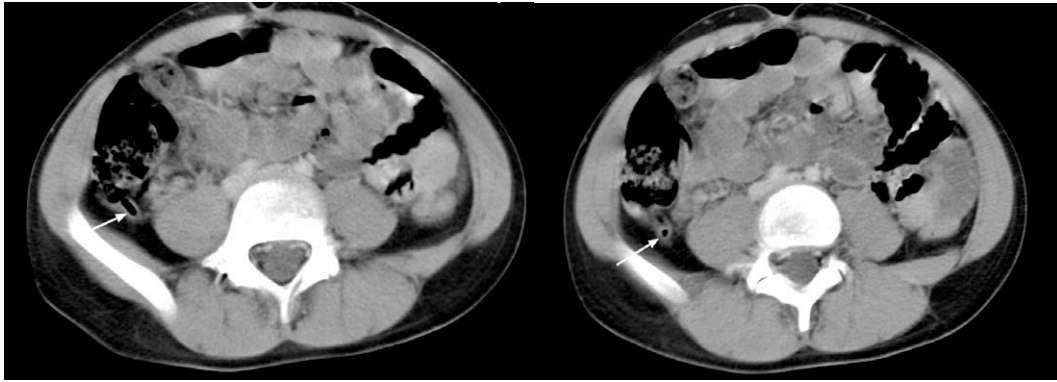
Two consecutive contrast-enhanced abdominal CT scans demonstrating a normal air-filled appendix (arrows).

In recent years, it has been suggested that ionizing radiation from diagnostic imaging carries a risk of later development of malignancy [199, 210, 211]. Children are at greater risk from ionizing radiation than adults, both because of a longer life span during which cancer can develop, and also because of the increased radiation sensitivity of developing tissues. Because of its frequent use, a major area of concern is the risk of radiation from CT scanning. Mettler et al. found that CT scans were responsible for 67% of the effective dose to the population from all diagnostic imaging studies, and 11% of these CT scans were performed in children [212]. Paterson et al. reported that the majority of CT studies performed at different institutions did not use techniques appropriate for children, which included both factors resulting in increased radiation dose and factors decreasing diagnostic accuracy [213]. An example of a non-medical activity that increases radiation exposure is high altitude airline flight. It has been estimated that 10,000 miles of long distance airline travel result in an increase in the cancer risk rate for children of 1 in 5,000 [214], which is similar to the single CT risk calculated, using the modern lower dose techniques.

Therefore, CT scanning should be ordered with attention to both the risk and the benefit. In most cases, the benefit greatly outweighs the risk [215]. All CT scans should be performed using the lowest dose that provides the radiologist with the necessary information [215]. Donnelly et al. described a table that can be used to choose the single-detector CT scanning technique for adjusting the radiation dose, depending on the part of the body scanned and on the patient's size. The use of this technique in young children provided a decrease in radiation dose of up to 75% without loss of diagnostic confidence [216]. Models for dose reduction for multidetector CT are also being increasingly discussed [217]. Still, the greatest possible decrease in risk occurs when an unnecessary study is not performed.

Magnetic resonance imaging offers the advantages of excellent soft tissue contrast, multiplanar imaging capability, and no ionizing radiation exposure. There are, however, only a small number of studies regarding evaluation of possible appendicitis in selected populations [218-220]. The method has several limitations; i.e., high cost, it is time-consuming and therefore frequently requires sedation in children, and is rarely available on an emergency basis. Furthermore, since faecoliths and intestinal gas produce similar signal voids on MRI, they may be difficult to distinguish. There is a need for further studies, but currently MRI cannot be advocated over US or CT for the evaluation of appendicitis, especially not in children.

Treatment of appendicitis

Appendectomy

Open appendectomy is the treatment of choice in the vast majority of patients with appendicitis. The surgical technique used today has evolved from tradition and experience during several decades. Detailed descriptions are available in textbooks of surgery, e.g., P. Myers description from 1994 [23]. Laparoscopic appendectomy was performed for the first time in 1983 [221], and is now performed routinely at numerous institutions, in both adults and children.

