Diagnosis and treatment of acute appendicitis

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Chapter 1

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INTRODUCTION

Diagnosing patients with suspected acute appendicitis remains a challenge to the clinician. In the Western world, the lifetime risk of acute appendicitis is 7 per cent for females and 9 per cent for males. However, the chance of undergoing an appendectomy during lifetime is much higher; 23 per cent in females and 12 per cent in males. The discrepancy between frequency of appendectomy and acute appendicitis reflects the number of incidental and unnecessary appendectomies. To prevent unnecessary appendectomies, diagnostic accuracy demands improvement. Clinical investigation, a thermometer, and some laboratory results are simply not enough to diagnose acute appendicitis accurately in all cases. In this era of ultrasonography, computed tomography and laparoscopy it appears logical to apply these diagnostic tools to assist the often puzzled clinician. Is it justified to incur more costs or expose patients to radiation just to diagnose acute appendicitis and are these tools really better than the hands of an experienced surgeon?

It is obvious that treatment of acute appendicitis implies removal of the inflamed appendix. However, since no diagnostic modality is 100 per cent accurate, the surgical procedure includes diagnostic aspects as well. When McBurney described the possibility of performing an appendectomy through a gridiron incision in 1884, this was a minimally invasive approach compared to the usual midline laparotomy. His gridiron incision carried one major disadvantage: it hampered access to the other quadrants of the abdominal cavity in case the appendix was not inflamed. It took almost 100 years before the laparoscopic appendectomy challenged McBurney's operation. This novel technique combines a safe way to remove the inflamed appendix imposing less trauma to the abdominal wall and allows for an inspection of the entire abdominal cavity. Nevertheless, is laparoscopic appendectomy really the superior technique and worth the extra operative time and training? Many surgeons tend to doubt this, particularly in The Netherlands.

This thesis addresses questions regarding diagnosis and treatment of acute appendicitis in adults and provides some of the answers. It provides scientific evidence to modify the approach to a disease that affects annually 16,000 people in The Netherlands.

OUTLINE OF THIS THESIS

The optimal method to diagnose and treat acute appendicitis has been topic of much debate during the past century. Particularly in the past two decades, introduction of diagnostic modalities such as helical computed tomography (CT) and laparoscopy and wider application of laparoscopic appendectomy have created an abundance of clinical studies. In **chapter 2** this literature is reviewed to answer two key questions:

- *What is the current state of the art diagnosis and treatment of acute appendicitis?*
- *What evidence can be culled to support different diagnostic and treatment modalities?*

CT yields a high accuracy for acute appendicitis. This factor combined with the increasing availability of helical CT scanners has resulted in a wide application of this diagnostic procedure. However, enteral and intravenous contrast enhancement is often considered to be mandatory to establish high accuracy. In **chapter 3**, the question is answered:

- *Can unenhanced CT be used as a diagnostic tool in patients with suspected acute appendicitis?*

Implementation of routine CT scanning in patients with acute appendicitis requires 24 hours radiological expertise because these patients present at any time of day and they require prompt and accurate diagnosis and treatment. Consequently, the assessment of patients with suspected acute appendicitis and interpretation of US and CT scans are done by in house staff. **Chapter 4** addresses the following question:

- *What is the impact of experience of radiologists on accuracy of CT scanning in patients with suspected acute appendicitis?*

Treatment of acute appendicitis has undergone major changes as well. Removal of the inflamed appendix is obviously still the goal, but the technique has changed with the introduction of minimally invasive techniques in general surgery. In **chapter 5**, the operative technique of laparoscopic appendectomy is described. This chapter is definitely not based on a high level of evidence but describes tips and tricks from the author's personal experience with laparoscopic appendectomy and answers the following question:

- *What is the optimal operative technique for laparoscopic appendectomy?*

Technically, the procedure is straight forward except for securing the appendiceal stump. This can be done with pre-knotted loops or laparoscopic linear staplers. Both techniques have shown to be safe but both entail potential drawbacks. Linear staplers are expensive, they require a 12 mm port for introduction and leave metal staplers on the stump and in the abdominal cavity, which have been shown to lead potentially to short bowel obstruction or pseudo-polyps. Endoloops on the other hand are associated with more intense manipulation of the stump and they can slip, which can potentially lead to more deep and superficial postoperative infections and they cannot be placed safely over the cecum if the base of the appendix is involved in the inflammation. Complications solely attributable to stump closure are rare, which means that large studies are required to show superiority of either fashion. In **chapter 6**, data are pooled from the literature to overcome this sample size problem and to answer the following question:

- *What is the optimal fashion to secure the appendiceal stump in laparoscopic appendectomy?*

During the advent of laparoscopic appendectomy, there was much scepticism whether the already 'minimally invasive' grid iron incision could be improved. There were also safety concerns about the potential negative effects of a CO_2 pneumoperitoneum in patients with perforated appendicitis and generalised peritonitis. In **chapter 7**, these issues are dealt with in a multi-centre randomised, controlled trial. The power of the randomised trial described in chapter 7 did not allow assessing all potential complications or mortality after laparoscopic appendectomy. To overcome this sample size problem, data from published randomized controlled trials are pooled in **chapter 8**. In chapter 7 and 8 the following question is answered:

- *What are the advantages and disadvantages of laparoscopic appendectomy as compared to open appendectomy in patients with acute appendicitis?*

Chapter 9 describes the history and current status of laparoscopic appendectomy in The Netherlands to answer the following question:

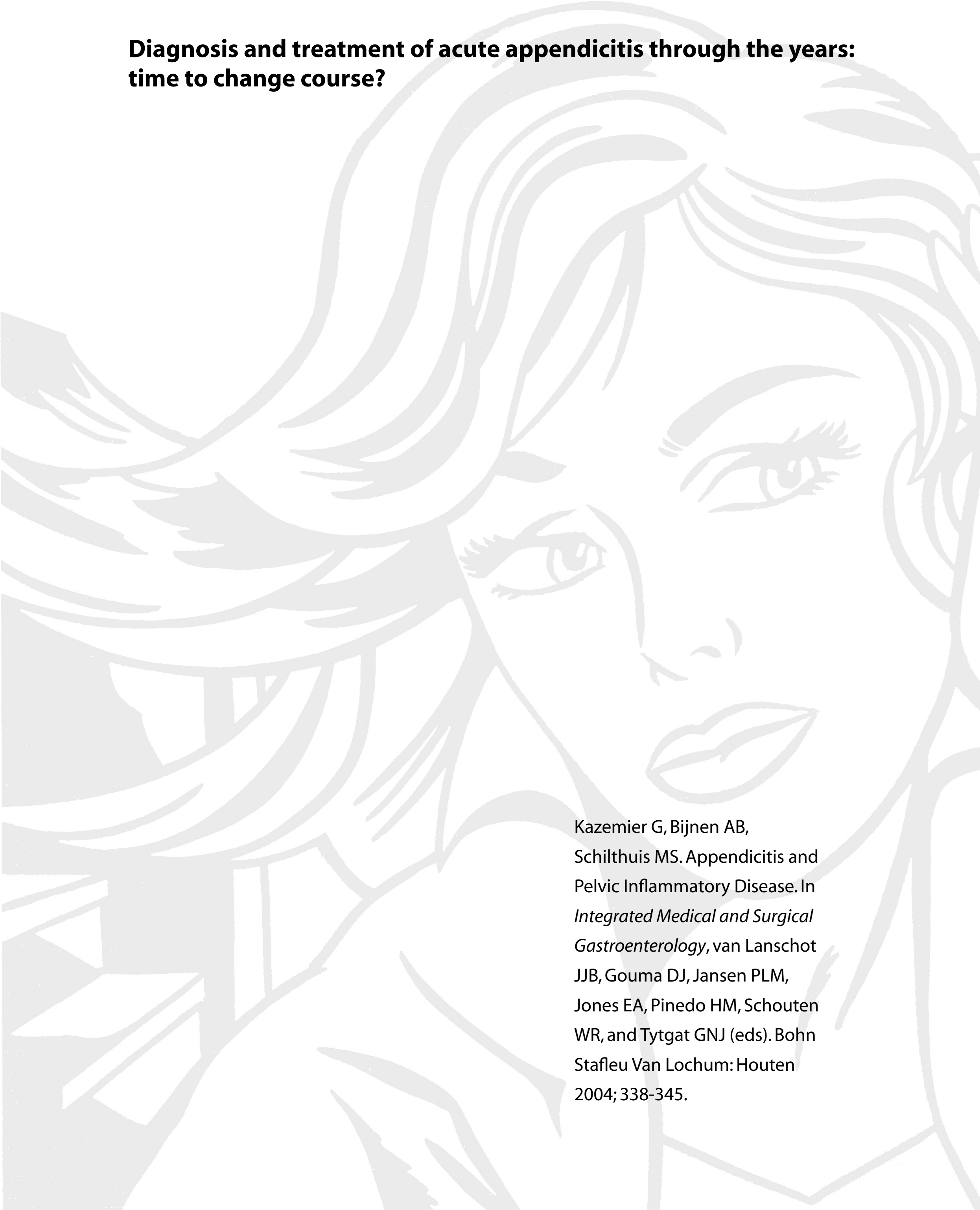
- *What is the current status of laparoscopic appendectomy in The Netherlands?*

Chapter 10 presents a general discussion and summarizes the findings of this thesis.

Chapter 11 is a Dutch summary.

Chapter 2

Diagnosis and treatment of acute appendicitis through the years: time to change course?



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INTRODUCTION

Since the drainage of an abscess in the right lower abdominal quadrant of Prince Edward VII (1841-1910), only few days before his coronation in 1902, the diagnosis and treatment of acute appendicitis have changed considerably. In those days the timing of surgery was under debate. While Frederick Treves (1853-1923) and Lord Lister (1827-1912) treated acute appendicitis of the Prince with opiates and only operated upon him after an abscess had formed, the young Harvey Cushing, as a surgical resident, had already insisted on emergency operation at the moment he realized he had developed acute appendicitis himself on September 26, 1897. The debate on timing of the operation is nowadays settled in favour of acute operation, but the price paid for this dogma of emergency surgery for suspected appendicitis is a high rate of unnecessary appendectomies.

Appendectomy is the most commonly performed emergency operation, accounting for 6 per cent of all operations in The Netherlands. In the European Union 700,000 appendectomies are performed annually [107]. Mortality following appendectomy is low, 0-0.24 per cent; it is largely contributable to the severity of peritonitis present at the initial operation [18,68,108,109]. Morbidity following appendectomy is also low, 5.2 per cent-11.3 per cent; it correlates with the presence of perforation and the severity of peritonitis at the time of operation [68,108,109].

EPIDEMIOLOGY

In the Western world, the lifetime risk of acute appendicitis is 6.7 per cent for females and 8.6 per cent for males [10]. However, the chance of undergoing appendectomy during a lifetime is higher, 23.1 per cent in females and 12 per cent in males [10]. The discrepancy between frequency of appendectomy and acute appendicitis reflects the number of incidental and unnecessary appendectomies.

The overall incidence of acute appendicitis has decreased by 40 per cent in females and 34 per cent in males in the period from 1975 to 1994 in the United Kingdom [11]. This trend has also been noted in the United States and other Western countries [10,12-15]. Appendicitis is rare in most of Asia and Central Africa, but the incidences in developing countries are increasing [16]. The causes of these changes are unclear, but could be attributed to dietary changes [14,17].

In the West, the perforation rate has remained the same, about 20 per cent from 1936 to 1993[18]. Thus, despite progress in medicine, the number of perforations has not changed in the past fifty years. Improvements in health care are apparently not associated with fewer perforations. This finding probably indicates that most perforations occur before patients are admitted to hospital with acute appendicitis. This phenomenon is more apparent in the very young and old patients, because in these groups the rates of perforation tend to be higher [18-21].

PATHOGENESIS AND CLINICAL PRESENTATION

Acute appendicitis is an inflammation of the entire wall of the appendix, which is infiltrated with granulocytes. Bacteria in the inflamed appendix are those of the normal colon flora, which suggests secondary invasion of the appendix wall from the lumen of the bowel. The pathogenesis of acute appendicitis is unclear. It has often been postulated that obstruction of the lumen of the appendix, either by swelling of the surrounding lymphoid tissue or a fecolith, and subsequent retention of mucus and swelling of the appendix, results in disturbance of the capillary blood flow in the appendix, followed by necrosis. Other foreign bodies, such as food debris, gallstones or worms have been reported to obstruct the lumen of the appendix. However, it has been shown that appendicitis can occur without obstruction, possibly due to bacterial invasion of the lymphoid tissue in the appendix wall, which may subsequently lead to ulceration. The latter form should perforate less easily.

The classical symptoms of acute appendicitis include the onset of referred, central or upper abdominal pain, which is sometimes colicky, followed by nausea and one or more episodes of vomiting. The cause of this referred pain is stretching of the appendix. This period of pain and discomfort may be mild: pain is sometimes not mentioned by the patient. After several hours the pain usually shifts to the right lower abdominal quadrant and becomes continuous and severe; movement becomes uncomfortable. This shifting of the pain is due to the involvement of the parietal peritoneum. With progression of the disease, the pain may spread diffusely over the abdomen, as occurs in generalized peritonitis due to a perforation. If an abscess develops following a localized perforation of the appendix, the pain remains in the right lower quadrant.

Difficulties in making the diagnosis are common; not all cases exhibit the clinical features just described. Particularly in young children, the elderly, pregnant women, and obese patients the diagnosis may be particularly challenging. The position of the appendix as related to the cecum may also influence the clinical presentation and the differential diagnosis.

DIAGNOSTIC WORK-UP

Physical examination and medical history remain the cornerstones of good clinical practice in patients presenting with acute abdominal pain localized in the right lower abdominal quadrant. White blood cell (WBC) count, erythrocyte sedimentation rate, and, sometimes serum C-reactive protein (CRP) may be helpful. Urinary sediment examination and a pregnancy test should be undertaken to exclude urinary tract infection, urolithiasis, and pregnancy when applicable. However, a recent report on the diagnostic value of medical history, clinical presentation and indices of inflammation, including CRP in a group of 496 patients with suspected appendicitis showed that none of the individual variables had sufficiently high discriminating power to be used as a diagnostic test [22]. The presence of anorexia, nausea, and right-sided rectal tenderness had no diagnostic value. In this study, leukocyte and WBC counts, CRP, rebound tenderness, guarding and gender were independent predictors of appendicitis; the combined area under the receiver operating characteristic (ROC) curve was 0.93 for appendicitis, showing the value of combining several parameters. A normal serum CRP level was recently shown to correlate strongly with a normal appendix in patients with suspected appendicitis [23]. A meta-analysis of studies addressing these issues has shown increased likelihood of appendicitis when a positive psoas sign, fever, or pain migrating to the right lower abdominal quadrant was present; vomiting before the onset of pain made appendicitis less likely [24]. A study by Bohner showed a maximum positive predictive value of 85 per cent when a combination of three out of five clinical parameters were present [25]. Rectal examination was not shown to contribute to a definite diagnosis of appendicitis [26].

Computer aided decision making and scoring systems Combining clinical history, physical examination and laboratory studies has led to the development of scoring systems and computer aided algorithms to help clinicians in the decision making in appendicitis. In clinical studies several of these computer aided algorithms can reduce the number of unnecessary appendectomies [27-29]. These modalities were shown to be cost beneficial but they require introduction of new and costly equipment and expertise [27,30,31].

In contrast to this computer aided decision making, scoring systems can be applied without special equipment and do not require new skills [31]. However, despite the reported excellent results, these systems are not routinely used [32-34]. Some studies reported even a negative effect of the introduction of such scoring systems. In a recent prospective multicentre study by Ohmann et al. [35], two groups of patients with acute abdominal pain were compared. In the first group of 870 patients no scoring system was used, in the second group of 614 patients a computer-supported diagnostic score was employed. There were no differences in the rates of perforated and normal appendices found at laparotomy or postoperative complications, but the diagnostic accuracy of the final examiner decreased using the diagnostic score. The authors concluded that the score could not be recommended as a standard tool for diagnostic decision making.

Overall, the actual gain of scoring systems appears small and the performance of these scores outside study conditions is often optimistically biased. In a German study, the value of 10 different scores for acute appendicitis was assessed using data of 1254 patients presenting with acute abdominal pain[31]. In this evaluation, the application of the scores to the prospectively collected data was disappointing because none of the scores fulfilled any of the performance criteria determined beforehand. A discrepancy exists between what can be achieved during studies using scoring systems and what is actually achieved in every day clinical practice. This limits the value of these scores considerably.

Imaging techniques Several imaging techniques have been advocated to improve diagnostic accuracy in patients with suspected acute appendicitis. In a recent study by Rao et al.[36] the diagnostic utility and hospital resource impact of plain abdominal radiography in patients with suspected appendicitis were evaluated. The authors reviewed medical records of 821 consecutive patients hospitalized for suspected appendicitis. Seventy-eight per cent had plain abdominal radiography, 64 per cent had appendicitis. Radiographic findings were noted in 51 per cent of patients with, and 47 per cent of patients without appendicitis. No individual finding on the plain abdominal radiographs was sensitive or specific. The authors found that plain abdominal radiographs in patients with suspected appendicitis are frequently misleading. They also found that they are costly in relation to making a specific and correct diagnosis. They concluded that abdominal radiographs should not be routinely obtained in such patients.

The value of preoperative ultrasonography has been shown in numerous studies. Puylaert et al.[37] showed a specificity of 100 per cent and a much lower sensitivity of 75 per cent for this technique. In patients with perforated appendicitis sensitivity was notably low (28.5 per cent). More recently, Allemann showed a specificity of 99 per cent and sensitivity of 91 per cent in patients with suspected appendicitis if the ultrasonography was undertaken by the attending surgeon [38]. However, Wise et al.[39] showed that ultrasonography has a high inter and intra-observer variability (kappa = 0.15-0.20 and 0.39-0.42, respectively). Additionally, Josephson et al.[40] showed that in patients with a body mass index exceeding 25, sensitivity was as low as 37 per cent. In a meta-analysis by Orr et al,[41] including 17 studies and a total number of 3358 patients, the overall sensitivity and specificity of ultrasonography were 85 per cent, and 92 per cent, respectively. Orr et al. showed that performance was largely dependent on pretest probability for appendicitis. In this study, ultrasonography proved most useful for patients with intermediate probability of appendicitis, based upon clinical examination [41]. Although the levels of accuracy of ultrasonography to be achieved under optimal conditions are high, they are largely dependent on patient characteristics and expertise of the individual ultrasonographer.

There is growing evidence that CT scanning is superior to ultrasonography in diagnosing acute appendicitis [39,42-44]. Although CT has the disadvantage of exposing the patient to radiation, its consistent sensitivity and specificity of over 90 per cent in many studies, and the low inter and intra-observer variability, have made CT the optimal non-invasive diagnostic procedure in a patient with suspected appendicitis [39,43,45-47]. A recent trial by Rao et al. [48] demonstrated that routine appendiceal CT, undertaken in patients who present with suspected appendicitis, results in improved patient care and reduced use of hospital resources. Focused, thin-section helical CT seems to be the optimal CT technique [49]. Enhancement with intravenous contrast in combination with contrast administered both orally and rectally is usually advocated but Rao has shown that equal results can be achieved without oral contrast [46]. In recent studies, unenhanced thin-section helical CT yielded results similar to those of enhanced CT, which questions the essence of contrast enhancement [42,50]. Wise et al. [39] recommend a standard abdominopelvic CT scan as the initial examination; the focused appendiceal CT using colonic contrast material can be kept in reserve for difficult cases.

Magnetic resonance imaging (MRI) is used incidentally in the work-up of patients with suspected appendicitis. It has been shown that MRI can diagnose and rule out acute appendicitis with high degrees of accuracy, but its current levels of availability, its high costs and certain patient restrictions limit its widespread use [51-54]. MRI has not been shown to be superior to helical CT, but it has the definite advantage of not involving radiation exposure, which is particularly important in pregnancy.

Diagnostic laparoscopy Laparoscopic inspection of the abdominal cavity enables the surgeon to diagnose acute appendicitis accurately [55]. Early laparoscopy in patients with acute non-specific abdominal pain is associated with higher diagnostic accuracy and better quality of life than occurs after close observation followed by surgical intervention, if signs of peritonism developed [56]. It has been shown that leaving an appendix that appears normal during laparoscopic inspection is safe [55,57-59]. Criteria for the diagnosis of appendicitis during laparoscopic inspection are the presence of unequivocal inflammatory changes, such as pus, fibrin, or vascular injection of the serosa. Rigidity and lack of mobility at manipulation are more uncertain signs of inflammation.

Removing a normal appendix is associated with a 6.7 per cent to 13 per cent risk of early complications and 4 per cent risk of late complications, such as incisional hernia and chronic pain in the first years after the operation [60,61]. If a normal appendix is left in situ during diagnostic laparoscopy, the number of unnecessary appendectomies will decrease, particularly in the group of fertile women (17 per cent-38 per cent), but also in men (11 per cent) [2,57,59,62-64]. The diagnostic yield of laparoscopy in patients suspected of appendicitis is high, but laparoscopy may be too invasive to justify its use only for diagnostic purposes. This reasoning seems particularly true in the era of helical CT.

TREATMENT OF ACUTE APPENDICITIS

Non-operative treatment Immediate operative treatment has been advocated for more than a century and is still the 'gold standard' in the treatment of acute appendicitis. There is some experience of antibiotic treatment without operation in the acute phase. The only randomized controlled trial comparing antibiotic and surgical treatment of appendicitis reported in the literature showed that 8 out of 20 patients (40 per cent) of the group initially treated with antibiotics required appendectomy within one year of the acute episode, because of recurrence [65]. For this reason, antibiotic treatment for acute appendicitis is only considered if surgical therapy is not available.

Operative treatment The surgical technique of appendectomy has undergone few changes. After introduction of the 'minimally invasive' operative technique, which was first undertaken by McArthur, but first described by McBurney in 1884, the gridiron incision has remained the standard access to the abdominal cavity, when acute appendicitis is suspected [4]. Laparoscopic appendectomy was first reported by the Dutch surgeon de Kok in 1977 and later by Semm [5-8]. The availability of this technique has resulted in the 'gold standard' of the gridiron incision and of always removing the appendix becoming debatable for the first time.

The laparoscopic technique combines possibly even less surgical trauma than the McBurney incision with the ability to inspect the entire abdominal cavity [9]. Laparoscopic removal of an inflamed appendix has been shown to be a feasible technique [66-68]. A large number of randomized controlled trials have been conducted, in which laparoscopic and open appendectomy have been compared [9,67,69-82]. A number of meta-analyses comparing these randomized trials has been performed [83-87]. The meta-analyses recognized methodological flaws in many of the trials but most concluded that laparoscopic appendectomy resulted in less wound infections, less postoperative pain, shorter hospital stay and faster recovery. The operative time is 16-18 minutes longer than for the open procedure. In particular, the reduction of wound infection rates and the possibility of patients returning to normal activities sooner may be the greatest medical and economical advantage of the laparoscopic procedure. A trend towards increased intra-abdominal abscess formation has been recognised after laparoscopic appendectomy [83,84].

De Wilde reported 70 per cent less intra-abdominal adhesions at laparoscopy 3 months after laparoscopic appendectomy than after open appendectomy [88]. However, there is no evidence that the number of long-term adhesion-related complications following laparoscopic appendectomy is less than after open appendectomy.

In most studies direct costs are higher for laparoscopic appendectomy [89-91]. Direct costs are related to the technique of appendiceal stump closure. To secure the stump at laparoscopic appendectomy, a linear stapler has been suggested to be superior to loops, but more costly [68,74]. Total costs associated with laparoscopic appendectomy have been shown to be lower, because of shorter hospital stay and faster recovery [92].

In the era of open appendectomy, invagination of the appendiceal stump has not been shown to be superior to simple ligation in an extensive randomized study by Engstrom et al. [93] It is not to be expected that introduction of the laparoscopic technique has changed these findings.

The most important disadvantage of using a gridiron incision and routine appendectomy following the suspicion of acute appendicitis is the high rate of negative appendectomies. This strategy used to be justified by the lack of adequate means of diagnosing or excluding acute appendicitis in patients presenting with acute right lower quadrant abdominal pain and the risk of perforation occurring during observation. Following the classical strategy of managing patients with suspected acute appendicitis results in a high rate of negative surgical explorations, particularly in certain groups of patients, such as women of childbearing age. Negative appendectomy rates of 19 per cent-34 per cent are still accepted in these groups, even in recent studies [1,2,18,110]. Introduction of diagnostic tools such as enhanced or even unenhanced helical CT or diagnostic laparoscopy has been shown to allow identifying or excluding acute appendicitis with great accuracy [39,43,45-47,55,57-59]. This means it should be possible to reduce the number of unnecessary appendectomies considerably when these tools are introduced routinely in the management of patients suspected of acute appendicitis.

Treating patients in whom acute appendicitis is suspected after a positive CT finding, deprives laparoscopy of one of its great advantages i.e. the possibility of using it as a diagnostic intervention only. On the other hand, many randomized controlled trials, in which open and laparoscopic appendectomy were compared and several meta-analyses of these studies have shown advantages for the laparoscopic procedure, even though in most studies uninflamed appendices were removed. In conclusion there is enough evidence to support laparoscopy in every patient suspected of acute appendicitis followed by laparoscopic appendectomy when the appendix is macroscopically abnormal.

Perioperative antibiotic treatment A large number of randomized controlled trials have been undertaken to determine the merits of perioperative use of antibiotics in patients undergoing appendectomy. Andersen et al. [94] reviewed 44 studies, in which any antibiotic regime was compared to placebo, in patients who underwent appendectomy. This review included 9298 patients. The overall conclusion was that the administration of antibiotics was associated with less wound infections and intra-abdominal abscesses than administration of placebo, regardless of inflammation of the nature of the removed appendix. The spectrum of the antibiotics should be effective against colonic flora; intraoperative cultures from the abdominal cavity are not helpful [95]. Monotherapy with a second-generation, broad- spectrum cephalosporin is an economical and effective antibiotic regimen in patients with complicated appendicitis [96]. In non-perforated appendicitis the antibiotic treatment should be single shot prophylaxis [97,98]. In the case of a perforated appendicitis, antibiotic treatment should be given over a period of time, depending on the clinical condition of the patient [99].

Appendiceal mass Patients presenting with a history of right lower quadrant abdominal pain of longer duration may have an appendiceal mass. Such a mass either consists of a large phlegmon or an abscess. Each entity requires different treatment, hence differentiating between these two lesions is crucial. Imaging techniques like ultrasonography and CT are able to do so [37,100]. An appendiceal abscess should be drained, preferably percutaneously under CT or ultrasonographic guidance [101]. In adult patients a phlegmon should be treated non-surgically, because the complication rate of early surgery range from 15-50 per cent and conservative treatment has been shown to be safe [64,101-104]. Following successful conservative treatment, interval appendectomy is often recommended, but only 6.6 per cent to 8.5 per cent of patients will develop recurrent appendicitis [101,105]. There is little support in the literature for routine interval appendectomy. However, thorough examination of the colon (barium enema or colonoscopy) should always be performed to rule out possible non-infectious causes of an appendiceal mass, such as adenocarcinoma of the right colon or appendix, carcinoid of the appendix, or Crohn's disease. The incidence of adenocarcinoma of the right colon can be as high as 8 per cent in patients presenting with an appendiceal mass [106].

CONCLUSION

Diagnostic and therapeutic options for patients with suspected acute appendicitis have changed considerably during the last century. However, routine use of preoperative CT or diagnostic laparoscopy in this group of patients is still not widely accepted. Consequently, the numbers of negative appendectomies have hardly changed through the years. Moreover, the majority of appendectomies are still performed open, although laparoscopic removal of an inflamed appendix has been shown to be the optimal way. In this era of evidence based surgery, these discrepancies are difficult to justify. It seems time to change course for both diagnosis and treatment of acute appendicitis.