Conservative treatment

Conservative treatment with antibiotics only (combined intravenous and oral treatment) has been used in acute appendicitis in small adult populations [7] but, to my knowledge, there are no studies restricted to children. Antibiotic treatment that may or may not be followed by an interval appendectomy, however, is frequently used in the management of appendiceal abscesses; sometimes combined with percutaneous drainage of the abscess. Prophylactic antibiotic treatment, preceding an appendectomy, is recommended especially in cases of advanced appendicitis [138].

Histopathologic analysis

The generally accepted histologic criterion for the diagnosis of acute appendicitis is polymorphonuclear leukocytic infiltration of the muscularis layer [46]. Usually, neutrophils and ulcerations are also present within the mucosa. The different stages of appendicitis are usually referred to as phlegmonous, gangrenous or perforated appendicitis.
However, the histopathological examination has been stated to be an "imperfect gold standard" [27], since the criteria for the diagnosis of appendicitis are not set and may vary between different institutions and interpreters.
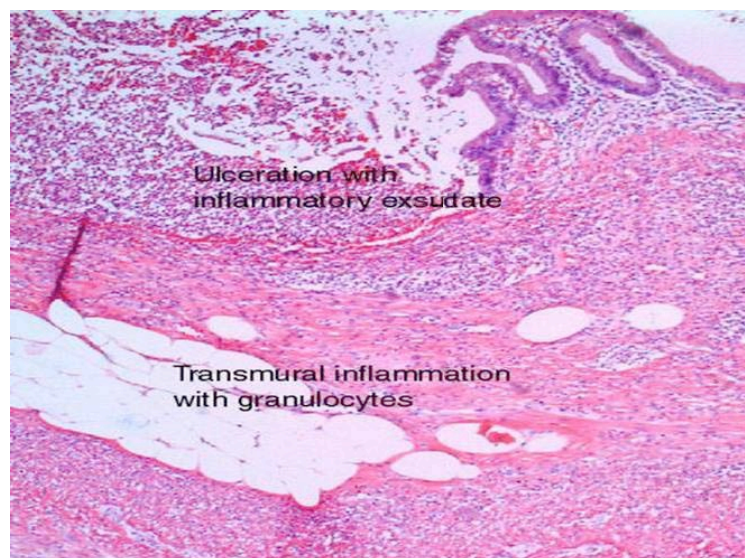
Histological section of an acute appendicitis with ulceration of the mucosa and intense inflammatory infiltration of neutrophile granulocytes through the appendiceal wall.

(Section provided by Edneia Tani, MD, PhD, Dept. of Cytology, Karolinska Hospital).

AIMS OF THE THESIS

The main aims of the present investigation were

- To evaluate the diagnostic accuracy of ultrasonography (US) and of abdominal computed tomography (CT) performed in addition to US in the diagnosis of appendicitis in children

- To compare the diagnostic accuracy of different CT techniques, namely non-enhanced helical CT limited to the lower part of the abdomen, CT of the entire abdomen after intravenously administered contrast medium, and the combination of both, in order to optimize the CT technique and possibly reduce the radiation dose

- To evaluate how the negative appendectomy rate and the perforation rate have changed during the past decade with the introduction of and increased use of US and CT

- To evaluate how the radiologic imaging procedures, including US only or US and CT, affect the surgeon's decision making process in the management of suspected appendicitis in children

MATERIAL AND METHODS

Prospective study

Study setting

The evaluation of suspected appendicitis was analysed in a prospective randomized study that constituted the basis for papers I, III and IV. The study was performed during a period of 9 months, from December 1999 to September 2000, and was approved by the local ethics committee at Karolinska Hospital. All children who were clinically suspected of having acute appendicitis and were admitted to the emergency department of Astrid Lindgren Children's Hospital, Stockholm, received oral and written information about the study. Patients with abdominal pain that was considered to be due to obstruction without inflammation were excluded. Informed consent was obtained from each child's parents. The vast majority of the consecutive patients chose to participate in the study. The study population consisted of 600 children, including 312 girls and 288 boys (average age, 10.4 years; age range, 2-15 years).

The initial examination was performed by a pediatric surgeon or a surgical resident on duty, who estimated the likelihood of each child having appendicitis on a scale from 0% to 100%. The initial clinical impression before performing radiologic investigation was recorded, designating the patient for operation, observation, or discharge, with or without a planned new visit for re-examination.
After this protocol, all patients were randomized to undergo US only (283 patients) or US and additional abdominal CT (317 patients).

US and CT Scan Interpretation

The US studies were performed and interpreted by either one of 12 pediatric radiologists or one of 9 senior residents who had completed rotations in general US and at least 2 months in pediatric radiology. All studies were performed by using a 7-MHz linear-array transducer (Sequoia; Acuson, Mountain View, Calif) and the graded compression technique described by Puylaert [139]. The criteria for the diagnosis of appendicitis were previously established [139, 193].

Helical CT scanning was performed on a single detector-row CT scanner (CT HiSpeed Advantage; GE Medical Systems, Milwaukee, Wis). Each CT study consisted of two scans. Initially, a limited scan of the lower part of the abdomen was performed without any contrast medium administration. After

that, a nonionic contrast medium was administered intravenously, and the entire abdomen was scanned. The injected dose was 2 mL per kilogram of body weight, with an upper limit of 100 mL. Patients with a history of asthma or possible previous reactions to contrast medium were excluded. There were no severe adverse drug reactions to the intravenous administration of contrast medium. No oral or rectal contrast medium was administered. All CT scans were analysed at a workstation, i.e. on computer monitors, and interpreted by either one of 12 pediatric radiologists or one of 9 senior residents. The diagnosis of appendicitis was based on criteria established in prior studies [54, 208, 222-224]. The CT study was always performed after the US study, and the time interval between the US and CT examinations was kept as short as possible. The interpreter of the CT study had access to the results of the US study.

Both the US scan interpreter and the CT scan interpreter stated whether appendicitis was present or not, and estimated their level of confidence in their finding on a scale from 0% to 100%.

These statements form the basis for the analysis performed in papers I and IV.

In paper III, a retrospective review of prospectively acquired data from the CT examinations referred to above was performed. All CT examinations were divided into three groups, which were evaluated by three pediatric radiologists, working independently: group A, all non-enhanced limited CT studies; group B, all contrast enhanced CT studies; group C, both all the non-enhanced and the enhanced sequences together. To avoid any recall bias, the readers evaluated the sequences in different order, and the patients appeared in different order within the groups. In this study, the readers were blinded to all clinical information and to the results of previous US and CT studies.

Final disposition, final diagnosis and follow-up

After the radiologic imaging was completed, the patient was re-examined by the surgeon, who made the final disposition for the patient as to operation, observation, or discharge. The final clinical outcomes were determined at surgery and histopathologic analysis in the patients who underwent laparotomy (n = 252). The nonsurgically treated patients (n = 348) were followed up with a questionnaire, which was sent to the child's parents 6 months after their emergency department admission. The questions about their state of health and possible treatment at other facilities, if any, after discharge from our hospital were designed to track any false-negative diagnoses. The questionnaire was completed by 327 (94%) of the 348 patients who were treated nonsurgically. The medical records of all patients were also reviewed.

Retrospective study

The changes in the negative appendectomy rate and the perforation rate during the past decade were studied in a retrospective study, which constituted the basis for paper II.
In the greater Stockholm area, pediatric surgery is centralized such that the vast majority of pediatric surgical cases up to 15 years of age have been provided care at St. Göran Children's Hospital until 1998, when it was closed and replaced by Astrid Lindgren Children's Hospital, located at the Karolinska Hospital area. The pediatric population in the greater Stockholm area has gradually increased during the past decade, and at present, the hospital has a referral area of approximately 350,000 children.