REFERENCES

1. Andersson RE et al. Why does the clinical diagnosis fail in suspected appendicitis? *Eur J Surg* 2000; **166**: 796-802.
2. Larsson PG et al. Laparoscopy reduces unnecessary appendicectomies and improves diagnosis in fertile women. A randomized study. *Surg Endosc* 2001; **15**: 200-2.
3. Flum DR, Morris A, Koepsell T, Dellinger EP. Has misdiagnosis of appendicitis decreased over time? A population- based analysis. *JAMA* 2001; **286**: 1748-53.
4. Meade RH. The evolution of surgery for appendicitis. *Surgery* 1964; **55**: 741-52.
5. de Kok HJ. A new technique for resecting the non-inflamed not-adhesive appendix through a mini-laparotomy with the aid of the laparoscope. *Arch Chir Neerl* 1977; **29**: 195-8.
6. de Kok HJ. Laparoscopic appendectomy: a new opportunity for curing appendicopathy. *Surg Laparosc Endosc* 1992; **2**: 297-302.
7. Fingerhut A, Millat B, Borrie F. Laparoscopic versus open appendectomy: time to decide. *World J Surg* 1999; **23**: 835-45.
8. Semm K. Endoscopic appendectomy. *Endoscopy* 1983; **15**: 59-64.
9. Kazemier G, de Zeeuw GR, Lange JF, Hop WC, Bonjer HJ. Laparoscopic vs open appendectomy. A randomized clinical trial. *Surg Endosc* 1997; **11**: 336-40.
10. Addiss DG, Shaffer N, Fowler BS, Tauxe RV. The epidemiology of appendicitis and appendectomy in the United States. *Am J Epidemiol* 1990; **132**: 910-25.
11. Williams NM, Jackson D, Everson NW, Johnstone JM. Is the incidence of acute appendicitis really falling? *Ann R Coll Surg Engl* 1998; **80**: 122-4.
12. Raguveer-Saran MK, Keddie NC. The falling incidence of appendicitis. *Br J Surg* 1980; **67**: 681.
13. Noer T. Decreasing incidence of acute appendicitis. *Acta Chir Scand* 1975; **141**: 431-2.
14. Arnbjornsson E, Asp NG, Westin SI. Decreasing incidence of acute appendicitis, with special reference to the consumption of dietary fiber. *Acta Chir Scand* 1982; **148**: 461-4.
15. Walker AR, Segal I. What causes appendicitis? *J Clin Gastroenterol* 1990; **12**: 127-9.
16. Ofili OP. Implications of the rising incidence of appendicitis in Africans. *Cent Afr J Med* 1987; **33**: 243-6.
17. Jones BA, Demetriades D, Segal I, Burkitt DP. The prevalence of appendiceal fecaliths in patients with and without appendicitis. A comparative study from Canada and South Africa. *Ann Surg* 1985; **202**: 80-2.
18. Hale DA, Molloy M, Pearl RH, Schutt DC, Jaques DP. Appendectomy: a contemporary appraisal. *Ann Surg* 1997; **225**: 252-61.
19. Wong SW, Haxhimolla H, Grieve DA, Fisher R, Keogh G. Insurance and the risk of ruptured appendix in the adult. *Aust N Z J Surg* 1999; **69**: 31-3.
20. Koepsell TD, Inui TS, Farewell VT. Factors affecting perforation in acute appendicitis. *Surg Gynecol Obstet* 1981; **153**: 508-10.
21. Kraemer M, Franke C, Ohmann C, Yang Q. Acute appendicitis in late adulthood: incidence, presentation, and outcome. Results of a prospective multicenter acute abdominal pain study and a review of the literature. *Langenbecks Arch Surg* 2000; **385**: 470-81.
22. Andersson RE et al. Diagnostic value of disease history, clinical presentation, and inflammatory parameters of appendicitis. *World J Surg* 1999; **23**: 133-40.
23. Asfar S, Safar H, Khoursheed M, Dashti H, al Bader A. Would measurement of C-reactive protein reduce the rate of negative exploration for acute appendicitis? *J R Coll Surg Edinb* 2000; **45**: 21-4.
24. Wagner JM, McKinney WP, Carpenter JL. Does this patient have appendicitis? *JAMA* 1996; **276**: 1589-94.
25. Bohner H, Yang Q, Franke K, Ohmann C. [Significance of anamnesis and clinical findings for diagnosis of acute appendicitis. Acute Abdominal Pain Study Group]. *Z Gastroenterol* 1994; **32**: 579-83.
26. Kremer K, Kraemer M, Fuchs KH, Ohmann C. [The diagnostic value of rectal examination of patients with acute appendicitis]. *Langenbecks Arch Chir Suppl Kongressbd* 1998; **115**: 1120-2.
27. Adams ID et al. Computer aided diagnosis of acute abdominal pain: a multicentre study. *Br Med J (Clin Res Ed)* 1986; **293**: 800-4.

28. Wellwood J, Johannessen S, Spiegelhalter DJ. How does computer-aided diagnosis improve the management of acute abdominal pain? *Ann R Coll Surg Engl* 1992; **74**: 40-6.
29. de Dombal FT, Dallos V, McAdam WA. Can computer aided teaching packages improve clinical care in patients with acute abdominal pain? *BMJ* 1991; **302**: 1495-7.
30. McAdam WA et al. Twelve years' experience of computer-aided diagnosis in a district general hospital. *Ann R Coll Surg Engl* 1990; **72**: 140-6.
31. Ohmann C, Yang Q, Franke C. Diagnostic scores for acute appendicitis. Abdominal Pain Study Group. *Eur J Surg* 1995; **161**: 273-81.
32. Alvarado A. A practical score for the early diagnosis of acute appendicitis. *Ann Emerg Med* 1986; **15**: 557-64.
33. Christian F, Christian GP. A simple scoring system to reduce the negative appendicectomy rate. *Ann R Coll Surg Engl* 1992; **74**: 281-5.
34. Fenyo G. Routine use of a scoring system for decision-making in suspected acute appendicitis in adults. *Acta Chir Scand* 1987; **153**: 545-51.
35. Ohmann C, Franke C, Yang Q. Clinical benefit of a diagnostic score for appendicitis: results of a prospective interventional study. German Study Group of Acute Abdominal Pain. *Arch Surg* 1999; **134**: 993-6.
36. Rao PM, Rhea JT, Rao JA, Conn AK. Plain abdominal radiography in clinically suspected appendicitis: diagnostic yield, resource use, and comparison with CT. *Am J Emerg Med* 1999; **17**: 325-8.
37. Puylaert JB et al. A prospective study of ultrasonography in the diagnosis of appendicitis. *N Engl J Med* 1987; **317**: 666-9.
38. Allemann F, Cassina P, Rothlin M, Largiader F. Ultrasound scans done by surgeons for patients with acute abdominal pain: a prospective study. *Eur J Surg* 1999; **165**: 966-70.
39. Wise SW et al. Comparative assessment of CT and sonographic techniques for appendiceal imaging. *AJR Am J Roentgenol* 2001; **176**: 933-41.
40. Josephson T, Styrud J, Eriksson S. Ultrasonography in acute appendicitis. Body mass index as selection factor for US examination. *Acta Radiol* 2000; **41**: 486-8.
41. Orr RK, Porter D, Hartman D. Ultrasonography to evaluate adults for appendicitis: decision making based on meta-analysis and probabilistic reasoning. *Acad Emerg Med* 1995; **2**: 644-50.
42. Pickuth D, Heywang-Kobrunner SH, Spielmann RP. Suspected acute appendicitis: is ultrasonography or computed tomography the preferred imaging technique? *Eur J Surg* 2000; **166**: 315-9.
43. Horton MD, Counter SF, Florence MG, Hart MJ. A prospective trial of computed tomography and ultrasonography for diagnosing appendicitis in the atypical patient. *Am J Surg* 2000; **179**: 379-81.
44. Stroman DL et al. The role of computed tomography in the diagnosis of acute appendicitis. *Am J Surg* 1999; **178**: 485-9.
45. Funaki B, Grosskreutz SR, Funaki CN. Using unenhanced helical CT with enteric contrast material for suspected appendicitis in patients treated at a community hospital. *AJR Am J Roentgenol* 1998; **171**: 997-1001.
46. Rao PM et al. Helical CT combined with contrast material administered only through the colon for imaging of suspected appendicitis. *AJR Am J Roentgenol* 1997; **169**: 1275-80.
47. Walker S et al. The value of limited computed tomography with rectal contrast in the diagnosis of acute appendicitis. *Am J Surg* 2000; **180**: 450-4.
48. Rao PM, Rhea JT, Novelline RA, Mostafavi AA, McCabe CJ. Effect of computed tomography of the appendix on treatment of patients and use of hospital resources. *N Engl J Med* 1998; **338**: 141-6.
49. Weltman DI, Yu J, Krumenacker J, Jr., Huang S, Moh P. Diagnosis of acute appendicitis: comparison of 5- and 10-mm CT sections in the same patient. *Radiology* 2000; **216**: 172-7.
50. Lane MJ et al. Suspected acute appendicitis: nonenhanced helical CT in 300 consecutive patients. *Radiology* 1999; **213**: 341-6.
51. Chung JJ, Semelka RC, Martin DR, Marcos HB. Colon diseases: MR evaluation using combined T2-weighted single-shot echo train spin-echo and gadolinium-enhanced spoiled gradient-echo sequences. *J Magn Reson Imaging* 2000; **12**: 297-305.
52. Incesu L et al. Acute appendicitis: MR imaging and sonographic correlation. *Am J Roentgenol* 1997; **168**: 669-74.
53. Rao PM, Boland GW. Imaging of acute right lower abdominal quadrant pain. *Clin Radiol* 1998; **53**: 639-49.

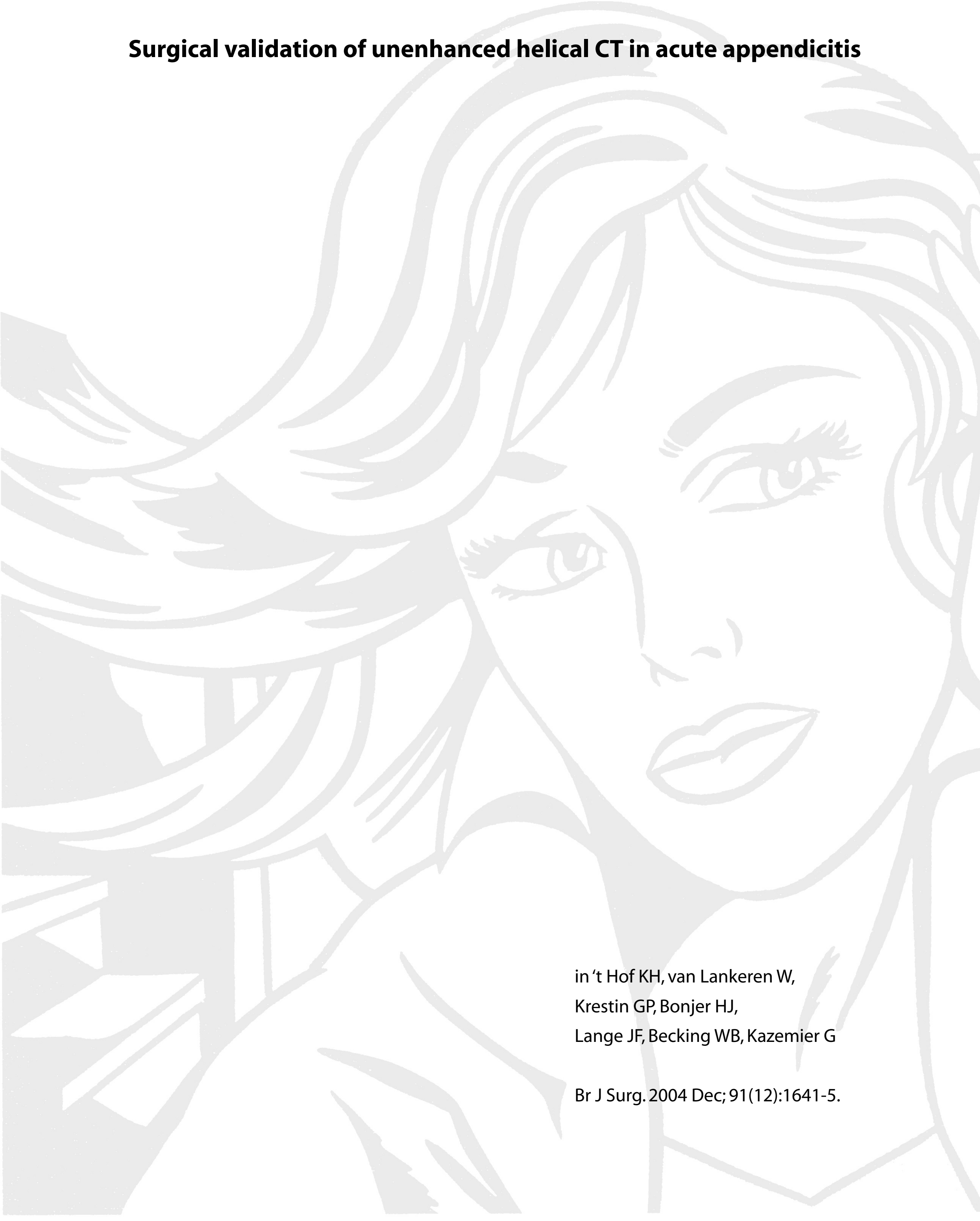
54. Gupta H, Dupuy DE. Advances in imaging of the acute abdomen. *Surg Clin North Am* 1997; **77**: 1245-63.
55. Kraemer M, Ohmann C, Leppert R, Yang Q. Macroscopic assessment of the appendix at diagnostic laparoscopy is reliable. *Surg Endosc* 2000; **14**: 625-33.
56. Decadt B et al. Randomized clinical trial of early laparoscopy in the management of acute non-specific abdominal pain. *Br J Surg* 1999; **86**: 1383-6.
57. van den Broek WT, Bijnen AB, van Eerten PV, de Ruiter P, Gouma DJ. Selective use of diagnostic laparoscopy in patients with suspected appendicitis. *Surg Endosc* 2000; **14**: 938-41.
58. Bouillot JL et al. Laparoscopic procedure for suspected appendicitis. A prospective study in 283 consecutive patients. *Surg Endosc* 1995; **9**: 957-60.
59. Barrat C, Catheline JM, Rizk N, Champault GG. Does laparoscopy reduce the incidence of unnecessary appendicectomies? *Surg Laparosc Endosc* 1999; **9**: 27-31.
60. Deutsch AA, Shani N, Reiss R. Are some some appendectomies unnecessary? An analysis of 319 white appendices. *J R Coll Surg Edinb* 1983; **28**: 35-40.
61. Gough IR et al. Consequences of removal of a "normal" appendix. *Med J Aust* 1983; **1**: 370-2.
62. Olsen JB, Myren CJ, Haahr PE. Randomized study of the value of laparoscopy before appendicectomy. *Br J Surg* 1993; **80**: 922-3.
63. Thorell A, Grondal S, Schedvins K, Wallin G. Value of diagnostic laparoscopy in fertile women with suspected appendicitis. *Eur J Surg* 1999; **165**: 751-4.
64. Jadallah FA, Abdul-Ghani AA, Tibblin S. Diagnostic laparoscopy reduces unnecessary appendicectomy in fertile women. *Eur J Surg* 1994; **160**: 41-5.
65. Eriksson S, Granstrom L. Randomized controlled trial of appendicectomy versus antibiotic therapy for acute appendicitis. *Br J Surg* 1995; **82**: 166-9.
66. Hill AD, Attwood SE, Stephens RB. Laparoscopy appendicectomy is feasible and safe in acute appendicitis. *Ir J Med Sci* 1991; **160**: 268-70.
67. Kazemier G, de Zeeuw GR, Lange JF, Hop WC, Bonjer HJ. Laparoscopic vs open appendectomy. A randomized clinical trial. *Surg Endosc* 1997; **11**: 336-40.
68. Schafer M, Krahenbuhl L, Frei E, Buchler MW. Laparoscopic appendectomy in Switzerland: a prospective audit of 2, 179 cases. *Dig Surg* 2000; **17**: 497-502.
69. Attwood SE, Hill AD, Murphy PG, Thornton J, Stephens RB. A prospective randomized trial of laparoscopic versus open appendectomy. *Surgery* 1992; **112**: 497-501.
70. Tate JJ, Dawson JW, Chung SC, Lau WY, Li AK. Laparoscopic versus open appendicectomy: prospective randomised trial. *Lancet* 1993; **342**: 633-7.
71. Kum CK, Ngoi SS, Goh PM, Tekant Y, Isaac JR. Randomized controlled trial comparing laparoscopic and open appendicectomy. *Br J Surg* 1993; **80**: 1599-600.
72. Hebebrand D et al. [Laparoscopic or classical appendectomy? A prospective randomized study]. *Chirurg* 1994; **65**: 112-20.
73. Frazee RC et al. A prospective randomized trial comparing open versus laparoscopic appendectomy. *Ann Surg* 1994; **219**: 725-8.
74. Ortega AE, Hunter JG, Peters JH, Swanstrom LL, Schirmer B. A prospective, randomized comparison of laparoscopic appendectomy with open appendectomy. Laparoscopic Appendectomy Study Group. *Am J Surg* 1995; **169**: 208-12.
75. Hansen JB et al. Laparoscopic versus open appendectomy: prospective randomized trial. *World J Surg* 1996; **20**: 17-20.
76. Cox MR et al. Prospective randomized comparison of open versus laparoscopic appendectomy in men. *World J Surg* 1996; **20**: 263-6.
77. Henle KP et al. [Laparoscopic versus conventional appendectomy: a prospective randomized study]. *Chirurg* 1996; **67**: 526-30.
78. Mutter D et al. Laparoscopy not recommended for routine appendectomy in men: results of a prospective randomized study. *Surgery* 1996; **120**: 71-4.
79. Hart R et al. Laparoscopic versus open appendectomy: a prospective randomized trial of 81 patients. *Can J Surg* 1996; **39**: 457-62.
80. Reiertsen O et al. Randomized controlled trial with sequential design of laparoscopic versus conventional appendicectomy. *Br J Surg* 1997; **84**: 842-7.

81. Minne L et al. Laparoscopic vs open appendectomy. Prospective randomized study of outcomes. *Arch Surg* 1997; **132**: 708-11.
82. Macarulla E et al. Laparoscopic versus open appendectomy: a prospective randomized trial. *Surg Laparosc Endosc* 1997; **7**: 335-9.
83. Golub R, Siddiqui F, Pohl D. Laparoscopic versus open appendectomy: a metaanalysis. *J Am Coll Surg* 1998; **186**: 545-53.
84. Sauerland S, Lefering R, Holthausen U, Neugebauer EA. Laparoscopic vs conventional appendectomy--a meta-analysis of randomised controlled trials. *Langenbecks Arch Surg* 1998; **383**: 289-95.
85. Garbutt JM, Soper NJ, Shannon WD, Botero A, Littenberg B. Meta-analysis of randomized controlled trials comparing laparoscopic and open appendectomy. *Surg Laparosc Endosc* 1999; **9**: 17-26.
86. Chung RS, Rowland DY, Li P, Diaz J. A meta-analysis of randomized controlled trials of laparoscopic versus conventional appendectomy. *Am J Surg* 1999; **177**: 250-6.
87. Temple LK, Litwin DE, McLeod RS. A meta-analysis of laparoscopic versus open appendectomy in patients suspected of having acute appendicitis. *Can J Surg* 1999; **42**: 377-83.
88. de Wilde RL. Goodbye to late bowel obstruction after appendicectomy. *Lancet* 1991; **338**: 1012.
89. Kald A et al. Cost-minimisation analysis of laparoscopic and open appendicectomy. *Eur J Surg* 1999; **165**: 579-82.
90. Martin LC et al. Open versus laparoscopic appendectomy. A prospective randomized comparison. *Ann Surg* 1995; **222**: 256-61.
91. Williams MD, Miller D, Graves ED, Walsh C, Luterman A. Laparoscopic appendectomy, is it worth it? *South Med J* 1994; **87**: 592-8.
92. Long KH et al. A prospective randomized comparison of laparoscopic appendectomy with open appendectomy: Clinical and economic analyses. *Surgery* 2001; **129**: 390-400.
93. Engstrom L, Fenyo G. Appendicectomy: assessment of stump invagination versus simple ligation: a prospective, randomized trial. *Br J Surg* 1985; **72**: 971-2.
94. Andersen BR, Kallehave FL, Andersen HK. Antibiotics versus placebo for prevention of postoperative infection after appendicectomy (Cochrane Review). *Cochrane Database Syst Rev* 2001; **2**: CD001439.
95. Bilik R, Burnweit C, Shandling B. Is abdominal cavity culture of any value in appendicitis? *Am J Surg* 1998; **175**: 267-70.
96. Hopkins JA, Wilson SE, Bobey DG. Adjunctive antimicrobial therapy for complicated appendicitis: bacterial overkill by combination therapy. *World J Surg* 1994; **18**: 933-8.
97. Schein M, Assalia A, Bachus H. Minimal antibiotic therapy after emergency abdominal surgery: a prospective study. *Br J Surg* 1994; **81**: 989-91.
98. Johnson CC, Baldessarre J, Levison ME. Peritonitis: update on pathophysiology, clinical manifestations, and management. *Clin Infect Dis* 1997; **24**: 1035-45.
99. Taylor E, Dev V, Shah D, Festekjian J, Gaw F. Complicated appendicitis: is there a minimum intravenous antibiotic requirement? A prospective randomized trial. *Am Surg* 2000; **66**: 887-90.
100. Oliak D, Sinow R, French S, Udani VM, Stamos MJ. Computed tomography scanning for the diagnosis of perforated appendicitis. *Am Surg* 1999; **65**: 959-64.
101. Bagi P, Dueholm S. Nonoperative management of the ultrasonically evaluated appendiceal mass. *Surgery* 1987; **101**: 602-5.
102. Nitecki S, Assalia A, Schein M. Contemporary management of the appendiceal mass. *Br J Surg* 1993; **80**: 18-20.
103. Skoubo-Kristensen E, Hvid I. The appendiceal mass: results of conservative management. *Ann Surg* 1982; **196**: 584-7.
104. Vargas HI, Averbook A, Stamos MJ. Appendiceal mass: conservative therapy followed by interval laparoscopic appendectomy. *Am Surg* 1994; **60**: 753-8.
105. Adalla SA. Appendiceal mass: interval appendicectomy should not be the rule. *Br J Clin Pract* 1996; **50**: 168-9.
106. Bleker RJ, Wereldsma JC. Colonic malignancy mimicking an appendiceal mass. *Neth J Surg* 1989; **41**: 42-6.
107. de Dombal FT, Clamp SE, Wardle KS. Measuring surgical performance in acute abdominal pain: some reflections from international studies. *Eur J Surg* 1997; **163**: 323-9.

108. Styrud J, Eriksson S, Segelman J, Granstrom L. Diagnostic accuracy in 2,351 patients undergoing appendicectomy for suspected acute appendicitis: A retrospective study 1986-1993. *Dig Surg* 1999; **16**: 39-44.
109. Baigrie RJ, Dehn TC, Fowler SM, Dunn DC. Analysis of 8651 appendicectomies in England and Wales during 1992. *Br J Surg* 1995; **82**: 933.
110. Wen SW, Naylor CD. Diagnostic accuracy and short-term surgical outcomes in cases of suspected acute appendicitis. *CMAJ* 1995; **152**: 1617-26.

Chapter 3

Surgical validation of unenhanced helical CT in acute appendicitis



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ABSTRACT

Introduction: Surgery for pain in the right lower quadrant of the abdomen remains a clinical dilemma. This prospective study assessed the accuracy of preoperative unenhanced helical computed tomography (CT) in the evaluation of patients with suspected acute appendicitis.
Patients and methods: One hundred-and-three adult patients with suspected acute appendicitis underwent unenhanced helical CT of the abdomen. Subsequently, all patients underwent laparoscopic inspection of the abdominal cavity by a surgeon who was blinded to the diagnosis suggested by CT. Patients underwent appropriate surgical therapy accordingly. Follow-up was at least 6 weeks.
Results: Appendicitis was diagnosed by CT in 83 patients (80.6 per cent). Acute appendicitis was identified during laparoscopy in 87 patients (84.5 per cent). Prospective interpretations of CT images yielded a sensitivity of 95.4 per cent, and a specificity of 100 per cent for the diagnosis of acute appendicitis. There were four false-negative scans. In 12 of 20 patients without signs of appendicitis on CT, the scan established the presence of other pathology. At operation no additional pathology was observed in this group and all other diagnoses proved to be correct.
Conclusions: Plain helical CT in patients suspected of acute appendicitis provides an accurate diagnosis without the disadvantages of contrast enhancement.

INTRODUCTION

Acute appendicitis affects over 700,000 patients annually in the European Community, 16,000 in The Netherlands [1]. A similar number of patients with suspected appendicitis are hospitalised with a subsequent diagnosis other than appendicitis [2].

At least 20 per cent of appendectomies should be considered unnecessary, because other or no pathology is found at operation [3,4]. However, surgical tradition dictates removal of the appendix whenever a gridiron incision has been made at open surgery. Diagnostic laparoscopy has been shown to improve diagnostic accuracy for acute appendicitis, and to reduce the number of redundant appendectomies, both in fertile women (by 17-38 per cent) and also in men (by 11 per cent) [4-9]. Preoperative computed tomography (CT) in patients suspected of acute appendicitis has also been demonstrated to be highly accurate in confirming or ruling out acute appendicitis [10].

Several studies on the value of CT in acute appendicitis have been performed with administration of contrast, either intravenously and/or in the digestive tract. The present study, was a prospective assessment of the accuracy of preoperative helical CT without contrast in confirming or excluding acute appendicitis and other pathology in patients with acute right lower quadrant pain.

PATIENTS AND METHODS

The study included 103 consecutive patients over 16 years of age with suspected acute appendicitis who presented to the emergency departments of the University Hospital Rotterdam and Medical Centre Rijnmond-Zuid between December 1999 and November 2001. The clinical diagnosis was established by senior surgeons in all patients. All patients were scheduled for emergency laparoscopy. Before operation each patients gave written informed consent and subsequently underwent abdominal CT. The study was approved by medical ethical committees of both participating hospitals.

Preoperative evaluation included medical history, physical examination, and laboratory tests, including pregnancy tests if appropriate, all at the discretion of the surgeon. Exclusion criteria were signs of acute bowel obstruction, contra-indication to laparoscopy, contra-indication to general anaesthesia or pneumoperitoneum, age under 16 years, pregnancy and sepsis. Sepsis was defined as a body temperature of 39 ^{0}C or above or 35.5 ^{0}C or less and dependence on catecholamines to maintain normal blood pressure, or positive blood cultures. Signs of acute pancreatitis or acute aneurysm of the abdominal aorta or iliac arteries on CT were considered to be stopping points.

CT was performed within 1 h of being requested. A LightSpeed Advantage™ scanner (GE Medical Systems, Milwaukee, Wisconsin, USA) was used to obtain a single breath-hold helical scan from the caudal edge of the T11 vertebral body to the pubic symphysis. A 7.5-mm beam collimation was used for the upper abdomen to the anterior iliac spine, and a 5 mm beam collimation was used for the lower abdomen to the pubic symphysis. The table speed was 10 m/sec (11.25 mm / rotation, pitch 2.0, 120 kV, 190 mAs). No intravenous, oral or rectal contrast was used.

The primary sign on CT for the diagnosis acute appendicitis was dilatation of the appendix greater than 6 mm in transverse diameter. Secondary signs were periappendiceal infiltration, thickening of the cecal wall, presence of an appendicolith, periappendiceal phlegmon or abscess, and adenopathy. If only positive secondary signs were present, the scan was considered positive for acute appendicitis. After completion of scans, a radiology resident and a senior radiologist reviewed the images. Their findings were noted on a record form for use by the surgeon after the diagnostic laparoscopy (see below). At the completion of the study, all scans were reviewed by an expert radiologist who was blinded to the clinical history and surgical findings. His scores were used to evaluate the final performance of preoperative CT.

After CT, all patients underwent a standardized diagnostic laparoscopy, which included inspection of the gallbladder, stomach, duodenum, sigmoid, transverse and ascending colon, distal 100 cm of ileum and internal genitals if applicable. The lesser sac was not routinely opened to allow inspection of the pancreas. The surgeon was blinded to the CT findings during laparoscopy until the explorative phase of the laparoscopy was considered complete, at which point the laparoscopic findings were noted on a record form. These findings were considered the 'gold standard', and were used to interpret the value of preoperative CT. Subsequently, the surgeon was free to use any extra information provided by CT in clinical decision making. Patients were treated with respect to the final diagnosis, non-surgically or by open or laparoscopic surgery. Non-inflamed appendices were not removed if treatment was laparoscopically. All removed specimens were sent for pathological examination.

Follow-up involved completion of postoperative record forms 1 and 2 days, and 1 and 6 weeks after surgery. Other data collected included hospital stay, pathological diagnosis, complications and change of diagnosis and treatment after discharge.

RESULTS

Sixty-four men and 39 women, ranging in age from 16 to 82 (median 36) years were enrolled in this study. During the study period no patients meeting inclusion criteria were excluded. Prospective interpretation of unenhanced helical CT images had a sensitivity of 95.4 per cent and a specificity of 100 per cent for the diagnosis of acute appendicitis. The appendix was demonstrated in all scans. There were no false-positive and four false-negative

CT interpretations. In patients with a false-negative interpretation, acute appendicitis was demonstrated during laparoscopy.

Acute appendicitis was diagnosed by CT in 83 patients (80.6 per cent). Whereas 87 patients (84.5 per cent) were diagnosed with acute appendicitis during laparoscopy (*Table 1*). Laparoscopic appendectomy was intended in all patients with signs of acute appendicitis during laparoscopy, but three patients eventually underwent open appendectomy for technical reasons. All 87 removed appendices were inflamed on microscopic examination.

Table 1 Laparoscopic and radiological characteristics of 103 consecutive patients suspected of acute appendicitis

	CT scan	Laparoscopy
appendicitis	83	87
no appendicitis	20	16
no pathology	8	5
gastric perforation	1	1
ileitis	2	2
colitis	1	1
enteritis	1	1
cecal infiltration	1	1
dermoid cyst	1	1
ileus	1	1
infiltration sigmoid	3	3
pyelonephritis	1	0
total	103	103

No appendicitis was diagnosed on CT scans in 20 patients (19.4 per cent). No pathology was revealed by CT in eight of these patients, but four were subsequently diagnosed with acute appendicitis during laparoscopy. Three cases of acute appendicitis involving only the tip of the appendix, and one of perforated appendicitis with micro-abscess were misdiagnosed by CT. Laparoscopy revealed no abdominal pathology in the other four patients.

Other pathology was observed on the scan in the remaining 12 patients without signs of appendicitis on CT. No additional pathology was found at operation and the diagnosis based on CT findings was correct. The radiological record form was used by the surgical team in six instances. In five patients no diagnosis could be found during laparoscopy which was confirmed by a negative CT scan. In one patient with a negative laparoscopy, pyelonephritis was diagnosed by CT.

A gastric perforation in one patient was sutured laparoscopically. Two patients with ileitis, one with colitis, one with enteritis, and one with mild infiltration of the cecum were treated conservatively. One patient with a dermoid cyst and one with a mild ileus of unknown origin were also treated non-operatively. Three patients were diagnosed with infiltration of the sigmoid wall, one of them underwent a Hartmann's procedure for perforated adenocarcinoma of the sigmoid. Two patients were diagnosed with diverticular disease of the sigmoid during laparoscopy. Their initial treatment was conservative, but one had a sigmoid resection after three months because of continuing obstructive complaints. One patient recovered completely and showed no tumour on colonoscopy and control CT after three months. The patient with pyelonefritis diagnosed by CT was treated with antibiotics. No laparoscopic procedure was converted to laparotomy because no specific diagnosis could be found laparoscopically.

In 11 patients (10.7 per cent) diagnostic laparoscopy was not followed by surgical treatment, in two patients because no signs of appendicitis or other pathology were shown during laparoscopy and in nine patients with various diagnoses as noted above.

Follow-up was at least 6 weeks for all patients. Directly after surgery, and at 6 weeks' follow-up, no patients had been diagnosed with additional pathology. Six patients had complications. Three patients with wound infections were treated by local wound drainage and two patients who developed an intra-abdominal abscess were treated successfully by percutaneous drainage under ultrasonographic guidance. One 57-year-old woman who developed tertiary peritonitis and enterocutaneous fistula after sigmoid resection for perforated sigmoid adenocarcinoma stayed in the hospital for 9 months. There were no deaths. Mean hospital stay was 2.8 (median 2) days, excluding the patient with perforated carcinoma of the sigmoid, who stayed in hospital for 282 days.

DISCUSSION

In the Western world, the lifetime risk of acute appendicitis is 6.7 per cent for females and 8.6 per cent for males [11]. However, the lifetime chance of appendectomy is higher, 23.1 and 12 per cent respectively [11]. This discrepancy reflects the number of incidental and unnecessary appendectomies. Removing a normal appendix is associated with an early complication rate of 6.7-13 per cent and a late complication rate of 4 per cent in the early years after surgery [12,13].

Several imaging techniques have been advocated to improve the diagnostic accuracy in patients suspected of acute appendicitis. The introduction of CT in clinical decision making has been shown to decrease the rate of negative appendectomies in this group of patients [10,14]. A sensitivity and specificity of 90.1 -97 per cent and 94.1-100 per cent respectively have been reported for CT [15,16]. This modality has been shown to be superior to ultrasonography in providing an adequate diagnosis in patients with possible acute appendicitis at the cost of a mild dose of ionising radiation [16-19].

The optimal CT technique is still under debate [20]. Several techniques, ranging from plain abdominal CT to thin section enhanced helical CT with oral and rectal contrast focussing on the appendix have been advocated [10,14,19-22]. Many studies that have attempted to evaluate specific CT techniques are flawed because they are either retrospective in design or use clinical follow-up to verify the final diagnosis in part of the study group, or both. In this study, the value of unenhanced helical CT without rectal or oral contrast was prospectively evaluated by comparing CT findings with findings at diagnostic laparoscopy in all patients. The implications of introduction of routine preoperative CT with respect to the requirement for 24-h availability of radiological expertise and interobserver variability were not investigated. In daily practise those items are of paramount importance and should be addressed in further studies.

Laparoscopic inspection of the abdominal cavity enables the surgeon to diagnose acute appendicitis accurately [23]. In this study it was considered the 'gold standard' in providing the diagnosis in patients with suspected acute appendicitis. This assumption proved to be correct because no patients required conversion to laparotomy purely for diagnostic purposes. Unenhanced CT without oral or rectal contrast yielded a high sensitivity and specificity of 95.4 and 100 per cent respectively for acute appendicitis. This method therefore represents a simple, rapid and relatively inexpensive technique with which to obtain an accurate diagnosis in patients with suspected acute appendicitis without possible allergic effects or patient discomfort related to the use of intravenous or enteral contrast. Avoiding contrast enhancement also has an economic cost advantage; in the authors' departments, use of intravenous and rectal contrast forms 25 percent of the total costs of CT.

Unenhanced CT without oral or rectal contrast was also able to diagnose other pathology accurately in this group of patients. Pre-operative CT could therefore provide information on the optimal surgical access to the abdomen in case of unexpected diagnoses such as gastric or sigmoid perforation that require a surgical approach other than a McBurney incision. In laparoscopic surgery, preoperative information on the exact location of the appendix or other intra- abdominal pathology is of less value because laparoscopy allows easy inspection of the entire abdominal cavity.

In this study, both men and women benefited from pre-operative CT; a McBurney incision would have been prevented in 9 women (23.0 per cent) and five men (7.8 per cent) if the intended treatment would have been changed on the basis of CT findings. Introducing diagnostic laparoscopy in the standard evaluation of patients with suspected acute appendicitis deprives preoperative CT of some of its benefits because it diagnosed with 99 per cent accuracy in this study and many conditions encountered, including acute appendicitis and gastric perforations, can be treated laparascopically. As a purely diagnostic modality, however, it is inferior to CT because it is more invasive. This is particularly disadvantageous to patients with a non-surgical disease. However, early laparoscopy in patients with acute non-specific abdominal pain is associated with a higher accuracy and improved quality of life compared with close observation followed by surgical intervention if signs of peritonism develop [24].

The four false-negative CT interpretations, particularly the missed case of perforated appendicitis, are of great concern. Reducing the collimation used in the appendiceal region (for example from 5 to 3.25 mm) might improve the accuracy, as only the tip of the appendix was affected in three of four with a false-negative scan. Reading the scans directly on the work station might also improve interpretation.

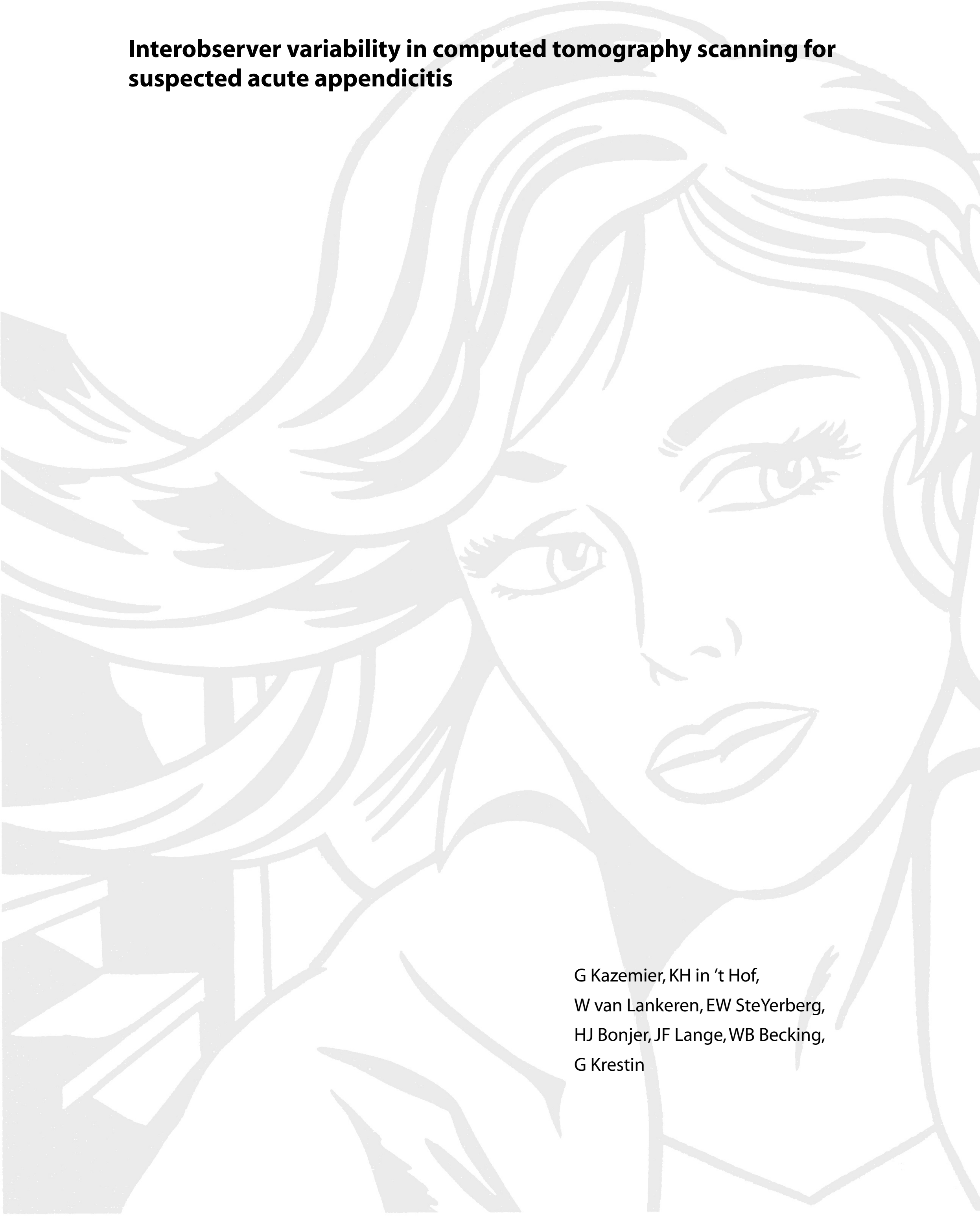
Rao et al. [10] showed in a North American study that routine contrast-enhanced appendiceal CT in patients with suspected acute appendicitis not only improved patient care but also reduced the use of hospital resources. In the light of the present finding that unenhanced helical CT can give an accurate diagnosis without the disadvantages of contrast enhancement, a randomized trial comparing its costs with those of diagnostic laparoscopy is now required.

REFERENCES

1. de Dombal FT, Clamp SE, Wardle KS. Measuring surgical performance in acute abdominal pain: some reflections from international studies. *Eur J Surg* 1997; **163**: 323-329.
2. Simmen HP, Decurtins M, Rotzer A, Duff C, Brutsch HP, Largiader F. Emergency room patients with abdominal pain unrelated to trauma: prospective analysis in a surgical university hospital. *Hepatogastroenterology* 1991; **38**: 279-282.
3. Andersson RE, Hugander AP, Ghazi SH, Ravn H, Offenbarl SK, Nystrom PO et al. Why does the clinical diagnosis fail in suspected appendicitis? *Eur J Surg* 2000; **166**: 796-802.
4. Larsson PG, Hendriksson G, Olsson M, Boris J, Stroberg P, Tronstad SE et al. Laparoscopy reduces unnecessary appendicectomies and improves diagnosis in fertile women. A randomized study. *Surg Endosc* 2001; **15**: 200-202.
5. Van Den Broek WT, Bijnen AB, van Eerten PV, De Ruiter P, Gouma DJ. Selective use of diagnostic laparoscopy in patients with suspected appendicitis. *Surg Endosc* 2000; **14**: 938-941.
6. Barrat C, Catheline JM, Rizk N, Champault GG. Does laparoscopy reduce the incidence of unnecessary appendicectomies? *Surg Laparosc Endosc* 1999; **9**: 27-31.
7. Olsen JB, Myren CJ, Haahr PE. Randomized study of the value of laparoscopy before appendicectomy. *Br J Surg* 1993; **80**: 922-923.
8. Thorell A, Grondal S, Schedvins K, Wallin G. Value of diagnostic laparoscopy in fertile women with suspected appendicitis. *Eur J Surg* 1999; **165**: 751-754.
9. Jadallah FA, Abdul-Ghani AA, Tibblin S. Diagnostic laparoscopy reduces unnecessary appendicectomy in fertile women. *Eur J Surg* 1994; **160**: 41-45.
10. Rao PM, Rhea JT, Novelline RA, Mostafavi AA, McCabe CJ. Effect of computed tomography of the appendix on treatment of patients and use of hospital resources. *N Engl J Med* 1998; **338**: 141-146.
11. Addiss DG, Shaffer N, Fowler BS, Tauxe RV. The epidemiology of appendicitis and appendectomy in the United States. *Am J Epidemiol* 1990; **132**: 910-925.
12. Deutsch AA, Shani N, Reiss R. Are some some appendectomies unnecessary? An analysis of 319 white appendices. *J R Coll Surg Edinb* 1983; **28**: 35-40.
13. Gough IR, Morris MJ, Pertnikovs EJ, Murray MR, Smith MB, Bestmann MS. Consequences of removal of a "normal" appendix. *Med J Aust* 1983; **1**: 370-372.
14. Rao PM, Rhea JT, Novelline RA. Helical CT of appendicitis and diverticulitis. *Radiol Clin North Am* 1999; **37**: 895-910.
15. Gwynn LK. The diagnosis of acute appendicitis: clinical assessment versus computed tomography evaluation. *J Emerg Med* 2001; **21**: 119-123.
16. Horton MD, Counter SF, Florence MG, Hart MJ. A prospective trial of computed tomography and ultrasonography for diagnosing appendicitis in the atypical patient. *Am J Surg* 2000; **179**: 379-381.
17. Balthazar EJ, Birnbaum BA, Yee J, Megibow AJ, Roshkow J, Gray C. Acute appendicitis: CT and US correlation in 100 patients. *Radiology* 1994; **190**: 31-35.
18. Pickuth D, Heywang-Kobrunner SH, Spielmann RP. Suspected acute appendicitis: is ultrasonography or computed tomography the preferred imaging technique? *Eur J Surg* 2000; **166**: 315-319.
19. Stroman DL, Bayouth CV, Kuhn JA, Westmoreland M, Jones RC, Fisher TL, McCarthy TM. The role of computed tomography in the diagnosis of acute appendicitis. *Am J Surg* 1999; **178**: 485-489.
20. Wise SW, Labuski MR, Kasales CJ, Blebea JS, Meilstrup JW, Holley GP et al. Comparative assessment of CT and sonographic techniques for appendiceal imaging. *AJR Am J Roentgenol* 2001; **176**: 933-941.
21. Lane MJ, Liu DM, Huynh MD, Jeffrey RBJr, Mindelzun RE, Katz DS. Suspected acute appendicitis: nonenhanced helical CT in 300 consecutive patients. *Radiology* 1999; **213**: 341-346.
22. Rao PM, Rhea JT, Novelline RA. Appendiceal and peri-appendiceal air at CT: prevalence, appearance and clinical significance. *Clin Radiol* 1997; **52**: 750-754.
23. Kraemer M, Ohmann C, Leppert R, Yang Q. Macroscopic assessment of the appendix at diagnostic laparoscopy is reliable. *Surg Endosc* 2000; **14**: 625-633.
24. Decadt B, Sussman L, Lewis MP, Secker A, Cohen L, Rogers C et al. Randomized clinical trial of early laparoscopy in the management of acute non-specific abdominal pain. *Br J Surg* 1999; **86**: 1383-1386.

Chapter 4

Interobserver variability in computed tomography scanning for suspected acute appendicitis



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ABSTRACT

Introduction: Computed tomography (CT) has been shown to improve diagnostic accuracy in patients suspected with acute appendicitis. This prospective study assessed the interobserver variability of CT scanning in these patients.

Patients and methods: One hundred-and-three adult patients with suspected acute appendicitis underwent unenhanced helical CT of the abdomen. Subsequently, all patients underwent laparoscopy by a surgeon who was blinded to the diagnosis suggested by CT. All CT scans were interpreted by group A, B, and C radiologists with different levels of expertise.

Results: Acute appendicitis was diagnosed on CT in 69 per cent, 74 per cent, and 80 per cent by group A, B, and C radiologists respectively. At laparoscopy, 83 per cent of patients were diagnosed with acute appendicitis. Sensitivity was: 81 per cent, 88 per cent, and 95 per cent caused by 16, 8, and 4 false-negative CT interpretations by group A, B, and C radiologists respectively. During laparoscopy 12 patients were diagnosed with other diseases. These were all correctly diagnosed by group C (specificity 100 per cent); group A and B both missed the diagnosis colitis in one patient, all other disorders were diagnosed correctly (specificity 94 per cent).

Conclusions: Sensitivity of CT for the diagnosis acute appendicitis differs considerably. This interobserver variability has to be considered in the implementation of routine CT scanning in patients with suspected acute appendicitis.

INTRODUCTION

Diagnosing acute appendicitis remains a challenge to the clinician. More than fifteen per cent of appendectomies are performed unnecessarily while in some high-risk populations, such as women of reproductive age, the population-based rate of unnecessary appendectomy is as high as 26% [1]. Preoperative imaging techniques, such as computed tomography (CT) and ultrasonography (US) have been shown to improve diagnostic accuracy in patients with suspected acute appendicitis [2-4]. In centres with dedicated expertise, sensitivity and specificity of over 95 percent in patients with suspected acute appendicitis have been reported using either technique [2-4]. In the majority of studies investigating the value of different preoperative imaging techniques, the expert interpretation of the images is provided. However, patients with acute illnesses such as appendicitis present at any time of the day and require prompt and accurate diagnosis and treatment. Consequently, the assessment of patients with suspected acute appendicitis and interpretation of US and CT scans is in the hands of in house staff. These health care professionals might have limited expertise in diagnosing appendicitis by US or CT. To assess the interobserver variability of CT scanning in patients with suspected acute appendicitis, a prospective study was performed.

MATERIALS AND METHODS

From December 1999 until November 2001, a prospective study was performed in a cohort of 103 consecutive patients over 16 years of age, suspected of acute appendicitis. All patients presented to the emergency departments of the Erasmus MC or the Medical Centre Rijnmond Zuid in Rotterdam, The Netherlands. Medical ethical committees of both participating hospitals approved of the study. The clinical diagnosis of acute appendicitis was established by staff surgeons in all cases. All patients were scheduled for emergency laparoscopy. Prior to surgery all patients signed informed consent and subsequently underwent abdominal CT. All CT scans were obtained within one hour after being requested by using a helical CT scanner (LightSpeed Advantage™; GE Medical Systems, Milwaukee, Wis, USA). A single breath-hold helical scan from the caudal edge of the 11th thoracic vertebral body to the pubic symphysis was obtained. A 7.5 mm beam collimation was used for the upper abdomen to the anterior iliac spine, and a 5 mm beam collimation was used for the lower abdomen to the pubic symphysis. A table speed of 10 m/sec (11.25 mm / rotation) was used (pitch 2.0; 120 kV; 190 mAs). No intravenous, oral or rectal contrast was used.

Exclusion criteria were signs of acute bowel obstruction, contra-indications to laparoscopy, general anaesthesia or pneumoperitoneum, age under 16 years, pregnancy and sepsis. Sepsis was defined as body temperature >39 ^{0}C or <35.5 ^{0}C and dependence on catecholamines to maintain normal blood pressure or positive blood cultures. Signs of acute pancreatitis or acute aneurysm of the abdominal aorta or iliac arteries on CT were considered stopping points.

All CT scans were reviewed by three different groups of radiologists. Promptly after completion of the CT, a radiology resident interpreted the images (Group A) and these findings were recorded. Subsequently, a staff radiologist blinded to the first findings reviewed the same images and noted these findings on a second blank record form (Group B). This last record was available to the surgeon upon completion of the diagnostic laparoscopy (see below). After closure of the study, all scans were reviewed by an expert radiologist (GPK) who was blinded to the clinical history, earlier CT evaluations and surgical findings (Group C).

The primary sign on CT establishing the diagnosis acute appendicitis was dilatation of the appendix greater than 6 mm in transverse diameter. Secondary signs were thickening of the cecal wall, periappendiceal infiltration, presence of an appendicolith, periappendiceal phlegmon or abscess, collection of air bubbles in the lumen of the appendix and lymphadenopathy.

After CT, all patients underwent a diagnostic laparoscopy. All laparoscopic inspections were supervised or performed by staff surgeons. The surgical team was blinded to the CT findings during surgery until the explorative phase of the laparoscopy was considered complete. At that time the surgeon noted the laparoscopic findings on a record form. These findings were considered the 'gold standard' and were used to interpret the value of preoperative CT scanning.

Subsequently, the surgeon was free to use any additional information from the CT in clinical decision making. Patients were treated with respect to the final diagnosis, either non-surgically or surgically, open or laparoscopically. Normal appendices were not removed. All removed specimens were sent for pathological examination.

To compare differences in performance between groups A, B and C, sensitivity, specificity and false-positive and false-negative interpretations were calculated. Level of agreement between groups was expressed by kappa coefficients. The kappa coefficient of reliability provides a pair wise indication of agreement between observers, corrected for chance and varies between –1 (perfect disagreement) and 1 (perfect agreement).

RESULTS

Sixty-four males and 39 females, ranging in age from 16 to 82 years (median 36 years) were enrolled in this study. During the study no patients meeting inclusion criteria were excluded. All CT scans were interpreted by group A and C radiologists while three CT scans were not interpreted by group B radiologists. Interpretation of scans by group A, B and C radiologists showed considerable differences (Table). Acute appendicitis was diagnosed on CT in 69 per cent, 74 per cent, and 80 per cent by group A, B, and C radiologists respectively. At laparoscopy, 83 per cent of patients were diagnosed with acute appendicitis. No laparoscopic proceduress were converted to laparotomy for diagnostic purposes.

The level of agreement (kappa) was good, 0.76 and 0.70 respectively between group A and B and between group B and C radiologists, but less between group A and C: 0.57. Specificity of CT interpretations for the diagnosis acute appendicitis in these 103 patients by Group A, B and C radiologists was comparable: 94 per cent, 94 per cent, and 100 per cent respectively (Table). However, sensitivity differed considerably between groups: 81 per cent, 88 per cent, and 95 per cent respectively. There were 16, 8, and 4 false-negative and 1, 1 and 0 false-positive CT interpretations in group A, B, and C respectively.

During laparoscopy 12 patients were diagnosed with other diseases (Table). These other diseases were correctly diagnosed by the expert radiologist (i.e. group C) in all patients; group A and B radiologists both missed the diagnosis colitis in one patient, while all other disorders were diagnosed correctly. Pathology confirmed surgical findings in all cases.

Follow-up was at least six weeks for all patients. Directly after surgery and at six weeks' follow-up, no patient had been diagnosed with additional pathology.

Table Accuracy of CT interpretations by group A, B, and C radiologists as compared to laparoscopy

	Group A	Group B	Group C	Laparoscopy
Cases (n)	**103**	**100**	**103**	**103**
Appendicitis (n)	**71**	**74**	**82**	**87**
No appendicitis (n)	**32**	**26**	**21**	**16**
no pathology	21	15	8	5
gastric perforation	1	1	1	1
Ileitis	2	2	2	2
Colitis	0	0	1	1
Enteritis	1	1	1	1
cecal infiltration	1	1	1	1
dermoid cyst	1	1	1	1
Ileus	1	1	1	1
infiltration sigmoid	3	3	3	3
Pyelonephritis	1	1	1	0
Sensitivity	**81%**	**88%**	**95%**	
# false negative	**16**	**8**	**4**	
Specificity	**94%**	**94%**	**100%**	
# false positive	**1**	**1**	**0**	

DISCUSSION

Morbidity associated with unnecessary appendectomies varies from three to six percent[5,6]. Particularly long-term complications such as bowel obstruction due to adhesions or incarcerated incisional hernias carry considerable risk and economical burden. In a recent study by Flum et al.[7], clinical and economical correlates of misdiagnosed acute appendicitis in the United States have been assessed. This study showed that in 1997 in the United States, 15.3 per cent of 261,134 non-incidental appendectomies were negative for acute appendicitis. The authors estimated that $741.5 million in total hospital charges resulted from admissions for unnecessary appendectomy. In our study, all patients were scheduled for emergency laparoscopy after they were diagnosed with acute appendicitis by a senior surgeon. Even in this group of patients with a high index of suspicion, 17 per cent did not have acute appendicitis at laparoscopic evaluation.