We retrospectively reviewed the medical records of the first 150 children during the years 1991, 1994, 1997 and 2000 who underwent appendectomy. Hence, the study population consisted of totally 600 children (343 boys, 257 girls; mean age 10 years, age range 0 – 15 years). The years were chosen with consideration to the time when US and CT were introduced as diagnostic tools in the evaluation of suspected appendicitis at St. Göran Children's Hospital. The total number of appendectomies and the total number of cases of appendicitis were recorded. In perforated appendicitis, the perforation was considered to have occurred after admission if the time interval between the first contact between the patient and any health professional (i.e., primary physician or surgical consultant at admission) and surgery exceeded 12 hours. Any performance of US and/or CT in order to investigate suspected appendicitis, as well as the results of the investigation, were recorded.

The study was scrutinized by the local ethics committee and considered quality assurance and therefore exempted from further ethical review.

Statistical analysis

Paper I

Measures of imaging examination validity – namely sensitivity, specificity, diagnostic accuracy, and positive and negative predictive values – in the diagnosis of appendicitis were calculated in each randomly selected group, and also for the diagnosis of appendicitis with US only in all 600 patients, and for the diagnosis of appendicitis with CT only in 317 patients. The standard Pearson χ^2 test was performed to compare the calculated values of US and CT

in each group. A *P* value of .05 or lower was considered to indicate a significant difference.

Paper II

The contingency tables were analysed by standard Pearson χ^2 test and tested for trend by Spearman correlation. Fisher's exact test was used for comparison of the negative appendectomy rates for the years studied. The computations were done with SPSS procedure crosstabs, release 10.0.1 (SPSS Inc., Chicago, Ill.). A *P* value of .05 or lower was considered to indicate a significant difference. The incidence of appendicitis for the years studied was correlated to the population statistics and an overall incidence was calculated.

Paper III

Individual and pooled sensitivity and specificity values for the three interpreters were calculated for the diagnosis of appendicitis for the limited non-enhanced CT, for the contrast enhanced CT of the entire abdomen, and for the combination of both. The standard Pearson χ^2 test was performed to compare the values between groups. A *P* value of .05 or less was considered to indicate a statistically significant difference. Receiver operating characteristic (ROC) curves were calculated by group for each reader.

Paper IV

Receiver operating characteristic (ROC) curves were calculated for the radiologist and for both the initial and the final surgical decision in the two randomized groups. The computations were done with SPSS for Windows, release 10.0.1 (SPSS Inc., Chicago, Ill.).

RESULTS

The main results are summarized below. For further details, see paper I – IV.

Diagnostic accuracy of US and CT

Of the 600 patients, 244 (41%) had a final diagnosis of appendicitis. US had an overall sensitivity of 80% (196 of 244 patients), an overall specificity of 94% (336 of 356 patients) and diagnostic accuracy of 89% (532 of 600 patients). In the group assigned to undergo US only, US had a sensitivity of 86% (94 of 109 patients), a specificity of 95% (165 of 174 patients) and diagnostic accuracy of 92% (259 of 283 patients). In the group of patients who were randomly assigned to undergo US and CT, CT had a sensitivity of 97% (131 of 135 patients), a specificity of 93% (170 of 182 patients) and diagnostic accuracy of 95% (301 of 317 patients). The combination of both US and CT had a sensitivity of 99% (133 of 135 patients), a specificity of 89% (162 of 182 patients) and diagnostic accuracy of 93% (295 of 317 patients). Positive and negative predictive values were also calculated. All values and clarifying data are listed in Tables 1-3, paper I.

Ultrasonographic image of a phlegmonous appendicitis with an appendicolith (arrow).

Table 2. *The most common differential diagnoses in patients who did not have a final diagnosis of appendicitis.*

Diagnosis	Number of patients (of the total of 356)	%
Non-specific abdominal pain	192	54
Mesenterial lymphadenitis	100	28
Gastroenteritis	20	5.6
Ovarian cyst	8	2.3
Urinary tract infection	8	2.3
Pneumonia	4	1.1
Ovarian torsion	3	0.8
Miscellaneous*	21	5.9

* The "miscellaneous" group included patients (n = 1 in each condition) with pancreatitis, intussusception, hematokolpos, small bowel obstruction, Wilms' tumor etc.

The rates of negative appendectomies and perforations

Of the total of 244 patients with appendicitis, 235 patients underwent appendectomy, and 8 were treated conservatively with antibiotics only for appendiceal abscess. One patient with an appendiceal abscess was identified at follow-up and treated by means of drainage.

A total of 252 patients underwent laparotomy. Eight patients underwent laparotomy because of diagnoses other than appendicitis, and all of these diagnoses were made using preoperative radiologic imaging.

In 9 patients, the results of appendectomy were negative for appendicitis. Of these, 6 patients had negative radiologic findings and appendectomy was performed on the basis of clinical symptoms. Consequently, the negative appendectomy rate in this study was 3.7%.

Perforated appendicitis was diagnosed in 52 of 244 patients, including 11 cases of appendiceal abscess. Consequently, the perforation rate was 21%. In 88% (46 of 52 patients), a correct diagnosis of appendicitis was made with US and/or CT. One patient had a false- negative diagnosis with both US and CT, but surgery was performed because the clinical findings were convincing for a diagnosis of perforated appendicitis.
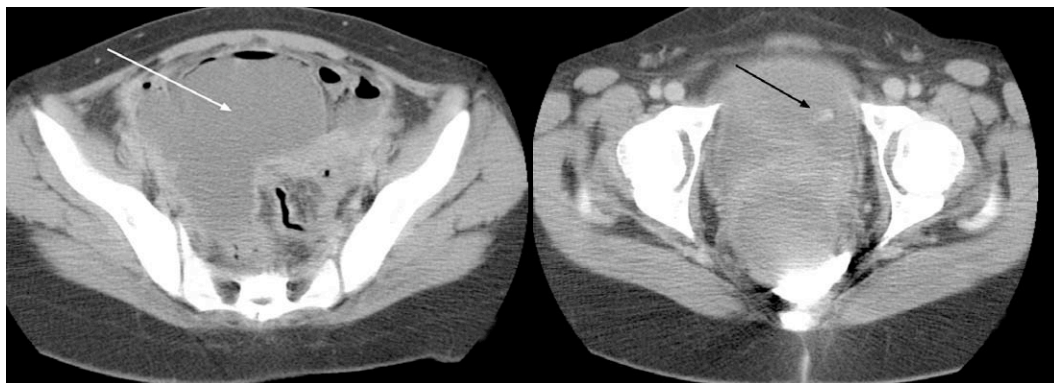
Two consecutive contrast-enhanced abdominal CT scans demonstrating perforated appendicitis. Pus in the peritoneal cavity (white arrow). An appendicolith surrounded by pus (black arrow).

Diagnostic accuracy of different CT techniques

From the original 317 patients who underwent CT, 11 were excluded from the retrospective review of the prospectively acquired data (paper III) because of technical difficulties in obtaining both CT sequences in each patient when the PACS software was upgraded. Hence, the study population consisted of 306 patients.

Of these, 129 (42%) had appendicitis. Interpreters diagnosed appendicitis with 66% pooled sensitivity and 96% pooled specificity with limited, non-enhanced CT. With contrast-enhanced CT of the entire abdomen, appendicitis was diagnosed with 90% pooled sensitivity and 94% pooled specificity. With the combination of both sequences together, readers diagnosed appendicitis with 90% pooled sensitivity and 94% pooled specificity. The individual results for each reader, by CT technique, are listed in Table 2 (paper III).

Transverse non-enhanced abdominal CT scan. The appendix, although visible, cannot be distinguished from bowel loops.