To decrease the number of unnecessary appendectomies, several imaging techniques such as CT and US have been advocated to improve diagnostic accuracy. Introduction of CT in clinical decision making has been shown to decrease the rate of negative appendectomies[2]. Sensitivity and specificity rates of 90.1 to 97 per cent and 94.1to100 per cent respectively have been reported for CT[2,4]. However, these high accuracies involve studies under optimal conditions with experts interpreting CT images. Under these conditions CT has been shown to be superior to US in providing an adequate diagnosis in patients with suspected acute appendicitis[8,9]. Interobserver variability in US for establishment of acute appendicitis is great because accurate ultrasonographic recognition of an inflamed appendix requires outstanding expertise in abdominal ultrasonography. Therefore, US has never been adopted routinely to diagnose appendicitis although US plays a role in pregnant women and children who have a thin abdominal wall which renders US more feasible[8]. The quality of CT images is far less dependent on the observer. However, this study shows that the interpretation of CT images carries a considerable interobserver variability. Although a positive CT is rarely erroneous, false-negative CT interpretations are more common when less experienced assessors review the images. The interobserver variability in CT scanning for suspected acute appendicitis has its consequences for training of medical doctors who are involved in the care of patients with right lower abdominal quadrant pain. Interpretation of CT images of such patients should be considered to be integrated into the early training of radiologists, surgeons and emergency medicine doctors. Another option is telesupervision of image interpretation, which is increasingly adopted and may become the standard of care in the near future. Information technology allows and will oblige the medical community to provide the highest degree of expertise at any time and any place.

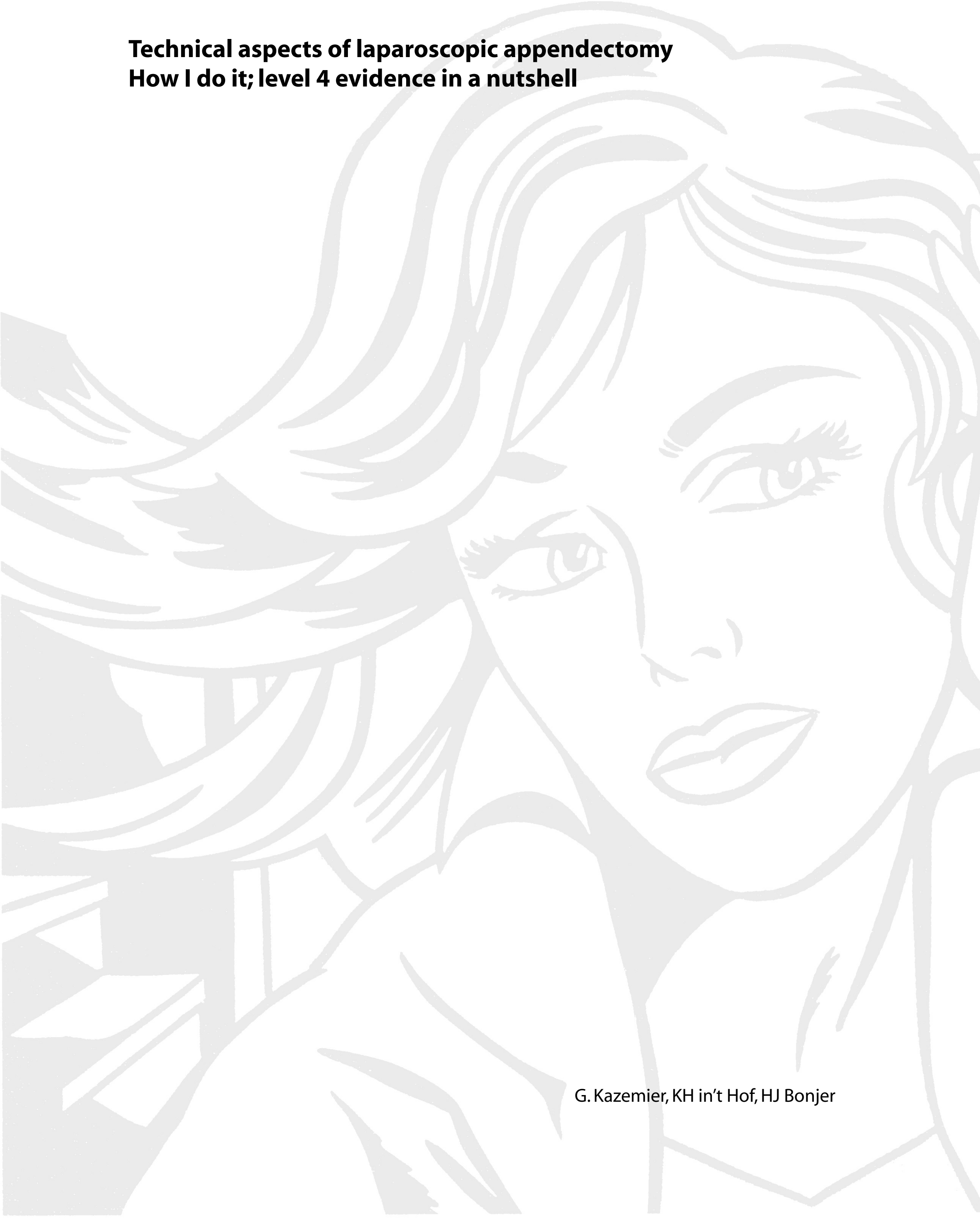
However, also in expert hands, false-negative CT interpretations do occur. In this study the expert radiologist interpreted four CT scans falsely negative. Reducing the collimation as used in the appendiceal region (for example from 5 to 3.25 mm), reading the scans directly on the working station or administering intravenous and enteral contrast in difficult cases might improve the quality of interpretation, but clinical assessment will continue to play a role. Clinical or outpatient observation and diagnostic laparoscopy are to be considered in patients with negative CT scans.

REFERENCES

1. Flum DR, Morris A, Koepsell T, Dellinger EP. Has diagnostic accuracy in appendicitis improved with time? *JAMA.* 2001;**286**:1748-1753.
2. Rao PM, Rhea JT, Rattner DW, Venus LG, Novelline RA. Introduction of appendiceal CT: impact on negative appendectomy and appendiceal perforation rates. *Ann Surg.* 1999;**229**:344-349.
3. Puylaert JB, Rutgers PH, Lalisang RI, de Vries BC, van der Werf SD, Dorr JP, Blok RA. A prospective study of ultrasonography in the diagnosis of appendicitis. *N Engl J Med* 1987 Sep 10;**317**:666-9.
4. in 't Hof KH, van Lankeren W, Krestin GP, Bonjer HJ, Lange JF, Becking WB, Kazemier G. Surgical validation of unenhanced helical computed tomography in acute appendicitis. *Br J Surg* 2004;**91**:1641-5.
5. Bijnen CL, Van den Broek WT, Bijnen AB, de Ruiter P, Gouma DJ. Implications of removing a normal appendix. *Dig Surg* 2003;**20**:215-9.
6. Tingsted B, Johansson J, Nehez L, Andersson R. Late abdominal complaints after appendectomy-readmissions during long-term follow-up. *Dig Surg* 2004;**21**:23-7.
7. Flum DR, Koepsell T. The clinical and economic correlates of misdiagnosed appendicitis: nationwide analysis. *Arch Surg.* 2002;137:799-804.
8. Wise SW et al. Comparative assessment of CT and sonographic techniques for appendiceal imaging. *Am J Roentgenol* 2001; **176**: 933-41.
9. Pickuth D, Heywang-Kobrunner SH, Spielmann RP. Suspected acute appendicitis: is ultrasonography or computed tomography the preferred imaging technique? *Eur J Surg* 2000; **166**: 315-9.

Chapter 5

Technical aspects of laparoscopic appendectomy
How I do it; level 4 evidence in a nutshell



G. Kazemier, KH in't Hof, HJ Bonjer

INTRODUCTION

Laparoscopic appendectomy has not yet been widely adopted by general surgeons in spite of clear evidence of its advantages. Inexperience with the laparoscopic approach to appendiceal pathology, subsequently long operating times and higher direct costs are halting wider diffusion. To implement laparoscopic appendectomy successfully into hospital practice, involved health care professionals require proper training and access to proper videoscopic equipment.

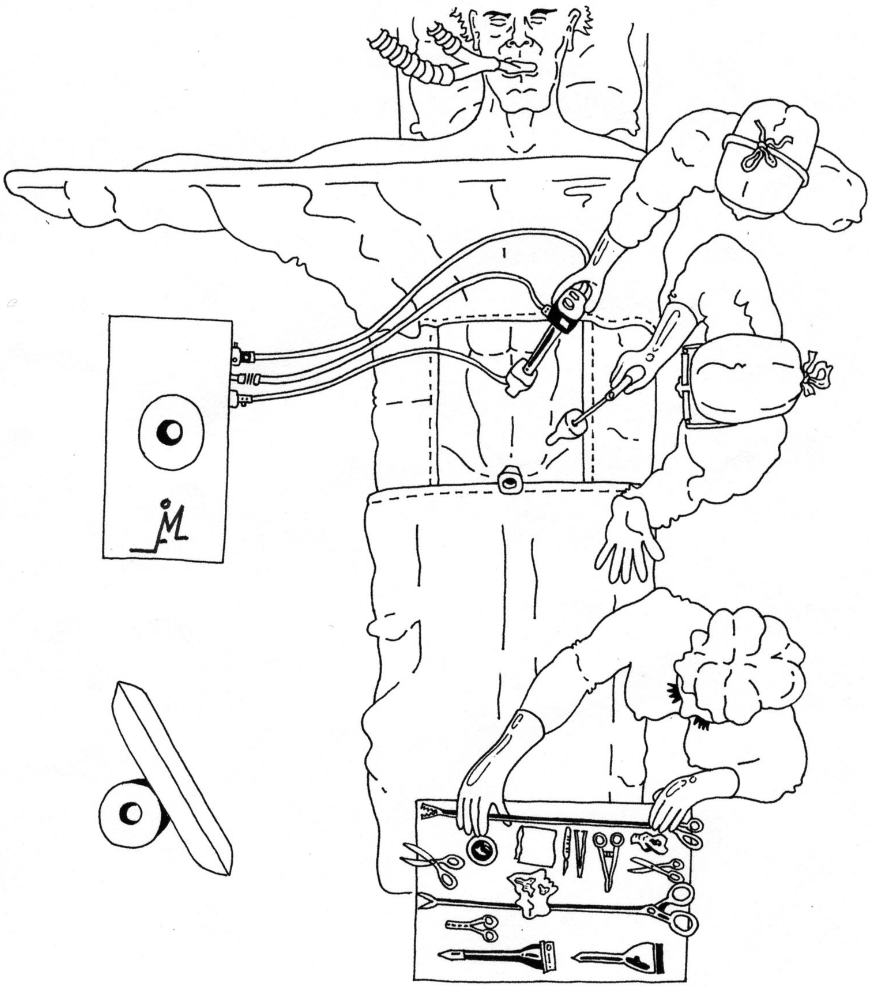


Figure 1 Positioning of the patient, surgical team and equipment

PRE-OPERATIVE WORK-UP

Laparoscopic appendectomy requires a surgical team with proficient training in basic laparoscopic procedures such as laparoscopic appendectomy and high quality videoscopic imaging to allow proper assessment of the appendix. If these criteria cannot be met, open appendectomy is to be preferred. Both patient and family should be informed pre-operatively that the incisions will be made in the left lower quadrant of the abdomen to remove the appendix laparoscopically, in order to avoid confusion among those who expect an incision in the right lower quadrant.

Prior to this laparoscopic procedure the intravenous line should be placed in the right arm to allow for positioning of the left arm along the body of the patient, since both the surgeon and camera driver stand on the left side of the patient (Figure 1). Insertion of a urinary catheter is not mandatory if the patient has voided prior to surgery. The patient is placed in supine position, optionally with the right side elevated to a tilt of 30 degrees in order to facilitate mobilization of the cecum. Either a cushion or a beanbag can be used to position the patient in right tilt.

FIRST TROCAR

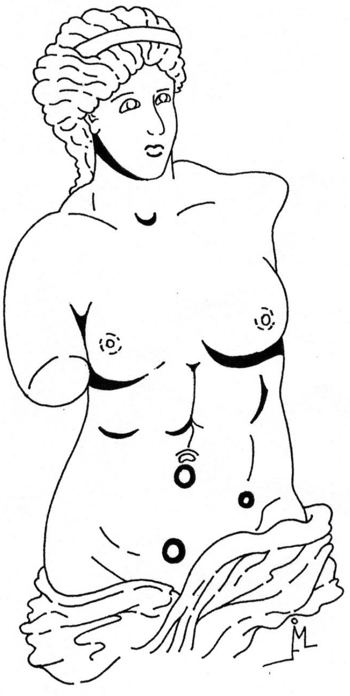


Figure 2 Trocar positioning

Establishment of the pneumoperitoneum is done in an open fashion in all patients since visceral and vascular lesions are more common after closed establishment of a pneumoperitoneum[1]. A semicircular incision is made in the lower or upper fold of the umbilicus depending on the anatomy of the umbilicus. In obese patients the position of the umbilicus tends to shift caudally. In these patients the optimal position of the first trocar can differ. Placement of the first trocar in the left upper quadrant is a safe alternative under these circumstances. In small patients this alternative should also be considered because placement at the umbilicus positions the trocar too close to the appendix. To introduce the Hasson's trocar, two Kocher clamps are placed on the fascia. Both fascia and peritoneum are opened under direct vision. Stay sutures are placed to secure the Hasson's cannula; at the end of the procedure these sutures will be used to close the fascia. In patients with abdominal scars due to previous surgery, the first trocar should be inserted in an area devoid of scars to allow for inspection and safe lysis of adhesions when present.

ADDITIONAL TROCARS AND INSPECTION OF THE ABDOMINAL CAVITY

The pressure of gas insufflation is determined per individual patient. The key is to work at the lowest pressure possible to limit adverse hemodynamic effects. After insufflating the peritoneal cavity, the patient is placed in a Trendelenburg position to displace the small bowels from the small pelvis. A zero degree 10-mm laparoscope is introduced to inspect the entire abdominal cavity. In most patients, placement of a second trocar allowing for introduction of an atraumatic grasper is required to retract small bowel loops and omentum. This second 5-mm trocar is placed just cranially to the pubic bone in the midline (Figure 2). The peritoneum tends to be very lax in the lower abdomen rendering introduction of this distal trocar difficult. Careful rotating this trocar during introduction and appropriate patience will contribute to its safe introduction.

The first step is the identification of the appendix. Laparoscopic inspection of the appendix involves assessment of color, consistency, mobility, fixation and possible perforation. Color assessment in videoscopic surgery is dependent on many variables such as light intensity, transparency of the laparoscope and quality of the camera and screen. A defective imaging chain can obscure or exaggerate redness of the appendix. An inflamed appendix is rigid while an unaffected appendix is floppy. Fixation of the appendix is indicative of appendicitis when previous generalized peritonitis has not occurred. Perforation of the appendix when present is obvious in most cases by the presence of pus or faeces in the peritoneal cavity. When the appendix is located posteriorly to the cecum, the cecum should be mobilized first by cutting the peritoneum at Told's line. This procedure will be facilitated by placing a third trocar. This third trocar is placed just medially to the left anterior superior iliac spine (Figure 2). Care should be taken not to damage the epigastric vessels. Laparoscopic inspection can accurately diagnose or rule out acute appendicitis [2,3]. If the appendix appears normal, inspection should continue and involve the gallbladder, stomach, duodenum, sigmoid colon, distal 100 cm of ileum, ovaries, Fallopian tubes and uterus if applicable. Inspection of the pancreatic body and tail requires opening of the lesser sac through the gastrocolic ligament and is not routinely performed. A normal appendix should be left in situ, even if no alternative diagnosis is confirmed [4]. Removing a normal appendix is associated with considerable morbidity and costs [5]. After negative diagnostic laparoscopy, patients should be well informed about the fact that the appendix was not removed. Murphy et al. [6] showed that 20 percent of patients was unaware of the status of their appendix after a diagnostic laparoscopy performed for right lower quadrant pain.

RESECTION OF THE APPENDIX

In the majority of patients a retrograde dissection of the appendix (from base to tip) is preferred; only dense infiltration of the base of the appendix may require antegrade dissection. Retrograde dissection requires skeletizing of the meso-appendix. To allow dissection of the meso-appendix, the appendix has to be retracted. The preferred method is retraction of the meso-appendix to avoid perforation of the appendix due to grasping. When the meso-appendix can not be grasped effectivily, a pre-tied loop at the tip of the appendix can serve as retraction handle. The meso-appendix harbors the appendicular artery that runs at the base of the meso-appendix (Figure 3). Depending on the caliber of this artery, occlusion can be accomplished by mono- or bipolar electrocautery, clips or an ultrasonic device. When diathermy is used, care should be taken to avoid contact between the tip of the dissection instrument and the terminal ileum or cecum. This can lead to unnoticed damage with late perforation of the ileum. Care should be taken that the entire appendix is freed as multiple reports exist on partial appendectomy during laparoscopic removal. The appendiceal stump can be taken care of by pre-tied loops at the base of the appendix. Application of diathermy during transsection of the appendix, which has been advocated to cauterize bacteria in the appendiceal lumen, should be avoided to prevent tearing the loop. The distal loop should not

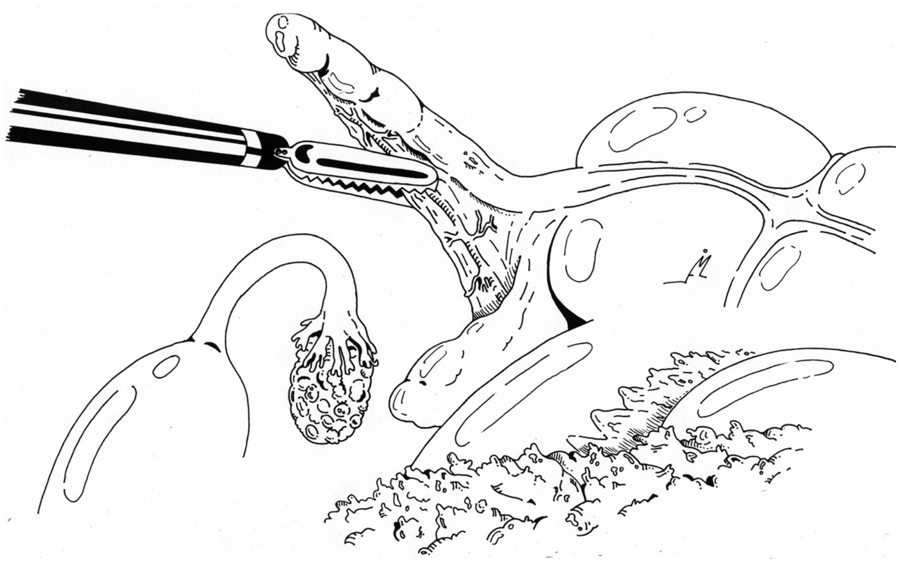


Figure 3 Anatomy of the appendix

be cut since it can be used to remove the appendix from the abdomen. As an alternative to pre-tied loops, the appendix can be occluded and transected by a 30-35 mm stapling device with a blue cartridge. When a stapling device is used, care should be taken not to include clips used on the meso-appendix in the staple line because this will cause misfiring. In case of bleeding at the staple line, compression with a gauze usually suffices. If bleeding persists, either a clip or a suture can be placed. Diathermy should be avoided to prevent necrosis at the staple line. Use of a stapling device requires change of the suprapubic 5 mm trocar for a 12-mm trocar. The use of a stapling device is mandatory when a perforation at the base of the appendix is present. In such cases, the stapler is placed over the cecum to exclude the perforation.

REMOVAL OF THE APPENDIX

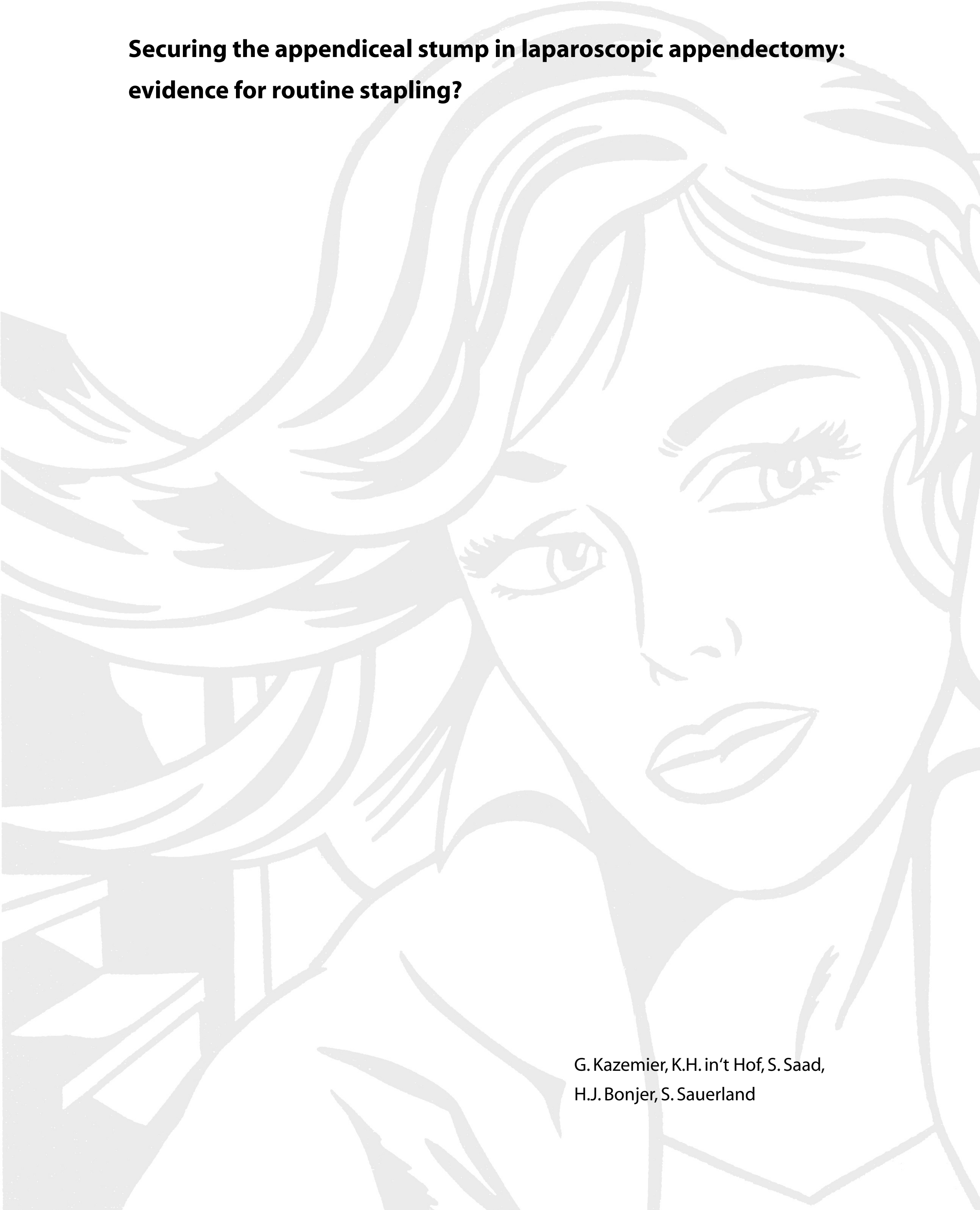
The appendix is removed from the abdominal cavity through the widest trocar that has been used during the procedure. In case one 10-mm trocar and two 5-mm trocars have been inserted, a 5-mm laparoscope can be inserted through one of the 5-mm trocars to allow removal of the appendix through the 10-mm trocar. When easy passage of the appendix through the trocar is unlikely, the appendix is placed in a plastic retrieval bag prior to removal. Drains are not left behind. Suction is performed routinely if blood or purulent material is present after removal of the appendix. All trocars are extracted under direct vision in order to identify possible bleeding at the port site. If a port site bleeding is noticed, coagulation with a laparoscopic instrument inserted through another port is attempted first to control the bleeding. If this is unsuccessful, compression with a balloon catheter or closure of the port site with suture passers that are inserted under laparoscopic monitoring is the next step. Intracutanous closure of the trocar sites is routinely performed.

REFERENCES

1. Bonjer HJ, Hazebroek EJ, Kazemier G, Giuffrida MC, Meijer WS, Lange JF. Open versus closed establishment of pneumoperitoneum in laparoscopic surgery. *Br J Surg* 1997; **84**: 599-602.
2. Kazemier G, de Zeeuw GR, Lange JF, Hop WC , Bonjer HJ. Laparoscopic vs open appendectomy. A randomized clinical trial. *Surg Endosc* 1997; **11**: 336-40.
3. Kraemer M, Ohmann C, Leppert R, Yang Q. Macroscopic assessment of the appendix at diagnostic laparoscopy is reliable. *Surg Endosc* 2000; **14**: 625-633.
4. Van den Broek WT, Bijnen AB, van Eerten PV, de Ruiter P, Gouma DJ. Selective use of diagnostic laparoscopy in patients with suspected appendicitis. *Surg Endosc* 2000;**14**:938-41.
5. Bijnen CL,Van den Broek WT, Bijnen AB, de Ruiter P, Gouma DJ. Implications of removing a normal appendix. *Dig Surg* 2003;**20**:215-9.
6. Murphy SM, Donnelly M, Fitzgerald T, Tanner WA, Keane FB, Tierney S. Patients' recall of clinical information following laparoscopy for acute abdominal pain. *Br J Surg* 2004;**91**:485-8.

Chapter 6

Securing the appendiceal stump in laparoscopic appendectomy: evidence for routine stapling?



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ABSTRACT

Background Despite the rapid proliferation of laparoscopic technology, many technical aspects of laparoscopic appendectomy are still a matter of debate. This meta-analysis aimed to compare endoscopic linear stapling versus loop ligatures in securing the base of the appendix.

Methods Randomized controlled trials on appendix stump closure during laparoscopic appendectomy were systematically searched (Medline, Cochrane and hand searches) and critically appraised. Results on complication rates, operating time, and hospital stay were pooled by standard meta-analytic techniques.

Results Data on 427 patients from four studies were included. The duration of surgery was 9 minutes longer if loops were used ($p = 0.04$). Superficial wound infection (OR 0.21; 95%-CI 0.06 to 0.71; $p = 0.01$) and postoperative ileus (0.36; 0.14 to 0.89; $p = 0.03$) were significantly less frequent when the appendix stump was secured by staples instead of loops. Of ten intraoperative ruptures of appendix, seven occurred in loop treated patients ($p = 0.46$). Hospital stay and frequency of postoperative intraabdominal abscess were also similar.

Conclusions The clinical evidence on stump closure methods in laparoscopic appendectomy favours routine use of endoscopic staplers. Higher direct costs will result from this strategy.

INTRODUCTION

Laparoscopic appendectomy (LA) is progressively accepted as the treatment of choice for acute appendicitis. Numerous randomized trials and meta-analyses have shown less post operative pain, less wound infections, faster recovery and shorter hospital stay after LA [1-7]. Although the surgical technique of laparoscopic appendectomy has been well established, controversy exists regarding closure of the appendiceal stump. In the early days of LA, the stump was closed with pre-knotted loops (Roeder loops or endoloops) [8-10]. After introduction of laparoscopic linear staplers, it became 'en vogue' to apply these for LA, particularly for difficult cases such as perforation at the appendiceal base [11-13]. Currently, some authors advise routine use of linear staplers during LA to avoid leakage from the appendiceal stump [14].

Both techniques have been shown to be safe but both entail potential drawbacks. Linear staplers are expensive and require a 12 mm port for introduction. Leaving metal staples on the stump and in the abdominal cavity can cause adhesion-related short bowel obstruction or formation of pseudo-polyps in the cecum [15-17]. Loops are associated with more manipulation of the stump and they can slip, which can potentially lead to more postoperative infections. Loops are not safe to close the cecum in case of perforation of the base of the appendix if the inflammation of the appendix has involved the cecum as well [18]. If loops are closed too tightly they also can cut into the tissue or cause local necrosis predisposing to stump leakage. Complications attributable to stump closure are rare, which means that large studies are required to show superiority of either fashion. Pooling data from the literature is potentially helpful to overcome this sample size problem [19]. The aim of this study is to determine the optimal technique to secure the appendiceal stump in LA from data available in the current literature.

MATERIALS AND METHODS

For this study, only data of patients who underwent laparoscopic surgery were assessed. All randomized controlled trials comparing different closing techniques of the appendiceal stump during laparoscopic appendectomy for acute appendicitis were included. Trials that allocated patients depending on the availability of staff or instruments were excluded. The aims of the surgical interventions under investigation were: (1) to remove an inflamed or uninflamed appendix and (2) to close the appendiceal stump with stapler or loops. The surgical tools applied to achieve these aims were: (1) LA with stapler; (2) LA with loops.

In order to be as comprehensive as possible, the following search strategies were employed to identify all relevant studies regardless of language after the year 1983. Electronically, the Cochrane Library (Version IV/2004), Medline, Embase, SciSearch and Biosis were searched. All searches were repeated until November 10, 2004. Reference lists were checked and authors of relevant articles and known international experts in the field of laparoscopic surgery were contacted to obtain information on any past, present or future studies. Abstracts presented to the international scientific societies focusing on endoscopic surgery were searched for by hand and the authors were asked to provide full information on their study.

All studies were assessed by 2 reviewers (KHH and SS) who checked the main criteria of study design and analysis, the method of randomization and allocation concealment, the blinding of outcome assessment, and how protocol violations were dealt with. These three aspects of quality were scored from 0 to 2, as proposed by Jadad et al. [20].

For dichotomous variables risk differences with their 95% confidence intervals were calculated. Since rare events were dealt with, the Peto odds ratio (OR) was calculated. For continuous variables, means with their corresponding standard deviations (SDs) are generally needed to calculate the mean differences and 95% confidence intervals. In case a study did not report SD for a mean value, we estimated SD to be equal to the mean. The effect measures were pooled within a random effects model. Heterogeneity was quantified by the I^2-statistics, which ranges from 0 percent (no heterogeneity) to 100 percent (maximum heterogeneity).

RESULTS

The five studies included in the review contributed to the results in the following way. One study compared double versus single loops at the base of the appendix [21], without showing major differences. Patients from this study were not included in the final analysis. Four studies compared LA using staplers and LA using loops [22-25]. Three of these studies had a three-armed design randomizing patients to laparoscopic appendectomy with loops or staplers or a third procedure. The third procedure was open appendectomy [25], extracorporeal stump ligation [23], or additional sinking of the appendix stump [22]. One trial was done in children [23]. The quality of all included studies was moderate to poor (table 1). Typical shortcomings were a lack of blinding and various types of protocol violations which made complete intention-to-treat analysis impossible. No study described the actual accrual rate of patients with suspected acute appendicitis during the study period nor included a longer follow-up to detect intra-abdominal adhesions and similar problems.

Table 2 summarizes therapeutic effects from the four above mentioned studies. Based on 427 patients, operative time was 9 minutes shorter ($p = 0.04$) if a stapler was used. Results on operative time however were heterogenous ($I^2 = 73\%$). Rupture of the appendix was as common in both groups ($p = 0.46$). Figure 1 shows that wound infections were significantly less likely if a stapler was used (OR 0.21; 95%-CI 0.06 to 0.71; $p = 0.01$). Figure 2 shows that postoperative ileus was significantly less common in the staple group (0.36; 0.14 to 0.89 ($p = 0.03$). Both outcomes were homogenous. Intraabdominal abscesses were seen at similar rates in both groups (0.62; 0.20 to 1.94). Hospital stay was apparently unaffected by stump closure technique. However, results on hospital stay were heterogenous (I^2=67 %). No study assessed costs in detail.

Table 1: Quality assessment of the included studies (according to Jadad et al. [20])

Author, Year	Concealment of random allocation	Blinding of patients or study staff	Intention-to-treat-analysis	Total score (0 to 6 range)
Ortega et al., 1995 [25]	**2** (telephone randomisation)	**2** (patients and nurses blinded)	**0** (five cross-over patients*)	**4**
Klima et al., 1998 [22,28]	**1** (methods unclear)	**0** (no blinding mentioned)	**1** (no conversions mentioned)	**2**
Lange et al., 1993 [24]	**1** (methods unclear)	**0** (no blinding mentioned)	**0** (methods unclear, abstract only)	**1**
Shalaby et al., 2001 [23]	**2** (envelope randomisation**)	**0** (no blinding)	**1** (no conversions mentioned)	**3**
Beldi et al., 2004 [21]	**0** (quasirandomisation)	**0** (no blinding)	**0** (over 20% excluded)	**0**

* In five patients assigned to stapled appendectomy the stapler was unavailable. These cases were treated by loops and analysed within the loop group.
** Personal written communication with Dr. Rafik Yousef Shalaby (October 2001)

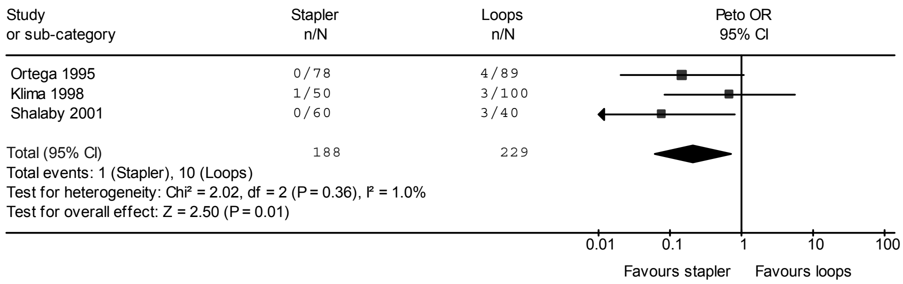


Figure 1: Superficial wound infection rates in randomized controlled trials comparing loops and stapling of the appendiceal stump

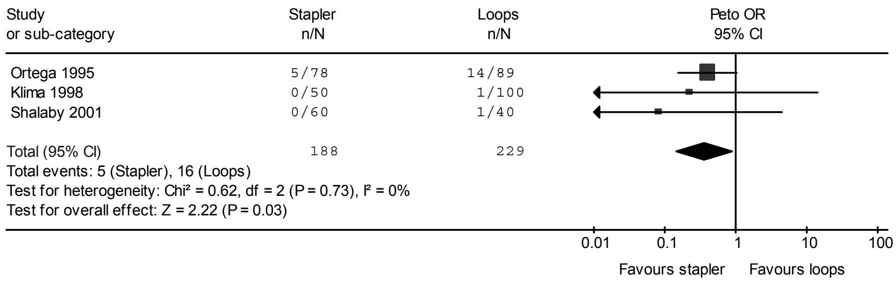


Figure 2: Postoperative ileus rates in randomized controlled trials comparing loops and stapling of the appendiceal stump

Table 2: Results of randomized controlled trials comparing loops and stapling of the appendiceal stump

Author, Year	Treatment groups (n)	Operative time (minutes)	Intraoperative rupture of appendix	Intraabdominal abscesses	Superficial wound infection	Postoperative ileus	Length of hospital stay (days)
Lange et al., 1993	endoloop** (n= 50)	57.3 ***	NA		7/50		4.5 ***
	stapler (n= 50)	48.7 ***	NA		6/50		3.7 ***
Ortega et al., 1995	two endoloops (n= 84*)	68 ±25	4/89	4/89	4/89	14/89	2.98 ±2.7
	stapler (n= 83*)	66 ±24	2/78	2/78	0/78	5/78	2.16 ±3.2
Klima et al., 1998	two endoloops with stump sinking (n= 50)	59 ***	1/50	0/50	1/50	0/50	NA
	two endoloops without stump sinking (n= 50)	54 ***	2/50	4/50	2/50	1/50	NA
	stapler (n= 50)	48.5 ***	1/50	2/50	1/50	0/50	NA
Shalaby et al., 2001	endoloop** (n= 40)	38.5 ±4.4	NA	1/40	3/40	1/40	1.48 ±0.68
	stapler (n= 60)	23.9 ±3.0	NA	0/60	0/60	0/60	1.73 ±0.80
Meta-analysis (with 95% CI)		-9 minutes (0 to -18)	OR 0.61 (0.17 to 2.22)	OR 0.62 (0.20 to 1.94)	OR 0.21 (0.06 to 0.71)	OR 0.36 (0.14 to 0.89)	-0.3 days (-1.2 to +0.6)

* In five patients assigned to stapled appendectomy the stapler was unavailable. These cases were treated by loops and analysed within the loop group.
** The trials do not make clear whether one or two loops were applied.
*** Data on SD not reported. SD was estimated to be equal to the reported mean.

DISCUSSION

Reduction of surgical trauma and prevention of postoperative morbidity are the pillars to provide patient safety. The laparoscopic approach to appendicitis has improved the outcome of appendectomy but requires laparoscopic skills of the surgical team [1]. Appendectomy is done by surgical teams with varying experience in laparoscopic surgery. Routine use of staplers to secure the appendiceal stump during laparoscopic appendectomy can contribute to reduction of the complexity of the procedure. This is confirmed by this study showing a decrease of operating time when the appendiceal stump is closed with a stapling device. The reduction of operating time in the staple group by nine minutes almost compensates for the average 12 minutes longer operating time for laparoscopic appendectomy as compared to the open approach [1]. This study also shows that routine use of staplers contributes to patient safety; it reduces the number of wound infections and frequency of postoperative ileus. However, the clinical impact of wound infections of trocar wounds of 1 cm or less in diameter should not be overestimated.

Optimization of technique applied to close the appendiceal stump with loops was not subject of this trial. However, techniques of loop placement play an important role in the final performance of this closure technique. One of the concerns of using a loop is partial transsection of the stump followed by leakage. Tightening the knot of a loop with due force requires experience, particularly when the stump of the appendix is fragile as in severe or longstanding inflammation. Placing two loops on the appendiceal stump has been suggested to provide more secure closure of the apendiceal stump although this will not avoid transsection per se [26]. Oversewing of the appendiceal stump possibly prevents complications but requires considerable expertise in laparoscopic suturing techniques [22]. The observation that numbers of intraabdominal abscesses were comparable in both groups and hospital stay did not differ can possibly be due to the sample size of this study although all currently available data from the literature were pooled.

If staplers were as cheap as loops, routine use of staplers in laparoscopic appendectomy was arguably the better option. However, considerable differences in costs between the two modalities exist. In the European Union, an increase of direct costs with 300 € is to be expected for every laparoscopic appendectomy. This represents more than half of the total costs for operating material (550 €). On the other hand, data from this study suggest that routine use of stapling can prevent an infectious complication in about every twentieth patient (i.e. the number needed-to-treat). Other studies found that one wound infection causes extra costs of about 3000 €, mainly by prolonging hospital stay by 6 days [27]. In terms of cost-effectiveness, stapling would prevent costs of 3000 €, but the use of the stapler in 20 patients would incur additional material costs of 6000 €.

Further studies are necessary to establish the costs of abdominal infections and postoperative ileus after appendectomy. In consequence, a future comparative trial should assess all types of local infection as the primary outcome measure. According to current data, superficial and intraabdominal infections occur in 3.5% and 1.5%, respectively. As some of the trials used a stapler, while other excluded perforated cases, the true infection rate is probably amounting to about 8%. Thus to test the hypothesis that routine use of staplers to secure the appendiceal stump reduces this 8% rate to 4% (or alternatively 2%) the trial requires 600 (or 240) patients per group. Until such a trial is completed, routine use of staplers during laparoscopic appendectomy appears preferable but at high direct costs.

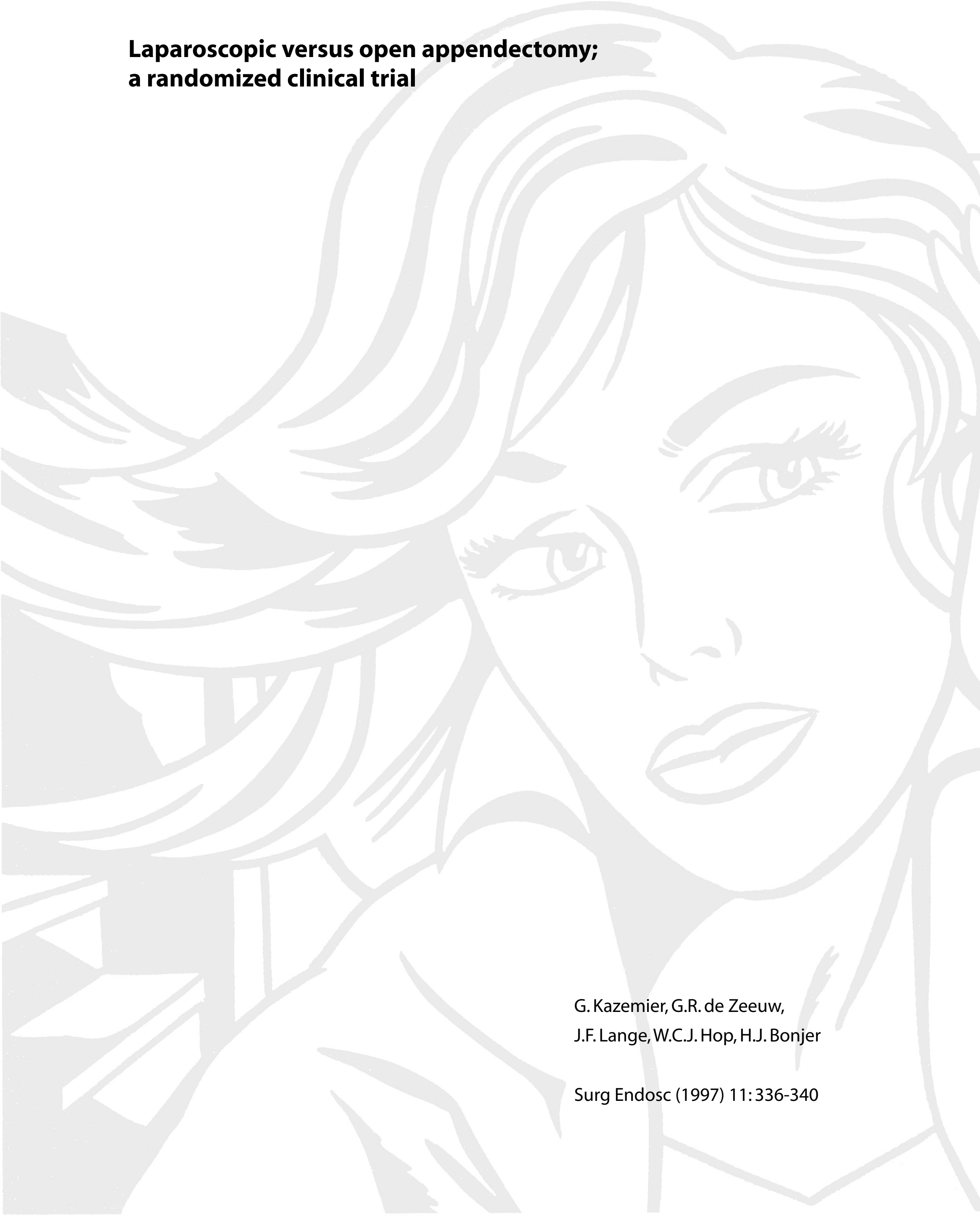
REFERENCES

1. Sauerland S, Lefering R, Neugebauer E. Laparoscopic versus open surgery for suspected appendicitis [Cochrane Review]. In: The Cochrane Collaboration, editor. The Cochrane Database of Systematic Reviews, Vol. IV/2004 [CD-ROM]. Oxford/UK: Update Software; 2004.
2. Sauerland S, Lefering R, Holthausen U, Neugebauer EAM. Laparoscopic vs conventional appendectomy - a meta-analysis of randomised controlled trials. Langenbeck's Arch Surg 1998; 383: 289-95.
3. Attwood SE, Hill AD, Murphy PG, Thornton J, Stephens RB. A prospective randomized trial of laparoscopic versus open appendectomy. Surgery 1992; 112: 497-501.
4. Heikkinen TJ, Haukipuro K, Hulkko A. Cost-effective appendectomy. Open or laparoscopic? A prospective randomized study. Surg Endosc 1998; 12: 1204-8.
5. Temple LK, Litwin DE, McLeod RS. A meta-analysis of laparoscopic versus open appendectomy in patients suspected of having acute appendicitis. Can J Surg 1999; 42: 377-83.
6. Kazemier G, de Zeeuw GR, Lange JF, Hop WCJ, Bonjer HJ. Laparoscopic vs open appendectomy. A randomized clinical trial. Surg Endosc 1997; 11: 336-40.
7. Pedersen AG, Petersen OB, Wara P, Ronning H, Qvist N, Laurberg S. Randomized clinical trial of laparoscopic versus open appendicectomy. Br J Surg 2001; 88: 200-5.
8. al Fallouji M. Making loops in laparoscopic surgery: state of the art. Surg Laparosc Endosc 1993; 3: 477-81.
9. Houben F, Willmen HR. Vereinfachte Appendektomie ohne Stumpfversenkung. Erfahrungen aus 20-jähriger konventioneller und 5-jähriger laparoskopischer Anwendung. Chirurg 1998; 69: 66-71.
10. Shimi SM, Lirici M, Vander Velpen G, Cuschieri A. Comparative study of the holding strength of slipknots using absorbable and nonabsorbable ligature materials. Surg Endosc 1994; 8: 1285-91.
11. Klaiber C, Wagner M, Metzger A. Various stapling techniques in laparoscopic appendectomy: 40 consecutive cases. Surg Laparosc Endosc 1994; 4: 205-9.
12. Daniell JF, Gurley LD, Kurtz BR, Chambers JF. The use of an automatic stapling device for laparoscopic appendectomy. Obstet Gynecol 1991; 78: 721-3.
13. Cristalli BG, Izard V, Jacob D, Levardon M. Laparoscopic appendectomy using a clip applier. Surg Endosc 1991; 5: 176-8.
14. Schäfer M, Krähenbühl L, Frei E, Büchler MW. Laparoscopic appendectomy in Switzerland: a prospective audit of 2179 cases. Dig Surg 2000; 17: 497-502.
15. Lörken M, Marnitz U, Schumpelick V. Freier intraperitonealer Clip als Ursache eines mechanischen Dünndarmileus. Chirurg 1999; 70: 1492-3.
16. Nottingham JM. Mechanical small bowel obstruction from a loose linear cutter staple after laparoscopic appendectomy. Surg Laparosc Endosc Percutan Tech 2002; 12: 289-90.
17. Petrocelli P, Corsale I, Giannessi S, Cerone M, Colugnat D, Matocci GC. Complicanze da suture meccaniche in chirurgia laparoscopica: occlusione intestinale da clip. Segnalazione di un caso clinico e revisione della letteratura. Minerva Chir 2003; 58: 591-4.
18. Paik PS, Towson JA, Anthone GJ, Ortega AE, Simons AJ, Beart RW, Jr. Intra-abdominal abscesses following laparoscopic and open appendectomies. J Gastrointest Surg 1997; 1: 188-193.
19. Sauerland S, Seiler CM. The role of systematic reviews and meta-analysis in EBM. World J Surg 2004: [accepted].
20. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 1996; 17: 1-12.
21. Beldi G, Muggli K, Helbling C, Schlumpf R. Laparoscopic appendectomy using endoloops: a prospective, randomized clinical trial. Surg Endosc 2004; 18: 749-50.
22. Klima S. Bedeutung der Appendixstumpfversorgung bei der laparoskopischen Appendektomie. Zentralbl Chir 1998; 123 Suppl 4: 90-3.
23. Shalaby R, Arnos A, Desoky A, Samaha AH. Laparoscopic appendectomy in children: evaluation of different techniques. Surg Laparosc Endosc Percutan Tech 2001; 11: 22-7.
24. Lange J, Zünd MR, Nägeli J. Prospektiv randomisierte Studie: Roederschlinge versus Endo-GIA bei der laparoskopischen Appendektomie [abstract]. Min Invas Chir 1993; 2(Suppl 1): 8.

25. Ortega AE, Hunter JG, Peters JH, Swanstrom LL, Schirmer B, Laparoscopic Appendectomy Study Group. A prospective, randomized comparison of laparoscopic appendectomy with open appendectomy. Am J Surg 1995; 169: 208-13.
26. Guillem P, Mulliez E, Proye C, Pattou F. Retained appendicolith after laparoscopic appendectomy: the need for systematic double ligature of the appendiceal base. Surg Endosc 2004; 18: 717-8.
27. Kirkland KB, Briggs JP, Trivette SL, Wilkinson WE, Sexton DJ. The impact of surgical-site infections in the 1990s: attributable mortality, excess length of hospitalization, and extra costs. Infect Control Hosp Epidemiol 1999; 20: 725-30.
28. Klima S, Schyra B. Technik und Bedeutung der Stumpfversorgung für das Ergebnis der laparoskopischen Appendektomie. Langenbecks Arch Chir Suppl Kongressbd 1996; 113: 556-558.

Chapter 7

Laparoscopic versus open appendectomy; a randomized clinical trial



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Surg Endosc (1997) 11: 336-340

ABSTRACT

Background. A randomized clinical trial was performed to compare open appendectomy (OA) and laparoscopic appendectomy (LA).

Methods. 201 patients with similar characteristics of appendicitis were randomized to either OA or LA. Operative time and technique, reintroduction of diet, postoperative pain, use of analgesia, hospital stay and complications were documented.

Results. 104 patients were allocated to the OA group, 97 to the LA group. Postoperative pain was significantly less in the LA group on the first ($p<0.001$) and second ($p<0.001$) postoperative day, resulting in less use of analgesics on both days ($p<0.001$). Restoration of diet was similar in both groups. Mean operative time was longer in the LA group: 61 vs 41 min. ($p<0.001$). Postoperative complications did not differ in either group, except for wound infections (six OA group vs zero LA group, $p< 0.05$). Mean hospital stay was similar in both groups.

Conclusions. LA results in less postoperative pain and fewer wound infections. The laparoscopic procedure is technically more demanding to perform, resulting in longer operative time.

INTRODUCTION

Appendectomy is done annually in almost 16,000 patients in The Netherlands, accounting for 6% of all surgical procedures performed yearly[8]. Laparoscopic techniques to remove the appendix were described prior to laparoscopic cholecystectomy[5,9,16]. In spite of the high incidences of appendicitis, widespread employment of laparoscopic appendectomy (LA) did not follow. Reluctance to create a pneumoperitoneum in patients with peritonitis, the use of small incisions for open appendectomy (OA) and performance of appendectomy at nightly hours appear to have held back most surgeons from employing laparoscopic techniques in patients with appendiceal disease. However OA has several disadvantages. Exploration of the entire abdominal cavity is impossible through a McBurney muscle splitting incision, which increases the chance to miss, e.g. pelvic inflammatory disease, sigmoiditis, cholecystitis and gastric perforation in patients with normal appendices. Due to the highly variable clinical picture of appendicitis, the rate of negative appendectomies is 20-30% in adults[2]. Wound infection is a common complication following OA, occurring in 8.5-20 per cent of all patients[12]. Laparoscopy allows thorough exploration of the peritoneal cavity and appears to be associated with less wound infections than open surgery, as LA is associated with minimal contact between the appendix and the skin.

To answer questions on superiority and safety of LA compared to OA we performed a randomized clinical trial in our teaching hospitals focusing on operative time, postoperative pain, use of analgesics, restoration of diet, complications and hospital stay.

PATIENTS AND METHODS

Pre-operative course and trial entry

Patients were asked to participate in this trial if a clinical diagnosis of acute appendicitis was most likely, if a McBurney muscle splitting incision in the right lower quadrant was considered a suitable approach, and if they were suitable for laparoscopy and laparotomy. Trial entry started in November 1 1993 and ended in March 1996. Patients were excluded if they were pregnant, were under 11 years of age or were thought unable to understand fully the aspects of randomization or were otherwise incapable of providing informed consent. Patients requiring elective appendectomy were also excluded. The study protocol was reviewed and approved by the ethics committees of both participating institutions.

After the decision to operate had been taken and after fully informed consent was obtained, the type of procedure was determined for each patient by drawing a card – on which the type of surgery to be performed was written – from an opaque envelope. Computer-generated blocked random numbers were used to assign LAP or OPEN to either card. Age, gender and duration of symptoms in hours of every patient were recorded.

Pre-operative care and antibiotics

Surgery was done under general anaesthesia. All patients received 1 g cefotaxime and 500 mg metronidazole intravenously at the time of induction. In the case of non-perforated appendicitis, antibiotics were not continued; in the case of perforated appendicitis, patients received 750 mg cefuroxime per 6 h and 500 mg metronidazole per 8 h intravenously until temperature remained below 37.5°C for 48 h, with a maximum of 5 days. All patients had a nasogastric tube during surgery. Patients did not receive a urinary catheter routinely.

Operative care

All open or laparoscopic surgery was performed or supervised by surgeons or surgical trainees with experience of more than 15 open and laparoscopic appendectomies. Normal training practices were continued during the trial.

Open appendectomy

Open surgery was done through a 6 cm McBurney muscle splitting incision in the right lower quadrant. The appendix was removed with ligation of the stump with an absorbable suture; the appendiceal stump was not buried routinely. The incision was extended if necessary. A normal appendix was always removed at open surgery. In that case, an attempt was made to visualize the right ovary and right fallopian tube in women and the distal 100 cm of ileum to detect a possible Meckel's diverticula. Saline lavage was not performed routinely. Drainage tubes were not left in the abdominal cavity. The skin incision was closed with 3-0 Nylon (Ethilon; Ethicon, Sommerville, NJ, USA), unless a perforated appendicitis was found in which case the skin wound was left open.

Laparoscopic appendectomy

For LA the patient was in a supine position, with both surgeon and assistant on the left side and video monitor on the right side of the patient. The CO_2 pneumoperitoneum was established by use of a Veress needle in the St. Clara Hospital and by use of an open technique and a Hasson's trocar in the University Hospital Dijkzigt. The Veress needle and/or first trocar were placed below the umbilicus or in the left lower quadrant if an operative scar was present at the umbilicus. A 0° laparoscope was inserted at the umbilicus and two re-usable canulas were introduced under direct vision: one 10-12 mm trocar in the left lower quadrant laterally to the rectus muscle and one 5 mm trocar in the midline just above the pubic bone. The operation was performed with the operating table in Trendelenburg position, tilted 10-20° to the left. The abdominal cavity was explored, and after the diagnosis of acute appendicitis had been confirmed or other diagnoses had been excluded, appendectomy was begun by dissection and division of the appendicular artery between clips or by electrocautery. The appendix stump was secured after division of the mesentery and divided between Chromic catgut loops (Ethibinder; Ethicon, Sommerville, NJ, USA). If the base of the appendix was heavily inflamed, an endoscopic linear stapling device (Endo-GIA-30; US Surgical Corp, Norwalk, Connecticut, USA) was applied over the base of the cecum to resect the appendix safely. The stump of the appendix was never buried. The appendix was retrieved through the canula in the left lower quadrant or by use of a plastic bag (Endocatch; US Surgical Corp, Norwalk, Connecticut, USA). A normal appendix was always removed, unless a definite other diagnosis, responsible for the patient's clinical course was found on laparoscopic exploration of the abdominal cavity. Lavage was performed routinely using 1 L of 0.9% saline solution if blood or purulent material was left after appendectomy or if blood obscured adequate vision. Drainage tubes were not left in the abdominal cavity. The skin incisions were closed in every case using 3-0 Nylon (Ethilon; Ethicon, Sommerville, NJ, USA).

Operative time was taken as the time between the first incision and application of dressings to the wounds. Extension of the incision in open surgery or conversion from laparoscopic to open surgery was done at the surgeon's discretion. All removed appendices were sent for histological examination.