Transverse contrast-enhanced abdominal CT scan at the same level as the image above. The inflammed appendix clearly visible due to contrast enhancement of the thickened appendiceal wall (arrow).

Changes in the rates of negative appendectomies and perforations over time

The retrospective study (paper II) revealed that the total number of appendectomies performed because of presumed acute appendicitis during the years 1991, 1994, 1997 and 2000 varied from 334 to 406 (Table 1). The negative appendectomy rate for the years studied decreased gradually from 23% to 4.0%. During the same years, the use of US and CT increased gradually from 1.3% and 0.0% to 98% and 59%, respectively. In appendicitis, the overall perforation rate remained stable between 29% and 34%. The perforation rate after admission decreased from initially 12% to 2.1%. For details, see Fig 2-3 (paper II).

Because of the very low incidence of appendicitis below the age of 3 years (Fig. 1), the overall incidence of appendicitis was calculated for the age interval of 3 to 15 years. After adjusting for age, the population-based incidence of appendicitis for the years studied has not changed.

Impact of radiologic imaging on surgical decision-making process

The initial disposition called for 88 operations, 338 observations, and 167 discharges. In total 347 patients had their treatment plan changed from the initial disposition, resulting in 252 operations, 65 observations, and 276 discharges. A total of 7 patients were initially designated for "other treatment", such as medical treatment, referral to other departments etc, and were thus excluded from further analysis. In 11 patients, an unnecessary operation was possibly avoided. In 28 patients who turned out to have appendicitis, a possible inappropriate discharge was avoided. Eighteen patients had a false negative radiological diagnosis. Of these, 17 underwent surgery due to convincing clinical findings. For further details, see Fig. 2a-c (paper IV).
CT provided additional information for the surgeon only when the results of US and CT were discordant, which occurred in 16% (50 of 317 patients).

DISCUSSION

Suspected appendicitis is the most common cause of emergency abdominal surgery in children [225]. Despite its common occurrence, accurate diagnosis remains challenging. Appendicitis may be missed at initial clinical examination in 28-57% of children aged 12 years or younger and in nearly 100% of children younger than 2 years [226]. Delay in treatment increases the risk of perforation and its complications, including abscess formation, peritonitis, sepsis, bowel obstruction, tubal sterility in girls, and death [207].

Diagnostic imaging of appendicitis with graded-compression US and helical CT has steadily improved over the past decades, but the effect of radiologic imaging on negative appendectomy rates, perforation rates and management outcome has been a subject of discussion [11, 135, 227]. A minority of studies are prospective and focused on children [11, 142, 143, 178, 201, 206, 228-230].

The ideal diagnostic test should be safe, fast, non-invasive, highly accurate, inexpensive and readily available. Several studies have demonstrated that higher sensitivity can be achieved when using helical CT compared to US, and

it has been recommended as the method of first choice by several authors [231-233]. During recent years, however, concern over the risks of ionizing radiation generated by CT has increased, especially in the pediatric population [199, 210, 211].

Ultrasonography

The results of our prospective study demonstrate that both US and CT are excellent tools for making the diagnosis of appendicitis in children, and that CT outperforms US with respect to sensitivity, negative predictive value and overall diagnostic accuracy. It has also been shown, however, that CT provides additional information to the surgeon only when the results of the US and CT studies are discordant.

US is a generally available, relatively inexpensive and safe procedure, that does not involve the use of ionizing radiation, and requires no patient preparation. Although it is well known that US is highly operator-dependent, the fact that senior residents were included among the staff members who performed US in our study demonstrates that an acceptable value of sensitivity can be reached. The major disadvantage of US is the fact that a negative US examination does not exclude appendicitis unless a normal appendix is confidently visualized. Visualization rates vary widely in the published literature from 22 to 98% [142, 234]. Our studies demonstrated even lower visualization values; however, although a normal appendix has been seen occasionally, the possibility of mistaking a bowel loop for a normal appendix, and thus giving the surgeon the false impression that appendicitis has been ruled out, has led to some underreporting of this finding. Patient-dependent difficulties include body constitution and meteorism; bypassing an initial ultrasonogram in obese children has even been suggested [209, 235].

US should remain the method of first choice in the evaluation of suspected appendicitis in children. CT should be added to the imaging protocol for patients who have negative US findings but clinical presentations strongly suggestive of appendicitis, in inconclusive cases, and/or when the radiologist lacks experience with US.

Computed tomography

The additional CT study should be performed with intravenous contrast material. Our results of the retrospective review of the prospectively acquired CT studies have demonstrated a significant improvement in sensitivity values

with contrast-enhanced CT compared to non-enhanced. Our results do not support the need of rectal contrast administration since our sensitivity and specificity values are consistent with other studies performed both with and without rectal contrast [144, 178, 201, 202, 206]. Partial opacification of the appendix occurs frequently when contrast material is administered rectally [179, 180] and hence, distal appendicitis may not be excluded.

Our results have led to a modification of the previous CT protocol and the non-enhanced limited scan has been excluded at our department. The present protocol includes scanning of the entire abdomen similar to the scanning model used in the study. Previous studies have shown that limiting the scanning field may result in not including the appendix in the CT study and also adversely affect the interpreter's ability to diagnose alternative conditions [200, 236]. However, in our study, the total number of patients with substantially pathological conditions in the upper abdomen was low, representing approximately 2.6% (8 of the 306 patients). Hence, over 97% of the CT studies could have been limited to the lower abdomen without clinical consequence. There is a need for further studies regarding the extent of the scanning field.

The exclusion of the first, limited non-enhanced CT study from the imaging protocol has reduced the total radiation dose by approximately 31%, and the exposure to the gonads by approximately 50% compared to the original protocol that included two scans. As previously postulated, CT should be performed using the lowest dose that is reasonably achievable but still providing the radiologist with the necessary diagnostic information [199, 207], and scanning parameters should be optimized for children [217, 237-240]. Communication between the radiologist and the clinician is crucial for avoiding unnecessary CT studies (especially repeat examinations) and provides the greatest possible potential to minimize unnecessary ionizing radiation.

The sensitivity values achieved by the three interpreters in the retrospective CT review (paper III) were lower than those achieved in the prospective study (paper I), probably due to several reasons which are discussed in the paper. Still, the sensitivity and specificity values achieved are high enough to consider CT useful for long distance consultations between radiologists without access to clinical data or the results of an US study, if performed; e.g., using an inter-hospital teleradiology system.

Negative appendectomy rate

The results of our retrospective study have demonstrated a gradual decrease in the negative appendectomy rate during the past decade, and a contemporaneous increase of the use of US and CT in the evaluation of suspected appendicitis in children. Since the management of appendicitis has not changed apart from the increased preoperative use of imaging modalities, it may be assumed that the decrease in the negative appendectomy rate is attributable to the increased use of preoperative radiologic imaging.

The negative appendectomy rate of 3.7% achieved in our prospective study is very low compared with that in most studies, but rates of 4% [145, 241] and 6% [142] have been reported. Still, false negative imaging results may occur, and the final decision to operate or not remains the surgeon's. Thus, a small number of negative laparotomies cannot be completely avoided.

Perforation rate

It has been repeatedly shown in prior studies that the rates of perforated appendicitis are higher in children than in adults, probably due to several reasons that have been discussed previously. The majority of appendiceal perforations in children appear to occur before the patient's admission to the surgical service [112] limiting the possibility to affect the number of these perforations. The results of our retrospective study have demonstrated a stable overall perforation rate during the years studied, but a decreasing perforation rate after admission, from initially 12% to 2.1%. It has been suggested that preoperative imaging might contribute to an increase in perforation rate [11]. Our results do not support this hypothesis. Other authors have reported decreased perforation rate after implementation of an imaging protocol rather similar to ours [146]. On the basis of our results, it may be assumed that a decrease in the rate of perforations after admission may be achieved when preoperative radiologic imaging is used.