Postoperative care and follow-up

Analgesia was recorded and prescribed on demand and consisted of 1mg/kg pethidine, maximally every 6 h on the first day and 1 g of paracetamol, maximally every 6 h on the second postoperative day. Postoperative pain was scored by each patient every 6 h postoperatively on a visual analogue scale (VAS), consisting of a 10 cm long horizontal line without graduations, varying from "no pain at all" on the left side to "unbearable pain" on the right side. Afterward, the VAS was scored by measuring the length in mm left of the patient's mark. Reintroduction of a liquid diet was recorded, and was defined as the first day on which over 1000mL of fluid oral intake was tolerated. Reintroduction of a solid diet was defined as the first day on which a normal solid meal was tolerated. Hospital stay was recorded and defined as the number of postoperative days spent in hospital, including days spent in hospital after possible readmission because of causes related to the initial operation. Day 1 was defined as the day of operation. Postoperative complications were recorded both in the hospital and at follow-up. Wound infection was defined as oedema and redness around any wound or purulent discharge. Ileus was defined as the inability to tolerate over 1000mL of fluid on the third postoperative day. Pulmonary infection was defined as consolidation on a chest X-ray combined with positive cultures of sputum. Data were collected by two departmental secretaries and by surgical trainees not directly involved in the operations.

Statistical analysis

Means and standard deviations (SD) of variables were calculated and analyzed for both groups using Wilcoxon rank sum test and the Fisher exact test for proportions. A p-value of < 0.05 was considered significant. All analyses were performed on an intention-to-treat basis;

this included analyses of data of patients whose laparoscopic operation had to be converted to an open operation.

RESULTS

Patients and observations during operation

A total of 201 patients were enrolled in the trial. Ninety-seven patients (48.3%) were allocated to LA, 104 patients (51.7%) were allocated to OA. One patient who was allocated to LA underwent primarily an open operation due to miscommunication; this patient stayed in the LA group during analysis. There were no significant differences between the two groups with respect to mean age, gender and mean duration of symptoms at the time of enrolment (table 1). Numbers of other diagnoses found at exploration, and the numbers of histologically normal, inflamed and perforated appendices removed were comparable in both groups (table 2). One appendix was not removed in the LA group, because bilateral pelvic inflammatory disease was found. In all other cases, in both groups, the appendix was removed, because no other definite diagnosis could be found or because of involvement of the appendix in the process. Retrocecally located appendices were found in 24 (24.7%) patients in the LA group and in 32 (30.8%) patients in the OA group.

Conversion of laparoscopic to open operation was necessary in 12 patients (12 %). In this group, the appendix was located retrocecally in nine cases and was surrounded by dense infiltrate in ten cases. The laparoscopic operation was converted to a normal McBurney muscle-splitting incision in nine cases, to a transverse, transrectal incision in two cases (both because of cecal diverticulitis); in one case a lower midline laparotomy was necessary to perform a resection because of carcinoma of the right ovary. Extension of the McBurney muscle splitting incision in the OA group was necessary in six patients (5.8 %). In five cases, lateral extension of the incision was sufficient. Once a lower midline laparotomy was necessary to remove a perforated Meckel's diverticula. During LA, one ileal perforation caused by electrocautery, was oversewn laparoscopically during the initial operation. The skin was left open in 19.4% of patients in the OA group, while the skin was closed in all patients in the LA group. The

Table 1. Clinical characteristics of patients in both groups.

		LA (n=97)	OA (n=104)
Mean age in yr (±SD)		30.8 (±14.5)	33.7 (±17.6)
Gender:	male	52 (53.6%)	59 (56.7%)
	female	45 (46.4%)	45 (43.3%)
Mean duration of symptoms in hrs (±SD)		39.8 (±36.4)	36.3 (±27.6)

Table 2. Clinical and histological diagnoses in both groups.

	LA (n=97)	OA (n=104)
acute appendicitis	85 (87.6%)	90 (86.5%)
non-perforated	69 (83.5%)	72 (82.7%)
perforated	16 (16.5%)	18 (17.3%)
normal appendix	8 (8.3%)	11 (10.8%)
no other diagnosis	6 (6.2%)	9 (8.7%)
Meckel's diverticulum	-	1 (1%)
pelvic inflammatory disease@	1 (1%)	-
hyperplasia of lymphoid tissue in ileocaecal corner	1 (1%)	1 (1%)
carcinoma of appendix	-	1(1%)
carcinoid of appendix	1 (1%)	1 (1%)
carcinoma of right ovary#	1 (1%)	-
coecal diverticulitis#	2 (2.1%)	-
sigmoid diverticulitis#	-	1 (1%)

@appendix not removed
appendix involved in process

mean operative time was significantly longer for LA than for OA, being 61 ± 24 vs 41 ± 18 min. ($p<0.001$; mean ± SD).

Postoperative course

Postoperative pain was significantly less in the LA group on the first and second postoperative day, resulting in lower scores on the VAS and resulting in less use of analgesics (table 3). There were no statistically significant differences for reintroduction of diet, or hospital stay (table 3). Postoperative complications did not differ except for the number of wound infections which were significantly lower in the LA group compared to the OA group (0 vs 6 $p<0.05$) (table 4). Postoperative ileus was seen in five cases in the LA group and three cases in the OA group (p = NS). Ileus followed operation because of non-perforated appendicitis in four out of five in the LA group and in two out of three in the OA group. One patient in each group developed ileus after operation for perforated appendicitis. One intra-abdominal abscess was seen at the base of the cecum in the OA group in a patient operated on because of perforated appendicitis. This abscess was treated successfully with percutaneous drainage. Esophagitis, successfully treated with Omeprazole, was seen in one case following OA because of acute appendicitis in a patient with a history of alcohol abuse. Urinary tract infection occurred in one female patient who had a LA for acute appendicitis; she was treated successfully with antibiotics. One reoperation was necessary during the study. A 41-year old male in the OA group had to be reoperated two days after removal of an inflamed appendix because of high fever and persisting abdominal pain. At reoperation through a midline laparotomy, a long sigmoid colon was found with perforated diverticular disease and abscess in the right and middle abdomen. A Hartmann's procedure was performed. The

Table 3. Postoperative course in both groups.

	LA (n=97) mean (± SD)	OA (n=104) mean (± SD)
Postoperative pain		
VAS day 1	35.3 (±23.7)	58.7 (±25.0)@
VAS day 2	18.7 (±17.6)	34.0 (±24.5)@
Analgesia day 1	1.3 (±0.7)	2.2 (±0.9)@
Analgesia day 2	1.0 (±0.8)	1.8 (±0.9)@
Reintroduction of diet		
liquid diet in days	1.3 (±0.2)	1.4 (±0.3)#
solid diet in days	2.1 (±0.4)	2.2 (±0.3)#
Hospital stay		
stay in days	3.7 (±2.5)	4.4 (±3.9)#

@ $p<0.001$
# p: NS

Table 4. Per- and postoperative complications in both groups.

	LA (n=97)	OA (n=104)
wound infection	-	6 (5.8%)#
ileal perforation	1 (1%)	-
sigmoid perforation overlooked	-	1 (1%)
ileus	5 (5.2%)	3 (2.9%)
urinary tract infection	1 (1%)	-
pulmonary infection	1 (1%)	-
esophagitis	-	1 (1%)
intra-abdominal abscess	-	1 (1%)

# $p<0.05$

Patient recovered uneventfully, except for a pulmonary infection which was treated with antibiotics. Colon continuity was restored after 6 months without negative sequelae.

DISCUSSION

Laparoscopic techniques have revolutionalized gallbladder surgery without any randomized clinical trial supporting the change from open cholecystectomy to laparoscopic cholecystectomy. LA on the other hand has been shown in several randomized, controlled trials to be superior on the aspect of postoperative pain or use of analgesia[1,6,7,10,15], number of postoperative complications[1,10,14,15], hospital stay [1,13,14,15] and return to normal activities[1,6,7,10,15]. Despite this evidence LA has not become the gold standard in treating acute appendicitis. This may be partly because of inconsistence in the literature, because other studies show no differences at all between OA and LA or only disadvantages for the laparoscopic technique[17], or because of the fact that appendectomy through a muscle splitting incision is already considered minimally invasive surgery. Possibly, the often acute aspect of appendectomy, hampering surgical training and motivation of anaesthesiologists or even surgeons at night might also contribute to the reluctance to introduce LA as therapy of first choice to treat acute appendicitis in all cases. In our study we showed that even with normal training practices continued during the study, important advantages can be achieved with reduced postoperative pain, less use of analgesics and less wound infections. The only disadvantage for LA in our study was the considerably longer mean operative time for LA: 61 vs 41 min and possibly related higher operative costs.

Earlier reports showed or suggested lower rates of ileus and quicker restoration of diet following laparoscopic surgery. We did not find lower numbers of ileus in the LA group, nor did we find a quicker restoration of diet following LA. The presence of postoperative ileus was not related to perforated appendicitis, because four out of five patients in the LA group and two out of three patients in the OA group who developed ileus had only contained appendicitis. Only one patient in each group developed ileus after operation for perforated appendicitis.

Insufflation of CO_2 in the peritoneal cavity has been theorized to spread pus intraperitoneally when a purulent intra-abdominal infection is present. Therefore LA would be expected to result in a higher rate of postoperative intra-abdominal abscesses and conversion to open operation is advocated by many authors if there is evidence of complicated appendicitis[1,3]. In our study only one postoperative abscess was observed after OA and none after LA. We noticed that laparoscopic irrigation of the peritoneal cavity could be performed effectively. In our study, evidence is lacking that laparoscopy is deleterious in generalized peritonitis.

Laparoscopy has been advocated as a diagnostic tool to decrease the rate of negative appendectomies. This could not be analyzed in this trial because all appendices were removed in both groups unless a definite other diagnosis was found. Yet this rate could have been reduced by 9.5 per cent, if all normal appendices would have been left in situ. However, detecting all appendeceal pathology on the serosal side of the appendix can be difficult[11] and laparoscopic examination of an appendix is affected by laparoscopic experience and quality of the video imaging system. Therefore we advocate removal of the appendix if no definite other diagnosis can be found at explorative laparoscopy. We found that a rigid, inflexible appendix is a consistent feature of appendiceal pathology which dictates removal. Although the number of patients with a definite other diagnosis for whom a laparoscopic exploration could be beneficial was low in this trial, the patient who was found to have a perforated sigmoiditis at relaparotomy might have benefited from inspection of the entire abdominal cavity instead of only limited inspection as was performed through a McBurney incision at the initial operation. Our hypothesis is that in this patient, thickening of the appendix was due to generalized peritonitis, caused by sigmoiditis and mistaken as acute appendicitis. At laparoscopy a perforated sigmoiditis would probably not have been overlooked.

To determine whether the higher efforts and costs are worthwhile to perform LA instead of OA, one should take into account not only direct advantages like the use of the laparoscope to increase diagnostic power, less postoperative pain and less wound infections, but also long-term effects as possibly decreased number of adhesions following LA[4]. De Wilde performed laparoscopy 3 months after OA and LA. Eighty per cent of patients who had OA developed adhesions, and only 10 per cent of patients in the LA group. Especially if one wants to perform cost-benefit analyses this aspect could be of utmost importance to determine the long-term costs of open appendectomy.

In this trial it was shown that even in a teaching hospital setting, LA can be performed safely and effectively, although both trainer and trainee should be aware of specific risks of minimally invasive surgery. One of our intraoperative complications consisted of ileal perforation due to electrocautery. One of the clamps, used to coagulate the mesentery was held against the ileum unnoticed, because only part of the tip of clamp was shown on the screen before electrocautery was started. If only limited experience exists with laparoscopic procedures this can happen easily. We consider on the other hand LA to be a perfect teaching model following laparoscopic cholecystectomy in which to teach more advanced minimally invasive techniques.

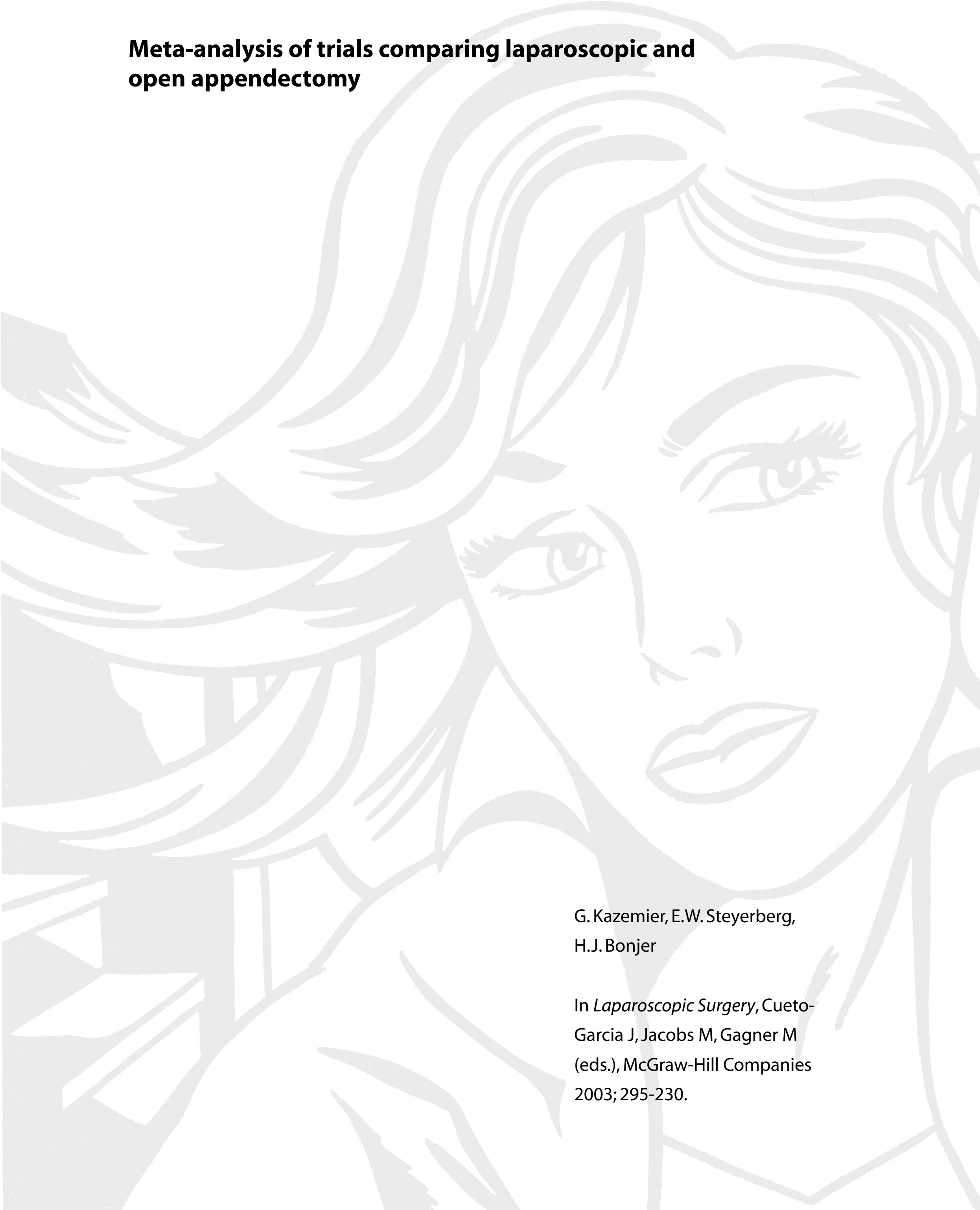
We think that LA is superior over OA regarding postoperative pain and postoperative complications. Long-term follow-up studies are necessary to determine a possible decrease of late bowel obstruction. Because of the increased operative time and possibly related higher direct costs, LA might not be the best way to treat every patient with acute appendicitis for every doctor at every hospital.

REFERENCES

1. Attwood SEA, Hill ADK, Murphy PG, Thornton J, Stephens RB (1992) A prospective randomized trial of laparoscopic versus open appendectomy. Surgery 112: 497-501
2. Berry J, Malt R (1984) Appendicitis near its centenary. Ann Surg 200: 567-575
3. Bonanni F, Reed J, Hartzell G, Trostle D, Boorse R, Gittleman M, Cole A (1994) Laparoscopic versus conventional appendectomy. J Am Coll Surg 179: 273-278
4. De Wilde RL (1991) Goodbye to late bowel obstruction after appendicectomy. Lancet 338: 1012
5. Dubois F, Icard P, Berthelot G, Levard H (1990) Coelioscopic cholecystectomy. Preliminary report of 36 cases. Ann Surg 211: 60-62
6. Frazee RC, Roberts, JW, Symmonds RE, Snyder SK, Hendricks JC, Smith RW, Custer MD, Harrison JB (1994) A prospective randomized trial comparing laparoscopic versus open appendectomy. Ann Surg 219: 725-731
7. Hansen JB, Smithers BM, Schache D, Wall DR, Miller BJ, Menzies BL (1996) Laparoscopic versus open appendectomy: prospective randomized trial. World J Surg 20: 17-21
8. Hesselink EJ (1995) In "Trends in surgery". SIG health care information. ISBN 90-70755-46-7
9. Kok de A. (1983) The laparoscopic mini appendectomy. Act Endosc Vol 13: 5-6
10. Kum CK, Ngoi SS, Goh PMY, Tekant Y, Isaac JR (1993) Randomized controlled trial comparing laparoscopic and open appendicectomy. Br J Surg 80: 1599-1600
11. Lau WY, Fan ST, Yiu TF, Chu KW, Suen HC, Wong KK (1986) The clinical significance of routine histopathologic study of the resected appendix and safety of appendiceal inversion. Surg Gynecol Obstet 162: 256-258
12. Lewis FR, Holcroft JW, Boey J, Dunphy JE (1975) Appendicitis: a critical review of diagnosis and treatment in 1,000 cases. Arch Surg 110: 677-684
13. Martin LC, Puente I, Sosa JL, Bassin A, Breslaw R, McKenney MG, Ginzburg E, Sleeman D (1995) Open versus laparoscopic appendectomy; a prospective randomized comparison. Ann Surg 222: 256-262
14. Mompean JAL, Campos RR, Paricio PP, Aledo VS, Ayllon JG (1994) Laparoscopic versus open appendicectomy: a prospective assessment. Br J Surg 81: 133-135
15. Ortega AE, Hunter JG, Peters JH, Swanstrom LL, Schirmer B and the Laparoscopic Appendectomy Group (1995) A prospective randomized comparison of laparoscopic appendectomy with open appendectomy. Am J Surg 169: 208-213
16. Semm K. Endoscopic appendectomy (1983). Endoscopy 15: 59-64
17. Tate JJT, Dawson JW, Chung SCS, Lau WY, Li AKC (1993) Laparoscopic versus open appendectomy: prospective randomised trial. Lancet 342: 633-637

Chapter 8

Meta-analysis of trials comparing laparoscopic and open appendectomy



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In *Laparoscopic Surgery*, Cueto-Garcia J, Jacobs M, Gagner M (eds.), McGraw-Hill Companies 2003; 295-230.

ABSTRACT

Background. The objective was to determine the merits of laparoscopic appendectomy (LA) with respect to operative time, postoperative pain and recovery, hospital stay and complications. A meta-analysis was performed of trials comparing LA and open appendectomy (OA) for acute appendicitis, because several randomised trials show conflicting or non-significant outcomes.

Methods. A systemic search of the literature was performed to identify randomised clinical trials on LA versus OA for acute appendicitis. Published data of these trials were used to perform a meta-analysis. We calculated mean variances and pooled mean differences (PMD) for continuous outcomes and pooled odds ratios (OR) for dichotomous outcomes.

Results. Fifteen studies were identified, including a total number of 1825 patients analysed. LA took longer than OA (PMD 15 [95% CI 12-18] min, p<10-5). LA resulted in less pain scored on a visual analogue scale (0-100) on day one (PMD 13 [10-17] points, p<10-5) and day two (PMD 11 [7-15] points, p<10-5), lower total number of dosages of parenteral pain medication (PMD 0.92 [0.69-1.16] doses, p<10-5), faster restoration of solid diet (PMD 0.27 [0.12-0.42] days, p=0.006), shorter hospital stay (PMD 0.69 [0.41-0.98] days, p<10-5) and faster return to normal activities (PMD 4.8 [3.7-5.9] days, p<10-5). We found no significant difference between the groups for total percentage of complications (OR 0.89 [95% CI 0.66-1.21], p=0.48), percentage of early bowel obstructions (OR 1.68 [0.96-3.01], p=0.08) or percentage of intra-abdominal abscesses (OR 1.78 [0.83-4.03], p=0.19). The percentage of postoperative wound infections was significantly less after LA (OR 0.37 [0.23-0.57], p<10-5).

Conclusions. LA requires more operative time and results in less postoperative pain, faster recovery, shorter hospital stay and less wound infections. Therefore, LA appears the preferable approach to acute appendicitis.

INTRODUCTION

Laparoscopic techniques have revolutionized general surgery in many fields. Particularly, laparoscopic cholecystectomy has gained widespread popularity. Laparoscopic removal of the gallbladder is now considered by many as the 'gold standard' in treatment of symptomatic gallbladder stones[1,2]. Laparoscopic appendectomy is also being performed on a regular basis in many hospitals, but has not yet become the treatment of choice in every patient with acute appendicitis. Reports on patients who had laparoscopic removal of the appendix were published prior to the first experiences with laparoscopic cholecystectomy[3-5]. In those first reports, possible advantages were described of minimally invasive appendectomy[3,4]. A number of randomized trials comparing laparoscopic (LA) and open appendectomy (OA) have been reported in the past years. Most of these trials showed considerable advantages of the laparoscopic technique[6-20].

In spite of these results and although appendectomy accounts for over 6% of all surgical procedures in daily practice and over 700,000 appendectomies are performed yearly in the European Union, widespread employment of LA did not follow[21,22]. Reluctance to create a pneumoperitoneum in patients with peritonitis, the use of already small incisions for OA, frequent performance of appendectomy at night, or presumed higher costs associated with laparoscopic appendectomy might have prevented many surgeons from converting from the open to the laparoscopic technique. One other factor that might possibly contribute to the hesitation to embrace this new technique is the seemingly inconsistent outcome or statistically insignificant results of some randomized trials. In order to provide a more definite answer to the question of how LA differs from OA, we combined data of all published, randomized clinical trials comparing LA and OA for acute appendicitis in a meta-analysis.

MATERIALS AND METHODS

A Medline (Silver Platter MEDLINE version 3.11) search was performed from January 1, 1966 to January 1, 1998 using the key words: append$ and laparos$ and randomi$. Using these items, randomized, clinical trials comparing LA and OA for acute appendicitis in adults were selected by two independent reviewers (GK and HJB).

Published data from these papers were used to perform a meta-analysis. Trials just focusing on the diagnostic value of laparoscopy or on specific subgroups of patients were excluded as were experimental or non-randomized studies and editorials and abstracts. Each included study was reviewed independently by two investigators (G.K. and H.J.B.). They were blinded to the name of the journal, authors and date of publication. Consensus was reached by both investigators afterwards on conflicting scores by reviewing these data together. Data on operative time, postoperative pain, restoration of diet, hospital stay, postoperative complications, and return to normal activities were extracted from each study. Results of this analysis were based solely on those trials that provided data on that specific aspect. Only data on items scored in three or more studies were analysed.

Postoperative pain was scored differently in several studies. To overcome some of these problems, visual analogue scale (VAS) scores for postoperative pain on day one and day two were all recalculated to percentages of the maximum score. Total dosages of parenteral and oral pain medication were scored as stated in the studies.

Outcomes were distinguished as continuous or dichotomous. We pooled differences between LA and OA as calculated within each study, using standard meta-analysis techniques, assuming homogeneity between studies[23].

Continuous Outcomes Operative time, VAS scores for pain on postoperative day one and day two, total number of dosages of parenteral and oral pain medication, number of days until tolerance of liquid and solid diets, number of postoperative days spent in hospital and number of postoperative days until restoration of normal activities were analyzed as continuous outcomes. For these continuous outcomes, variances (var) of differences were determined. Not all studies provided variances for all items. A mean variance was calculated using variances from the other studies. For every study and item a standard error (SE) was determined as $SE = \sqrt{var} \cdot \sqrt{(1/N_{LA}+1/N_{OA})}$. The weight (w) of each study was calculated as $w = 1/SE^2$. For each continuous outcome the precision weighted pooled difference (i.e., pooled mean difference [PMD]) was calculated as the weighted sum of the results per study: $PMD = \sum wb / \sum w$, where b is the difference between OA and LA in each study. The standard error of the PMD was calculated as $SE_{PMD} = 1/\sqrt{\sum w}$. Ninety-five per cent confidence intervals (95% CI) were calculated as $95\% \text{ CI} = PMD \pm 1.96 \cdot SE_{PMD}$. To test for statistical significance, a Z-test was performed: $Z = PMD/ SE_{PMD}$. The corresponding *p* value indicates the likelihood that the observed difference between the laparoscopic and the open group did exist while the difference was in fact zero.

A chi-square test was used to test for heterogeneity between studies: $\chi^2 = \sum w(b\text{-}PMD)^2$. Calculations were performed using a spreadsheet programme.

Dichotomous Outcomes Complications were classified in four groups: total, wound infection, early bowel obstruction or intra-abdominal abscess, and analysed as dichotomous outcomes. Odds Ratios were calculated per item per study and were pooled using the Mantel-Haenszel method[24]. Calculations, including tests on heterogeneity were performed using exact variance formulas as implemented in StatXact software (StatXact version 2, Cytel Software Corporation, Cambridge, MA, USA).

We also calculated the means (averages, weighted by number) and percentages (events divided by total N) in the laparoscopic and open group separately for illustrative purposes. The differences between these averages are not necessarily equal to the PMD for continuous outcomes. Similarly, pooled odds ratios can differ from those calculated with average percentages for dichotomous outcomes. *P* values of less than 5% (two-sided) were considered statistically significant.

The quality of methodology of the included trials was determined by scoring all studies according to a previously proposed quality assessment for surgical trials[25, 26]. In this assessment, trials are categorised according to their scores on eleven questions on methodology in category A, B or C. In this study, we considered category A as "good", category B as "intermediate" and C as "poor".

RESULTS

Fifteen studies were identified that described the results of a randomized, clinical trial comparing LA and OA[6-20]. In table 1 the studies are shown with the number of patients randomised, number of patients analyzed, reason for exclusion of analysis of patients, and qualitative category of methodology. Differences between open and laparoscopic groups with respect to demographic and preoperative clinical data and data on number of inflamed and perforated appendices were small; they are not shown because all studies were randomized. In the study by Lujan Mompean et al. [11] it is stated that formal randomisation was precluded by instrument availability. How the actual allocation to either LA or OA was done in this study is unclear.

A total number of 1907 patients were enrolled in these trials. Eighty-two randomised patients were not analyzed for various reasons (table 1). Operative techniques for LA and OA were comparable in each study, with the exception of the study by Ortega et al.[13]. In this study, 253 patients were randomized to either OA (86 patients) or LA using an endoscopic linear stapler (78 patients) or LA using catgut ligatures (89 patients). In the meta-analysis, all patients operated upon laparoscopically (167 patients) were pooled as LA and analyzed as one group.

Methodology was considered of poor quality, according to Slim's criteria in 12 of 15 trials and of intermediate quality in the remaining three[26]. Lack of intention-to-treat analysis was observed in seven trials.

Table 2 shows differences between LA and OA for continuous and dichotomous outcomes of different trials. Negative values indicate lower levels or rates in the LA group.