The radiological diagnosis of perforated appendicitis may be difficult. The results of our studies have demonstrated that the vast majority of cases with perforated appendicitis can be correctly diagnosed by means of CT, although occasional false negative results may occur. Therefore, a careful clinical examination is of utmost importance, as well as close communication between the radiologist and the surgeon.

Decision analysis

Despite the numerous studies that have demonstrated significantly improved diagnostic accuracy in detecting appendicitis [10, 139, 142, 143, 145, 185, 187, 200, 206, 242, 243], relatively little is known about the impact of various radiological investigations on the physician's diagnostic and therapeutic thinking. A hierarchical model for assessing the effectiveness of a radiological investigation has been described by Fineberg [244] and further developed by Fryback and Thornbury [245] and Dixon [246, 247]. In these models, the first two levels refer to technical and diagnostic-accuracy efficacy, respectively [245], or technical and diagnostic performance, respectively [248]. Most studies concentrate on these two levels [248]. A minority of studies are focused on the third and fourth levels, namely diagnostic thinking efficacy and therapeutic efficacy [245], or diagnostic and therapeutic impact [248]. The number of studies concerning the impact of radiologic imaging on the surgeon's decision-making process in suspected appendicitis in particular is relatively small [142, 186, 228, 249]. Previously, US has been reported to change initial treatment plans in 30-46% of patients [186, 228], and CT in up to 73% of patients [142, 249]. The results of our prospective study are in accordance with these reports, demonstrating that imaging findings have a high level of efficacy in level 3 and 4, according to Fryback and Thornbury [245], concerning diagnostic thinking and therapeutic efficacy. Radiologic imaging may guide whether a patient should be discharged home, admitted for observation, or given surgical treatment, which may lead to beneficial changes in management plans. The greatest influence on the surgeon's decision-making process was achieved in the group of patients initially designated for observation, since a large number of patients were discharged from the hospital after performing radiologic imaging which was negative for appendicitis. In minor groups of patients, unnecessary operations as well as unfortunate discharge were possibly avoided. Since the costs of radiologic imaging are minor compared to the cost of observation on a pediatric ward, unnecessary surgery or delayed diagnosis, the improvement in diagnosis provided by radiologic imaging can be obtained in a cost-effective manner.

CONCLUSIONS

- US is a valuable, highly specific tool in the diagnosis of appendicitis in children. The sensitivity of US is lower than that of CT but a positive US examination greatly helps rule in the diagnosis of appendicitis, making further imaging unnecessary. The well-known advantages of US make it suitable as the primary imaging modality in the evaluation of suspected appendicitis in children.

- Diagnostic accuracy can be increased significantly by performing abdominal CT in addition to US. Therefore, abdominal CT should be added to the imaging protocol when the US study fails to visualize the appendix but the patient has a clinical presentation strongly suggestive of, but not totally convincing for, appendicitis, when the US study is inconclusive, or when the radiologist lacks experience with US.

- Additional abdominal CT should be performed with intravenous contrast material administration. A limitation of the scanning field can probably be considered for the majority of patients but there is a need for further studies.

- During the past decade, the introduction and gradually increased use of US and CT in the evaluation of suspected appendicitis in children has led to a substantially decreased negative appendectomy rate. The overall perforation rate has remained stable. The rate of perforations after admission appears to decrease over time.

- Following the imaging protocol described above, the negative appendectomy rate can be reduced to a level of approximately 4% without an increase of the perforation rate.

- Radiologic imaging with US and/or CT provides valuable guidance as to whether a child with suspected appendicitis should be discharged, observed, or given surgical treatment, which may lead to beneficial changes in the management plan. The high diagnostic accuracy achieved by CT makes it an alternative for long distance consultations between radiologists, e.g., using an inter-hospital teleradiology system. Still, false negative results may occur and a close clinical re-examination is of utmost importance for the appropriate final decision.

ACKNOWLEDGEMENTS

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