Table 1 Trials included in the meta-analysis

First Author	Year of publication	Quality of methodology*	Journal	number of patients randomised	number of patients analysed	number of patients excluded and reason for exclusion
Attwood	1992	C	Surgery	62	62	-
Kum	1993	B	Br J Surg	137	109	28, normal or perforated appendix
Tate	1993	B	Lancet	140	140	-
Frazee	1994	C	Ann Surg	75	75	-
Hebebrand	1994	C	Chirurg	57	48	9, conversion from LA to OA
Lujan Mompean	1994	C	Br J Surg	200	200	-
Martin	1995	C	Ann Surg	169	169	-
Ortega	1995	C	Am J Surg	253	253	-
Hansen	1996	C	World J Surg	158	151	7, normal appendix or conversion from OA to midline laparotomy
Williams	1996	C	South Med J	39	37	2, conversion from LA to OA
Henle	1996	C	Chirurg	170	169	1, conversion from OA to LA
Hart	1996	C	Can J Surg	81	77	4, conversion from LA to OA
Kazemier	1997	B	Surg Endosc	201	201	-
Reiertsen	1997	C	Br J Surg	108	84	24, normal appendix, other pathology or conversion from LA to midline laparotomy
Minné	1997	C	Arch Surg	57	50	7, use of ketorolac tromethamine
			total	1907	1825	82

* Category A, B or C as described by Slim26

Table 2 Differences in outcomes between LA and OA. Values in the table represent outcomes in LA group minus values in OA group.

Outcomes	Attwood	Tate	Kum	Hebebrand	L. Mompean	Frazee	Ortega	Martin	Hansen	Williams	Henle	Hart	Kazemier	Reiertsen	Minné
# patients analysed	**62**	**140**	**109**	**48**	**200**	**75**	**253**	**169**	**151**	**37**	**169**	**77**	**201**	**84**	**50**
operative time (min)	10	24	3		5	22	10	20	23	6	4	29	19	26	15
VAS pain day 1 (0-100)		-6.0		-14.5			-14.6						-23.4	-4	-3
VAS pain day 2 (0-100)				-12.6			-6.7						-15.3		
total parenteral pain medication (dosages)		0.0	-0.3	-0.5					-2.0			-1.5	-0.9	-1.1	
total oral pain medication (dosages)			-2.2	-0.2					1.0				-0.8	0.1	
days to liquid diet		-0.1	-0.3										-0.1		
days to solid diet		-0.1	0.0			-0.8			-0.5	-0.7			-0.1		
days in hospital	-1.3	-0.1	-1.0	-2.3	-1.2	-0.8	-0.2	-2.1	0.0	-0.4	-1.0	0.2	-0.7	0.3	-0.1
days until normal activity			-13			-11.0	-5.0	-0.6	-7.0		-7.0	-7.2		-4.7	0.0
complications (%):															
total	-12.5	-2.9	-8.8	4.7	-4.0	2.5		1.0	-7.9	4.4	2.7		-3.3	14.3	10.5
wound infection	-3.1	-2.9	-8.8	-4.3	-6.0	-0.1	-10.4	-3.1	-8.6	-0.3	-2.9	-0.6	-5.8		
early bowel obstruction	-3.1	1.4	0.0	0.0	-1.0	0.0	4.4	3.8	1.1	-0.3	3.4		2.3		
intra-abdominal abscess	0.0	1.4	0.0	0.0	2.0	2.6	3.6	0.3	0.0	0.0	-1.3	3.1	-1.0	-2.4	3.1

Table 3 shows the results of the meta-analysis of continuous outcomes. The combined evidence from the trials indicated a statistically significantly longer operative time, less postoperative pain and less use of parenteral pain medication, faster restoration of solid diet, shorter hospital stay and faster restoration of normal activity for LA as compared to OA. Studies were heterogenic for the exact results of several continuous outcomes (operative time, VAS day 1, total doses of parenteral and oral pain medication, days to solid diet, hospital stay and days to normal activity).

Table 3 Results of meta-analysis of continuous outcomes and heterogeneity of outcomes

Outcomes	LA*	OA*	Pooled mean difference (95% CI)	Effect p-value	Homogeneity *p*-value
Operative time (min)	63	50	-15 (-12- -18)	$<10^{-5}$	$<10^{-3}$
VAS pain score day 1 (0-100)	35	51	13 (10-17)	$<10^{-5}$	0.005
VAS pain score day 2 (0-100)	11	25	11 (7-15)	$<10^{-5}$	0.111
Parenteral pain medication †	1.8	2.7	0.92 (0.69-1.16)	$<10^{-5}$	$<10^{-4}$
Oral pain medication †	2.4	3.5	0.42 (-0.08-0.92)	0.26	0.003
Days to liquid diet	1.2	1.4	0.15 (-0.02-0.31)	0.22	0.59
Days to solid diet	1.9	2.1	0.27 (0.12-0.42)	0.006	0.03
Days in hospital	3.2	3.9	0.69 (0.41-0.98)	$<10^{-5}$	0.01
Days till normal activity	14.7	19.3	4.8 (3.7-5.9)	$<10^{-5}$	$<10^{-5}$

* mean values of outcomes in laparoscopic (LA) and open appendectomy (OA) group
† total number of doses

Table 4 shows results of the meta-analysis of dichotomous data i.e. complications. We observed a statistically significant reduction in postoperative wound infections and no statistical differences in total number of complications, intra-abdominal abscesses and early bowel obstruction following LA as compared to OA. Insignificant trends were noticed towards increased percentages of early postoperative bowel obstruction and intra-abdominal abscesses following LA as compared to OA. All studies were rather homogenous for these outcomes.

Table 4 Results of meta-analysis of dichotomous outcomes and heterogeneity of outcomes

Complications	LA*	OA*	Pooled odds ratio (95% CI)	Effect p-value	Homogeneity p-value
total	12.6%	13.8%	0.89 (0.66-1.21)	0.48	0.18
wound infection	3.3%	7.7%	0.37 (0.23-0.57)	$<10^{-5}$	0.29
early bowel obstruction	4.7%	2.2%	1.68 (0.96-3.01)	0.076	0.69
intra abdominal abscess	2.2%	1.1%	1.78 (0.83-4.03)	0.19	0.28

* mean percentage of outcomes in laparoscopic (LA) and open appendectomy (OA) group

DISCUSSION

Laparoscopic removal of inflamed appendices has been performed for decades[3,4]. However, the majority of general surgeons have not adopted this technique. Laparoscopic appendectomy has been considered cumbersome and time-consuming, with few clinical advantages. The advent of laparoscopic cholecystectomy has incited renewed interest in the laparoscopic approach to acute appendicitis, but this has not yet resulted in its widespread application. Surprisingly, laparoscopical removal of the gallbladder became the 'gold standard' treatment for symptomatic gallbladder stones even before solid evidence of its superiority over open cholecystectomy was evident[27]. Laparoscopic appendectomy has by now been evaluated in 15 randomized clinical trials. Although the numbers of patients were small in some of these studies, advantages of the laparoscopic approach to appendicitis were shown in almost all studies. Due to the small numbers of patients included in individual studies, trends rather than significant differences were shown for some outcomes. Conflicting results also became apparent while reviewing these trials. In order to allow proper evaluation of the merits of laparoscopic appendectomy a meta-analysis was done. This analysis graded the impact of the studies, depending on the number of patients included in each study. A qualitative weigh factor was assessed but not introduced, because qualitative scoring adds the analyst's subjective bias to the results and is therefore generally not advocated [28].

Methodology of none of the included trials was good, intermediate in some and poor in the majority of trials. Some studies showed major flaws in the statistical analysis. One of the shortcomings was lack of intention-to-treat analysis. Another flaw was found in eight studies that only documented ranges of outcomes, without standard deviation, standard error or 95 per cent confidence interval. In the study by Lujan Mompean et al,[11] formal randomisation was precluded by instrument availability. Because consecutive patients were studied and because instrument availability might only have a minor influence on outcomes, this study was nevertheless included in this meta-analysis. With exclusion of the trial by Lujan Mompean however, no substantial differences with the initial meta-analysis were noticed. Blinding of the patients and postoperative observers to the surgical approach was only partially performed in one study[13].

In this analysis, outcomes of trials were largely heterogenic for seven out of nine continuous outcomes. This means that outcomes of different trials were poorly comparable with respect to the actual numeric value of the outcome. However, in all cases a negative or positive effect of laparoscopy was consistently reported by the majority of trials. For instance, every trial reported longer operative time for LA, but differences between LA and OA for operative time ranged from 3 to 29 minutes among the trials. This large range resulted in clear statistical heterogeneity between trials for operative time, although all trials were highly homogenic on the question whether LA took longer than OA.

Operative time showed an average increase of 15 minutes for LA compared to OA. Part of this increased operative time for LA could perhaps be contributed to the fact that most surgeons have less experience with the laparoscopic approach than the open. The impact of a learning curve could not be assessed, because the experience of the operative teams was not reported consistently in the reviewed studies. In our experience, LA remains technically more demanding even with growing experience, particularly in those patients with extensive inflammatory adhesions between the appendix and surrounding structures. When dissecting these adhesions, the surgeon relies more on his tactile sensations, which are diminished in laparoscopic surgery. Operative time has become increasingly important in this era of financial scrutiny of surgical practice, and the longer operative time of LA appears a financial disadvantage. However, LA was associated with significantly shorter hospital stay and earlier return to normal activities. These variables are all of paramount importance, when considering direct and indirect costs, but other factors such as instrument costs, costs of medication and costs related to possible (late) readmissions should be taken into account as well in a proper cost-effectiveness assessment.

Assessing acute postoperative pain is difficult and comparing different scoring systems might be even more difficult. However, less pain was shown following LA by objective standards such as visual analogue scales scores on postoperative days one and two. Diminished postoperative pain was also shown by less use of parenteral analgesia after LA, but use of oral pain medication was not clearly different, indicating an advantage of LA for pain immediately after the procedure, when most parenteral pain medication is used. Although postoperative pain and postoperative recovery are very important factors in the postoperative course, safety of the procedure may never be jeopardized for these reasons.

In this analysis, the published percentages of complications in the trials were pooled. The percentage of early small bowel obstructions was not clearly different between LA and OA, although a trend towards increased incidence was seen following LA. Surprisingly, general restoration of solid diet was significantly faster following LA, although the clinical significance of a difference of 0.27 days may be quite small. The general belief that laparoscopic surgery is associated with faster recovery of normal bowel function was not supported by the studies included in this analysis.

LA resulted in less wound infections. However, intra-abdominal abscesses were seen more frequently in the LA group, although the overall incidence was low in both groups and not significantly different. This finding is in concordance with earlier studies[29, 30]. The reason for this seemingly increased number of intra-abdominal abscesses could be the fact that the entire laparoscopic operation is performed intra-abdominally, while the open operation is performed mainly extra-abdominally, causing more wound infections. On the other hand, larger, uncontrolled series of laparoscopic appendectomies have shown considerably lower incidences (0.2-0.3 per cent) of intra-abdominal abscesses[31,32]. Thus insufficient laparoscopic irrigation of the abdominal cavity during early experience or other factors related to the learning curve effect could explain the insignificantly higher number of intra-abdominal abscesses in the LA group. The consequences of a learning curve were assessed in one study, which showed sixty per cent of complications occurred in the first twenty per cent of patients operated laparoscopically[16].

Late complications were not reported in any of these trials as follow-up was either not stated or very short. The majority of these late complications following appendectomy are bowel obstructions due to adhesions, which were reported in previous studies to occur in five to ten per cent of patients who underwent OA[33, 34]. De Wilde[35] showed that at second-look laparoscopy, performed three months after appendectomy, 80 per cent of patients developed adhesions following OA compared to 10 per cent following LA. Although not yet firmly proven, late bowel obstruction could be less common following LA.

Reduction of unnecessary appendectomies might be another possible advantage of LA not assessed in this analysis. Due to the highly variable clinical picture of acute appendicitis, especially in women of child bearing age, the rate of removal of normal appendices can be as high as 20-35 per cent[22,36]. When a grid-iron incision is made for suspected acute appendicitis, it is common practice to remove the appendix, even if it is normal. Laparoscopy has been shown to improve diagnostic accuracy for acute appendicitis with a reported sensitivity and specificity of over 95 per cent[37]. With the introduction of laparoscopic inspection of the abdominal cavity instead of laparotomy and standard removal of the appendix, reduction of redundant appendectomies has been shown to be possible in 30-35 per cent of patients presenting with acute right lower abdominal pain[19,34,35].

In this analysis LA was shown to result in less postoperative pain, faster restoration of solid diet, fewer wound infections, shorter hospital stay, and faster recovery to normal activities. On the other hand operative time was shown to be longer compared to OA. It is true that laparoscopic appendectomy can be performed safely, with certain benefits for the patient, but only a long-term cost-effectiveness analysis can show whether laparoscopic appendectomy is the optimal approach to treat every patient with acute appendicitis in every hospital by every surgeon.

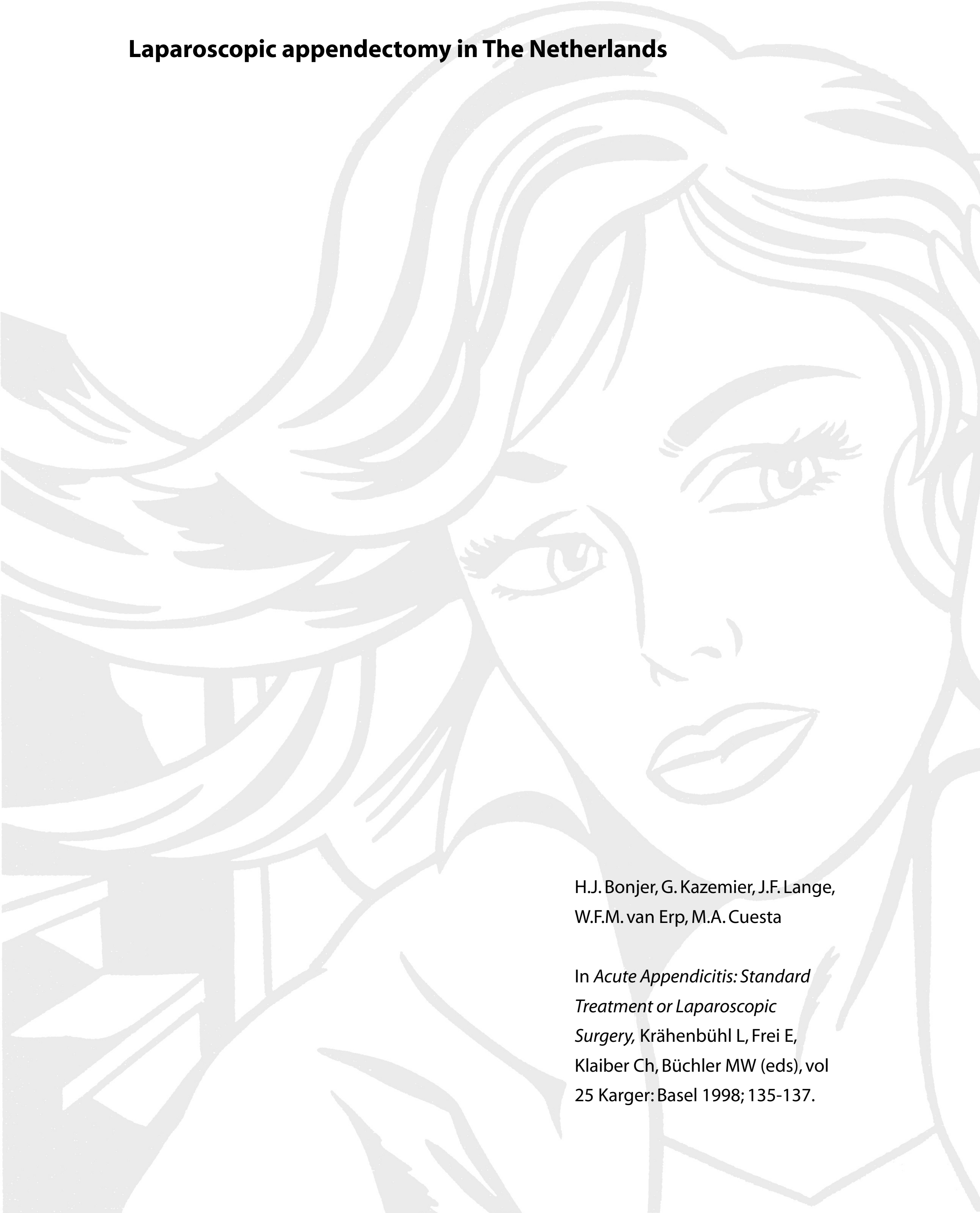
REFERENCES

1. The Southern Surgeons Club. A prospective analysis of 1518 laparoscopic cholecystectomies. N Eng J Med 1991; 213: 2-12.
2. Neugebauer E, Troidl H, Spangenberger W, et al. Conventional versus laparoscopic cholecystectomy and the randomized controlled trial. Br J Surg 1991; 78: 150-54.
3. de Kok A. The laparoscopic mini appendectomy. Act Endosc 1983; 13: 5-6.
4. Semm K. Endoscopic appendectomy. Endoscopy 1983; 15: 59-64.
5. Dubois F, Icard P, Berthelot G, Levard H. Coelioscopic cholecystectomy. Preliminary report of 36 cases. Ann Surg 1990; 211: 60-62.
6. Attwood SEA, Hill ADK, Murphy PG, Thornton J, Stephens RB. A prospective randomized trial of laparoscopic versus open appendectomy. Surgery 1992; 112: 497-501.
7. Kum CK, Ngoi SS, Goh PMY, Tekant Y, Isaac JR. Randomized controlled trial comparing laparoscopic and open appendicectomy. Br J Surg 1993; 80: 1599-1600.
8. Tate JJT, Dawson JW, Chung SCS, Lau WY, Li AKC. Laparoscopic versus open appendectomy: prospective randomised trial. Lancet 1993; 342: 633-637.
9. Frazee RC, Roberts, JW, Symmonds RE, Snyder SK, Hendricks JC, Smith RW, Custer MD, Harrison JB. A prospective randomized trial comparing laparoscopic versus open appendectomy. Ann Surg 1994; 219: 725-731.
10. Hebebrand D, Troidl H, Spangenberger W, Neugebauer E, Schwalm T, Günther MW. Laparoskopische oder klassische Appendektomie? Chirurg 1994; 65: 112-120.
11. Lujan Mompean JA, Robles Campos R, Parilla Paricio P, Soria Aledo V, Garcia Ayllon J. Laparoscopic versus open appendicectomy: a prospective assessment. Br J Surg 1994; 81: 133-135.
12. Martin LC, Puente I, Sosa JL, Bassin A, Breslaw R, McKenney MG, Ginzburg E, Sleeman D. Open versus laparoscopic appendectomy; a prospective randomized comparison. Ann Surg 1995; 222: 256-262.
13. Ortega AE, Hunter JG, Peters JH, Swanstrom LL, Schirmer B and the Laparoscopic Appendectomy Group. A prospective randomized comparison of laparoscopic appendectomy with open appendectomy. Am J Surg 1995; 169: 208-213.
14. Hansen JB, Smithers BM, Schache D, Wall DR, Miller BJ, Menzies BL Laparoscopic versus open appendectomy: prospective randomized trial. World J Surg 1996; 20: 17-21.
15. Williams MD, Colloins JN, Wright TF, Fenoglio ME. Laparoscopic versus open appendectomy. South Med J 1996; 89: 668-674.
16. Henle KP, Beller S, Rechner J, Zerz A, Szinicz G, Klinger A. Laparoskopische versus konventionelle Appendektomie: eine prospektive, randomisierte Studie. Chirurg 1996; 67: 526-527.
17. Hart R, Rajgopal C, Plewes A, Sweeney J, Davies W, Gray D, Taylor B. Laparoscopic versus open appendectomy: a prospective randomized trial of 81 patients. Can J Surg 1996; 39: 457-462.
18. Kazemier G, de Zeeuw GR, Lange JF, Hop WCJ, Bonjer HJ. Laparoscopic versus open appendectomy: a randomized clinical trial. Surg Endosc 1997; 11: 336-340.
19. Reiertsen O, Larsen S, Trondsen E, Edwin B, Færden AE, Rosseland AR. Randomized controlled trial with sequential design of laparoscopic versus conventional appendectomy. Br J Surg 1997; 84: 842-847.
20. Minné L, Varner D, Burnell A, Ratzer E, Clark J, Haun W. Laparoscopic vs open appendectomy. Arch Surg; 132: 708-711.
21. Hesselink EJ. In: Trends in surgery. SIG health care information. ISBN 90-70755-46-7, 1995.
22. de Dombal FT, Clamp SE, Wardle KS. Measuring surgical performance in acute abdominal pain: Some reflections from international studies. Eur J Surg 1997; 163: 323-329.
23. Greenland S. Quantitative methods in the review of epidemiologic literature. Epidemiologic Reviews 1987; 9: 1-30.
24. Robins JM, Greenland S, Breslow NE. A general estimator for the variance of the Mantel-Haenszel odds ratio. Am J Epidem 1986; 124: 719-723.
25. Hall JC, Mills B, Nguyen H, Hall JL. Methodologic standards in surgical trials. Surgery 1996; 119: 466-472.
26. Slim K, Bousquet J, Kwiatkowski F, Pezet D, Chipponi J. Analysis of randomized trials in laparoscopic surgery. Br J Surg 1997; 84: 610-614.

27. Majeed AW, Troy G, Nicholl JP, Smythe A, Reed MWR, Stoddard CJ, Peacock J, Johnson AG. Lancet 1996; 347: 989-994.
28. Greenland S. Invited commentary: a critical look at some popular meta-analytic methods. Am J Epidemiol 1994; 140 (3): 290-296.
29. Frizelle FA, Hanna GB. Pelvic abscess following laparoscopic appendectomy (letter). Surg Endosc 1996; 10: 947-948.
30. Tang E, Ortega AE, Anthone GJ, Beart RW. Intraabdominal abscesses following laparoscopic and open appendectomies. Surg Endosc 1996; 10: 327-328.
31. Pier A, Gotz F, Bacher C, Ibad R. Laparoscopic appendectomy. World J Surg 1993; 17: 29-33.
32. El Ghoneimi A, Valla JS, Limonne B, Valla V, Montupet, Chavrier Y, Grinda A. Laparoscopic appendectomy in children; report of 1379 cases. J Pediatr Surg 1994; 29: 786-789.
33. Metger U, Schwartz H. Bridenileus oder Perforationsperitonitis. Helv Chir Acta 1975; 42: 571.
34. Zbar RI, Crede WB, McKahnn CF, Jekel F. The postoperative incidence of small bowel obstruction following standard open appendectomy and cholecystectomy: a six-year retrospective cohort study at Yale-New Haven Hospital. Conn Med 1993; 57: 123-127.
35. de Wilde RL. Goodbye to late bowel obstruction after appendicectomy (letter). Lancet 1991; 338: 1012.
36. Berry J, Malt R. Appendicitis near its centenary. Ann Surg 1984; 200: 567-575.
37. Wagner M, Aronsky D, Tschudi J, Metzger A, Klaiber C. Laparoscopic stapler appendectomy. A prospective study of 267 consecutive cases. Surg Endosc 1996; 10: 895-899.
38. Olsen JB, Myren CJ, Haahr PE. Randomized study of the value of laparoscopy before appendicectomy. Br J Surg 1993; 80: 922-923.
39. Jadallah FA, Abdul-Ghani AA, Tibblin S. Diagnostic laparoscopy reduces unnecessary appendectomy in fertile women. Eur J Surg 1994; 60 : 41-45.

Chapter 9

Laparoscopic appendectomy in The Netherlands



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INTRODUCTION

Laparoscopic appendectomy was introduced in The Netherlands in the seventies by de Kok[1]. The technique that de Kok advocated involved laparoscopic identification and mobilization of the appendix, followed by extraction of the appendix with its mesoappendix through a small incision in the right lower quadrant of the abdomen. Dissection and ligation of the appendiceal base were done extracorporeally. This technique was only suitable for patients with chronic abdominal pain because an acutely inflamed appendix with a thickened mesoappendix could not be readily extracted. Upon the advent of laparoscopic cholecystectomy to The Netherlands in 1990, the popularity of laparoscopy in patients with suspected acute appendicitis increased. Van Erp was one of the first Dutch surgeons to propagate laparoscopic inspection of the abdomen and laparoscopic removal of the appendix in patients with the clinical picture of acute appendicitis. Van Erp reported successful laparoscopic appendectomy in 66 of 68 patients with an acute inflammation of the appendix[2]. While almost 10% of the patients had a perforated appendicitis, postoperative infection was only observed in 1 patient at one of the port sites. Abdominal abscesses did not occur in this series of patients. The hospital stay after laparoscopic appendectomy was 4 days in van Erp's report. This implied a reduction of hospital stay of 3 days considering the data on appendectomy of the Dutch National Registry (SIG 1990). In a nonrandomized study by Boekhoudt et al. comparing 231 conventional appendectomies with 55 laparoscopic appendectomies, hospital stay was reduced by 1 day after laparoscopic appendectomy[3]. Wound infections were documented in 14.7% of patients after conventional appendectomy and in 3.8% after laparoscopic appendectomy in spite of a similar distribution of normal appendix, acute and perforated appendicitis in both groups. Laparoscopic appendectomy required 20 min extra operative time in this study.

To assess the diagnostic potential of laparoscopy in the acute abdomen, Hamming et al. performed laparoscopy in 34 fertile women with a clinical picture of acute appendicitis. Half of these patients had acute appendicitis[4]. Gynaecological pathology was found in 21% and other disorders such as cholecystitis and internial herniation in 6%. Normal appendices were observed in 21% of all patients. Borgstein et al. performed laparoscopy in 203 female patients from 16 to 50 years suspected of acute appendicitis[5]. Fifty-five percent of these patients had acute appendicitis while gynaecological disease was present in 23%. Laparoscopy was negative in 14% of all patients. Of 23 postmenopausal women suspected of acute appendicitis, inflammation of the appendix was confirmed in 96%. In 137 male adults with a median age of 23 years, the appendix was approached through a muscle splitting McBurney incision. Acute appendicitis was present in 92% of all patients. Therefore, the diagnosis potential of laparoscopy in acute appendicitis appears of greatest benefit in fertile women.

Proper evaluation of laparoscopic appendectomy can only be done in a randomized clinical trial. Kazemier et al. performed a trial randomizing patients over 16 years in age with a clinical picture of acute appendicitis for either laparoscopic or open appendectomy[6].

A total of 201 patients were enrolled into this study. Mean operative time of laparoscopic appendectomy was significantly longer than that of open appendectomy (61 vs. 41 min). Conversion from laparoscopy to open operation occurred in 12% of patients mostly for retrocecally appendicular infiltrates. In the open group, extension of the McBurney incision was necessary in 5.8%. Extra-appendicular pathology was observed in 4% in the laparoscopic arm and in 3% in the open arm. A normal appendix without other disease was encountered in 6.2% of the patients in the laparoscopic group, and in 8.7% in the open group. Postoperative pain, measured on the first and second postoperative day with a visual analogue scale, was less after laparoscopic appendectomy. Restoration of normal gastrointestinal motility was similar in both groups. Wound infections occurred more frequently after open than after laparoscopic appendectomy (5.8 vs. 0%). Perforated appendicitis was observed in 17% in both groups. Only one intra-abdominal abscess was noted after open appendectomy in these patients. Hospital stay was significantly shorter after laparoscopic appendectomy than after open appendectomy (3.7 vs. 4.4 days).

To determine the definitive place of laparoscopic appendectomy in daily surgical practice requires a complete cost-effectiveness study which includes calculations of direct and indirect costs. In anticipation of the final results of such a study, direct costs of laparoscopic appendectomy can be commented upon. Considering the widespread use of reusable trocars and reusable laparoscopic instruments in The Netherlands, additional costs for disposable products appear limited. Ligation of the base of the appendix with pretied loops costs USD 30. In case of a thickened appendix, removal in a disposable plastic bag can be indicated. The costs of such a bag vary from Euro 20 to 100. Therefore, total additional costs for disposable products in laparoscopic appendectomy will vary from Euro 30 to 130. Adhesions due to appendectomy and late ileus due to these adhesions should be part of a complete cost-effectiveness study. The incidence of bowel obstruction after conventional appendectomy can be as high as 3.4% particularly after perforated appendicitis[7]. Long-term follow-up after laparoscopic appendectomy is not available to our knowledge. However, de Wilde performed 'second look' laparoscopies after either laparoscopic or open appendectomy for acute appendicitis[8]. Adhesions were found in 10% of the patients who had laparoscopic appendectomy, and in 80% of the patients who had open appendectomy. Krähenbühl et al. also observed in an experimental study less adhesions after laparoscopic fundoplication than after open fundoplication[9]. Further clinical studies are needed to assess if the incidence of late bowel obstruction is less after laparoscopic appendectomy.

Concern has been expressed that the laparoscopic approach to perforated appendicitis would be associated with a greater chance for intra-abdominal abscesses[10]. Intraperitoneal insufflation of gas has been suggested to spread bacteria through the abdominal cavity causing remote abscesses. In the reported Dutch studies, this assumption has not been validated[2,3,6]. Laparoscopy provides an excellent access to the entire peritoneal cavity, and allows thorough irrigation. Therefore, clinical suspicion of perforated appendicitis is not a contraindication for laparoscopy in The Netherlands.

The operative strategy in patients with macroscopically normal appendices without other intra-abdominal pathology remains controversial. Van Erp reported in his study of 68 laparoscopic appendectomies that 4 macroscopically normal appendices were considered inflamed at microscopic examination[2]. In this same study, 7 appendices that appeared laparoscopically inflamed lacked signs of inflammation at microscopy. While Kazemier et al. recommend removal of normal appendices in patients without other abdominal pathology[6]. Boekhoudt et al. propagate to leave the appendix in situ in such instances[3].

In spite of several distinct advantages of laparoscopic appendectomy in comparison to conventional appendectomy, the use of laparoscopy in acute appendicitis remains limited in The Netherlands. In 1995 only 5.3% of 16,000 appendectomies was done laparoscopically in The Netherlands[11]. Unawareness of specific advantages of the laparoscopic approach, limited laparoscopic experience and restricted availability of laparoscopic facilities outside office hours are probably factors that impede wider application of laparoscopic appendectomy. Inclusion of laparoscopic appendectomy in formal surgical training, further studies on the value of laparoscopic appendectomy and patient's demand are likely to increase the number of laparoscopic appendectomies in The Netherlands in the near future.

REFERENCES

1. de Kok HJM: The laparoscopic mini appendectomy. Acta Endosc 1983; 13:5-6.
2. Van Erp WFM: Laparoscopie goed bruikbaar bij diagnostiek en chirurgie wegens appendicitis acuta. Ned Tijdschr Geneesk 1993; 137:1500-1504.
3. Boekhoudt FD, Bijnen AB, de Ruiter P: Gunstige ervaringen met laparoscopische appendectomie. Ned Tijdschr Heelk 1993;5:153-156.
4. Hamming JF, Bonjer HJ, ten Hoope CA: Laparoscopy for suspected appendicitis in fertile women. Surg Endosc 1994;8:945.
5. Borgstein PJ, Gordijn RV, Eijsbouts QAJm Cuesta MA: Acute appendicitis – A clear-cut case in men, a guessing game in young women. Surg Endosc 1997;11:923-927.
6. Kazemier G, de Zeeuw GR, Lange JF, Hop WCJ, Bonjer HJ: Laparoscopic vs open appendectomy. A randomized clinical trial. Surg Endosc 1997;11:336-340.
7. Ahlberg G, Bergdahl S, Rutqvist J, Soderquist C, Frenchner B: Mechanical small-bowel obstruction after conventional appendectomy in children. Eur J Pediatr Surg 1997;7:13-15.
8. De Wilde RL : Goodbye to late bowel obstruction after appendicectomy. Lancet 1991; 338: 1012
9. Krähenbühl L, Schäfer M, Kuzinkovas V, Baer HU, Büchler MW :Less adhesion formation in rats after laparoscopic versus open fundoplication. Surg Endosc 1997;11:204.
10. Tang E, Ortega AE, Anthone GJ, Beart RW: Intraabdominal abscessess following laparoscopic and open appendectomies. Surg Endosc 1996;10:327-328.
11. Bonjer HJ, Cuesta MA, Bemelman WA, Janssen IMC, de Wit LT, ten Cate Hoedmaker HO, de Brauw MA: Diffusion of endoscopic surgery in the Netherlands. Surg Endosc 1997;11:597.

Chapter 10

Summary and implications of this thesis

In **chapter 1** a general outline of this thesis and an introduction to the topic of diagnosis and treatment of acute appendicitis are provided and the main questions are lined out.

In **chapter 2** an extensive review of the literature describes epidemiology, pathogenesis, and developments in diagnosis and treatment of acute appendicitis. This review shows that rates of negative appendectomies and incidences of perforated appendicitis have hardly changed through the years in the Western countries. It assesses different diagnostic modalities to improve diagnostic accuracy. Preoperative computed tomography (CT) appears the best diagnostic tool in patients with suspected acute appendicitis. However, the optimal CT technique is still under debate. Laparoscopic inspection has a higher accuracy than preoperative CT, but is obviously more invasive. Laparoscopic appendectomy seems the optimal technique to treat acute appendicitis, but certain aspects as the optimal fashion to secure the appendiceal stump and incidences of rare complications remain uncertain.

In **chapter 3** the question whether unenhanced CT can help to diagnose acute appendicitis more accurately is answered positively. This chapter presents the results of a prospective evaluation of 103 consecutive patients with suspected acute appendicitis. All patients were scheduled for emergency surgery after the diagnosis was approved by senior surgeons. Preoperatively all patients underwent a helical CT without contrast enhancement. Subsequently, a laparoscopic inspection of the abdominal cavity was done and appropriate surgical therapy was performed by a surgeon who was blinded to the diagnosis suggested by CT. Appendicitis was diagnosed by CT in 83 patients (80.6 per cent). Acute appendicitis was identified during laparoscopy in 87 patients (84.5 per cent). Prospective interpretations of CT images yielded a sensitivity of 95.4 per cent, and a specificity of 100 per cent for the diagnosis of acute appendicitis. There were four false-negative scans. In 12 of 20 patients without signs of appendicitis on CT, the scan established the presence of other pathology. At operation no additional pathology was observed in this group and all other diagnoses proved to be correct. In this study it was shown that contrast enhancement is not necessary to provide an accurate diagnosis in patients with suspected acute appendicitis. This means that with this CT technique contrast related complications such as allergic reactions can be prevented and considerable costs can be saved.

In **chapter 4** implementation of routine preoperative CT scanning in patients with suspected acute appendicitis is discussed. In the majority of studies that investigate the value of different preoperative imaging techniques, the expert interpretation of the images is provided. However, patients with acute illnesses such as appendicitis present at any time of day and they require prompt and accurate diagnosis and treatment. Consequently, the assessment of patients with suspected acute appendicitis and interpretation of US and CT scans are done by in house staff. These health care professionals might have limited expertise in diagnosing appendicitis by CT. Chapter 4, describes the results of a prospective evaluation of 103 consecutive patients with suspected acute appendicitis. All patients were scheduled for emergency surgery after the diagnosis was approved by senior surgeons. Preoperatively they underwent a helical CT without contrast enhancement. Al CT scans were interpreted by three groups of radiologists with different levels of expertise. Group A consisted of radiology residents, group B consisted of senior radiologists, and group C was an expert radiologist. After the CT was made, all patients underwent laparoscopic inspection of the abdominal cavity which was considered the 'gold standard'. Specificity for the diagnosis acute appendicitis was comparable: 94 per cent, 94 per cent, and 100 percent for group A, B, and C radiologists respectively. However, sensitivity differed considerably: 81 per cent, 88 per cent, and 95 per cent for group A, B, and C radiologists respectively. Other diseases in patients without appendicitis were diagnosed correctly in almost all cases by all three groups of radiologists. This interobserver variability for the diagnosis acute appendicitis hampers the implementation of routine CT scanning in patients with acute appendicitis. It is recommended that in this phase, all patients with negative CT interpretations undergo diagnostic laparoscopy or close clinical or outpatient observation.

In **chapter 5** technical aspects of laparoscopic appendectomy are described. Tips and tricks are provided to perform laparoscopic appendectomy safely. The optimal patient positioning, position of the surgical team and configuration of trocar sites are described. Technical difficulties and possible methods to solve these are discussed. In **chapter 6** the optimal way to secure the appendiceal stump during laparoscopic appendectomy is studied. In a meta-analysis, randomized controlled trials on appendiceal stump closure during laparoscopic appendectomy were systematically reviewed. Data on 427 patients from four studies were included. It was shown that surgery took 9 minutes longer if loops were used ($p = 0.04$). Superficial wound infection (OR 0.21; 95%-CI 0.06 to 0.71; $p = 0.01$) and postoperative ileus (0.36; 0.14 to 0.89; $p = 0.03$) were significantly less frequent when the appendix stump was secured by staples instead of loops. Of ten intraoperative ruptures of the appendix, seven occurred in loop treated patients ($p = 0.46$). Hospital stay and frequency of postoperative intraabdominal abscess were also similar. The conclusion of this systemic review of the literature shows that stump closure in laparoscopic appendectomy is best performed with an endoscopic stapler, but higher direct costs will result from this strategy.

In **chapter 7** a randomized, clinical trial answers questions about feasibility and safety of laparoscopic appendectomy. In this study 201 patients with similar characteristics of appendicitis were randomized to either open appendectomy or laparoscopic appendectomy. Operative time and technique, resumption of normal diet, postoperative pain, use of analgesia, hospital stay and complications were documented. One hundred-and-four patients were allocated to the open group, 97 to the laparoscopic group. Postoperative pain was significantly less in the laparoscopic group on the first ($p<0.001$) and second ($p<0.001$) postoperative day, resulting in less use of analgesics on both days ($p<0.001$). Restoration of diet was similar in both groups. Mean operative time was longer in the laparoscopic group: 61 vs 41 min ($p<0.001$). Postoperative complications did not differ in either group, except for wound infections (six in the open and zero in the laparoscopic group, $p< 0.05$). Mean hospital stay was similar in both groups. This randomized, controlled trial shows that laparoscopic appendectomy takes longer to perform but results in less postoperative pain and fewer wound infections. The power of 201 patients may be too small to show differences between laparoscopic and open appendectomy with respect to mortality or rare complications such as intra-abdominal abscesses.

To overcome this problem, a meta-analysis is described in **chapter 8** which reviews randomized, controlled trials comparing laparoscopic and open appendectomy for acute appendicitis. In this analysis, mean variances and pooled mean differences (PMD) for continuous outcomes such as operative time and postoperative pain and pooled odds ratios (OR) for dichotomous outcomes such as postoperative complications were calculated. Fifteen studies were identified, including a total number of 1825 patients analysed. Laparoscopic appendectomy took longer than open appendectomy (PMD 15 [95% CI 12-18] min, $p<10^5$). Laparoscopic appendectomy resulted in less pain scored on a visual analogue scale (0-100) on day one (PMD 13 [10-17] points, p<10-5) and day two (PMD 11 [7-15] points, $p<10^5$), lower total number of dosages of parenteral pain medication (PMD 0.92 [0.69-1.16] doses, $p<10^5$), faster restoration of solid diet (PMD 0.27 [0.12-0.42] days, p = 0.006), shorter hospital stay (PMD 0.69 [0.41-0.98] days, $p<10^5$) and faster return to normal activities (PMD 4.8 [3.7-5.9] days, $p<10^5$). We found no significant differences between the groups for total percentage of complications (OR 0.89 [95% CI 0.66-1.21], p = 0.48), percentage of early bowel obstructions (OR 1.68 [0.96-3.01], p = 0.08) or percentage of intra-abdominal abscesses (OR 1.78 [0.83-4.03], p = 0.19). The percentage of postoperative wound infections was significantly less after laparoscopic appendectomy (OR 0.37 [0.23-0.57], $p<10^5$). The meta-analysis concludes that laparoscopic appendectomy requires more operative time and results in less postoperative pain, faster recovery, shorter hospital stay and less wound infections. Therefore, laparoscopic appendectomy appears the preferable approach to acute appendicitis.

Despite the available evidence, laparoscopic removal of the inflamed appendix is still not considered the 'gold standard' by many surgeons. Particularly in The Netherlands, despite the early description of the technique by de Kok in the seventies, only a small percentage of appendectomies is performed laparoscopically. In **chapter 9**, the history and current status of laparoscopic appendectomy in the Netherlands are described.

CONCLUSION

It seems time to change course for both diagnosis and treatment of acute appendicitis. Removing an uninflamed appendix in patients with suspected acute appendicitis should be considered a complication. To prevent this complication, preoperative imaging appears pivotal. This thesis shows that routine unenhanced helical CT can diagnose acute appendicitis accurately. However, to reach this high level of diagnostic yield, expert interpretation of the scans is of paramount importance. Consequently, interpreting CT scans of patients with suspected acute appendicitis should be integrated into the training of radiologists. Telesupervision of the CT images by expert radiologists might be helpful to bridge the period of less broad distribution of specific expertise. Alternatively, routine diagnostic laparoscopy can be recommended in all patients with CT interpretations without a definitive diagnosis. A normal appearing appendix at laparoscopy can be left in place, while other disorders can be treated accordingly. In patients with evident appendicitis, laparoscopic appendectomy using a stapler to secure the stump appears to be the superior technique. It is obvious that laparoscopic appendectomy should be integrated into the formal training of general surgeons. The standard grid iron incision in all patients with suspected acute appendicitis is long overdue, and routine CT and laparoscopic appendectomy have met all criteria to be adopted as the new 'gold standard' for these patients. Thank you Dr. McBurney for over 100 years of dedicated service!

Chapter 11

Dutch summary

Hoofdstuk 1 beschrijft de opzet van het proefschrift en geeft een algemene introductie over diagnose en behandeling van appendicitis acuta. De belangrijkste vragen worden beschreven.

In **Hoofdstuk 2** worden in een uitgebreid overzicht van de literatuur de epidemiologie, de pathogenese en ontwikkelingen op het gebied van diagnose en behandeling van appendicitis acuta beschreven. Dit literatuuroverzicht laat zien dat de frequentie van het verrichten van een negatieve appendectomie en de incidentie van geperforeerde appendicitis door de jaren eigenlijk niet veranderd is in de Westerse wereld. In dit hoofdstuk worden meerdere diagnostische modaliteiten besproken die de preoperatieve accuratesse bij patiënten met appendicitis acuta zouden kunnen verbeteren. Preoperatieve computer tomografie (CT) blijkt het optimale diagnostisch hulpmiddel bij deze groep patiënten, maar welke CT-techniek de beste resultaten geeft is nog niet uitgekristalliseerd. Diagnostische laparoscopie heeft weliswaar een nog hogere accuratesse dan CT, maar is natuurlijk ook meer invasief. Laparoscopische appendectomie lijkt beter dan open appendectomie, maar bepaalde aspecten, zoals de optimale manier om de appendixstomp te verzorgen en incidenties van zeldzame complicaties blijven nog onzeker.

In **hoofdstuk 3** blijkt dat met een CT zonder contrast de diagnose appendicitis acuta goed te stellen is. In dit hoofdstuk worden de resultaten gepresenteerd van een prospectieve studie waarin 103 patiënten die door de chirurg verdacht werden van appendicitis acuta preoperatief een spiraal CT zonder contrast ondergingen. Vervolgens werd bij allen een diagnostische laparoscopie verricht door een chirurg die niet op de hoogte was van de door de CT gesuggereerde diagnose. Appendicitis acuta werd gediagnoseerd door de CT bij 83 patiënten (80.5%). Tijdens laparoscopie bleken echter 87 patiënten (84.5%) appendicitis acuta te hebben. Daarmee bleek CT 95.4% sensitief en 100% specifiek voor de diagnose appendicitis acuta. Er waren 4 foutnegatieve CT beoordelingen. Bij 12 van 20 patiënten zonder tekenen van appendicitis bij CT, werd op de scan andere pathologie gediagnostiseerd. Tijdens laparoscopie bleken al deze diagnosen correct en werd geen additionele pathologie gevonden. Deze studie laat zien dat het gebruik van intraveneus of enteraal contrast niet nodig is om de diagnose te stellen bij patiënten die verdacht worden van appendicitis acuta. Dit betekent dat contrast gerelateerde nadelen, zoals allergische reacties en kosten vermeden kunnen worden in deze groep patiënten.

In **hoofdstuk 4** wordt het probleem van het implementeren van routine CT bij patiënten die verdacht worden van appendicitis acuta besproken. De meerderheid van de studies die de waarde beoordelen van preoperatieve CT scanning bij patiënten die verdacht worden van appendicitis acuta gaat uit van interpretatie van de scans door experts. Patiënten met aandoeningen zoals appendicitis acuta presenteren zich echter op elk willekeurig moment van de dag en vragen acuut een correcte diagnose en behandeling. Dientengevolge worden deze patiënten veelal opgevangen door de dienstdoende chirurg en wordt het afbeeldend onderzoek geïnterpreteerd door de dienstdoende radioloog. Deze radioloog kan minder expertise hebben dan nodig is om tot de in studies gemelde accuratesse te komen bij het beoordelen van de scan. Hoofdstuk 4 beschrijft de resultaten van een studie waarin de CT scans van dezelfde 103 patiënten die door de chirurg verdacht werden van appendicitis acuta uit hoofdstuk 3 door drie groepen radiologen werden beoordeeld. De expertise van de radiologen in de verschillende groepen varieerde. Groep A bestond uit assistenten in opleiding tot radioloog, groep B bestond uit stafradiologen, groep C werd gevormd door een expert-radioloog. Nadat de CT was gemaakt en beoordeeld was door groep A en B radiologen werd bij alle patiënten een diagnostische laparoscopie verricht door een chirurg die niet op de hoogte was van de door de CT gesuggereerde diagnose. Deze laparoscopie werd gebruikt als 'gouden standaard'. De specificiteit voor de diagnose appendicitis acuta was vergelijkbaar: respectievelijk 94%, 94% en 100% voor groep A, B, en C radiologen. De sensitiviteit verschilde echter aanzienlijk: respectievelijk 81%, 88%, en 95% voor groep A, B en C radiologen. Er waren namelijk 16, 8 en 4 valsnegatieve CT beoordelingen in de verschillende groepen. Andere aandoeningen bij patiënten die geen appendicitis acuta hadden, werden alle door de expert-radioloog en op één na door groep A en B radiologen correct gediagnostiseerd. Deze interobserver variabiliteit maakt het implementeren van een routine CT bij alle patiënten die verdacht worden van appendicitis acuta lastig. Het is aan te raden om in deze fase bij alle patiënten die een negatieve CT beoordeling hebben toch een diagnostische laparoscopie uit te voeren of de patiënt klinisch te observeren.

In **hoofdstuk 5** worden technische aspecten van de laparoscopische appendectomie besproken. Er worden praktische tips gegeven hoe men veilig een laparoscopische appendectomie verricht. De beste ligging van de patiënt en de optimale opstelling van het chirurgische team en trocarplaatsing worden beschreven. Daarnaast worden technische problemen en hun oplossingen besproken.

In **hoofdstuk 6** wordt de beste manier onderzocht om de stomp van de appendix tijdens laparoscopische appendectomie te verzorgen. Data over 427 patiënten uit 4 studies werden bestudeerd. Het bleek dat de operatie 9 minuten langer duurt als er 'loops' werden gebruikt (p=0.04). Oppervlakkige wondinfecties (OR 0.21; 95%-CI 0.06 tot 0.71; p=0.01) en postoperatieve ileus (0.36; 0.14 tot 0.89; p=0.03) kwamen significant minder vaak voor bij het gebruik van 'staplers'. Van de 10 keer dat de appendix peroperatief ruptureerde, gebeurde dat 7 keer in patiënten bij wie de appendixstomp met een 'loop' was verzorgd (p=0.46). De duur van de ziekenhuisopname en de frequentie van voorkomen van een intra-abdominaal abces waren in beide groepen eveneens vergelijkbaar. In conclusie lijkt het beter om elke appendixstomp tijdens laparoscopische appendectomie te verzorgen met een 'stapler'. Dit zal wel hogere directe kosten met zich meebrengen.

In **hoofdstuk 7** wordt een gerandomiseerd, klinisch onderzoek beschreven dat laparoscopische en open appendectomie vergelijkt. In deze studie werden 201 patiënten die alle verdacht werden van appendicitis acuta gerandomiseerd tussen laparoscopische (LA) of open appendectomie (OA). Operatieduur en –techniek, hervatting van dieet, postoperatieve pijn, gebruik van analgetica, duur van het verblijf in het ziekenhuis en complicaties werden gescoord. Er vielen 104 patiënten in de OA groep en 97 in de LA groep. Postoperatieve pijn was significant minder in the LA groep op de eerste ($p<0.001$) en tweede ($p<0.001$) postoperatieve dag. Dit resulteerde in minder gebruik van analgetica op beide dagen ($p<0.001$). Herstel van dieet was vergelijkbaar in beide groepen. De gemiddelde operatieduur was langer in the LA groep: 61 versus 41 minuten ($p<0.001$). Postoperatieve complicaties verschilden niet in beide groepen, behoudens het aantal wondinfecties (6 in de OA and 0 in de LA groep, $p<0.05$). Het gemiddelde ziekenhuisverblijf was vergelijkbaar in beide groepen. Dit onderzoek laat zien dat laparoscopische appendectomie langer duurt, maar resulteert in minder postoperatieve pijn en minder wondinfecties. Het aantal patiënten in de studie is echter te klein om verschillen in mortaliteit en andere zeldzame complicaties zoals intra-abdominale abcessen aan te tonen.

In **hoofdstuk 8** wordt, om dit groepsgrootte probleem te omzeilen een meta-analyse beschreven die meerdere gerandomiseerde studies bevat die LA en OA vergelijken. In deze analyse werden gemiddelde varianties en gepoolde gemiddelde verschillen (PMD) voor continue uitkomsten, zoals operatieduur en postoperatieve pijn en gepoolde odds ratio's (OR) voor dichotome uitkomsten, zoals postoperatieve complicaties bepaald. Vijftien studies werden betrokken in het onderzoek. In deze 15 studies werd een totaal aantal van 1825 patiënten geanalyseerd. LA duurde langer dan OA (PMD 15 [95% CI 12-18] min, $p<10^{5}$). LA veroorzaakte minder pijn zoals gescoord op een visueel analoge schaal (0-100) op dag 1 (PMD 13 [10-17] punten, p<10-5) en dag 2 (PMD 11 [7-15] punten, $p<10^{5}$) postoperatief. Dit resulteerde in gebruik van minder doses parenteraal toegediende pijnstillers (PMD 0.92 [0.69-1.16] doses, $p<10^{5}$). Er was na LA een sneller herstel van normaal dieet (PMD 0.27 [0.12-0.42] dagen, $p=0.006$), kortere opnameduur (PMD 0.69 [0.41-0.98] dagen, $p<10^{5}$) en sneller hervatten van normale activiteiten (PMD 4.8 [3.7-5.9] dagen, $p<10^{5}$). Er werden geen verschillen aangetoond wat betreft totaal percentage complicaties (OR 0.89 [95% CI 0.66-1.21], $p=0.48$), percentage postoperatieve ileus (OR 1.68 [0.96-3.01], $p=0.08$) of percentage intra-abdominale abcessen (OR 1.78 [0.83-4.03], $p=0.19$). Het percentage postoperatieve wondinfecties was wel significant minder na LA (OR 0.37 [0.23-0.57], $p<10^{5}$). De meta-analyse concludeert dat LA een langere operatieduur vraagt, maar resulteert in minder postoperatieve pijn, sneller herstel, kortere opnameduur en minder wondinfecties. Dientengevolge is laparoscopische appendectomie de te prefereren methode om appendicitis acuta te behandelen.

Ondanks het voorhanden zijnde wetenschappelijk bewijs wordt de laparoscopische operatietechniek nog niet altijd gezien als de 'gouden standaard' bij het behandelen van appendicitis acuta. Met name in Nederland wordt slechts een klein percentage van de appendectomieën laparoscopisch verricht, ondanks het feit dat de Nederlandse chirurg de Kok al in de jaren 70 deze techniek beschreef.

In **hoofdstuk 9** worden de historie en huidige status van de laparoscopiche appendectomie in Nederland beschreven.

CONCLUSIE

Het lijkt tijd om een andere koers te varen wat betreft diagnose en behandeling van appendicitis acuta. Het verwijderen van een niet ontstoken appendix bij patiënten die verdacht worden van appendicitis acuta moet gezien worden als een complicatie. Om deze complicatie te vermijden, is het gebruik van afbeeldende technieken cruciaal. Dit proefschrift laat zien dat een spiraal CT zonder contrast appendicitis accuraat kan diagnostiseren. Om deze hoge diagnostische opbrengst te bereiken is het wel van het grootste belang dat er bij de radioloog voldoende expertise is met betrekking tot het stellen van deze diagnose op CT. Dit betekent dat het leren interpreteren van CT scans van patiënten met mogelijke appendicitis geïncorporeerd moet worden in de training van radiologen. Telesupervisie door een expert-radioloog kan behulpzaam zijn tijdens deze leerfase. Men zou er overigens ook voor kunnen kiezen om bij onvoldoende radiologische expertise bij alle patiënten die op CT geen duidelijke diagnose hebben een diagnostische laparoscopie te verrichten. Als de appendix niet ontstoken blijkt, kan deze in-situ blijven; wanneer er een andere chirurgische aandoening wordt gevonden, moet deze uiteraard behandeld. Als de appendix wel ontstoken is, moet deze zowel bij vrouwen als mannen laparoscopisch worden verwijderd met behulp van een 'stapler'. Dit betekent dat de laparoscopische appendectomie in het standaard opleidingsprogramma van een heelkunde assistent thuishoort. De standaard wisselsnede bij alle patiënten die verdacht worden lijkt obsoleet; routinematige CT and laparoscopiche appendectomie voldoen inmiddels aan alle criteria om de nieuwe 'gouden standaard' voor deze patiënten te worden. Hartelijk dank dokter McBurney voor meer dan 100 jaar trouwe dienst!

Appendix

LIST OF PUBLICATIONS

1. Kazemier G, Hesselink EJ, and Terpstra OT. "Hepatic anatomy." Transplantation 49.5 (1990): 1029-30.
2. Kazemier, G.; Hesselink, E.J.; Lange, J.F.; Terpstra, O.T. «Dividing the liver for the purpose of split grafting or living related grafting: a search for the best cutting plane.» Transplant.Proc. 23.1 Pt 2 (1991): 1545-46.
3. Berends, F.J.; Kazemier, G.; Bonjer, H.J.; Lange, J.F. "Subcutaneous metastases after laparoscopic colectomy." Lancet 344.8914 (1994): 58.
4. Borel, Rinkes, I; Bijma, A.; Kazemier, G.; Sinaasappel, M.; Valerio, D.; Terpstra, O.T. "Proliferative response of hepatocytes transplanted into spleen or solid support." J.Surg.Res. 56.5 (1994): 417-23.
5. Kazemier, G.; Bonjer, H.J.; Berends, F.J.; Lange, J.F. «Port site metastases after laparoscopic colorectal surgery for cure of malignancy.» Br.J.Surg. 82.8 (1995): 1141-42.
6. Bonjer, H.J.; Bruining, H.A.; Kazemier, G.; Lange, J.F.; Pols, H.A.; De Herder, W.W. "Endoscopic retroperitoneal adrenalectomy: a surgical improvement." Ned.Tijdschr.Geneeskd. 141.9 (1997): 426-29.
7. Bonjer, H.J.; Hazebroek, E.J.; Kazemier, G.; Giuffrida, M.C.; Meijer, W.S.; Lange, J.F."Open versus closed establishment of pneumoperitoneum in laparoscopic surgery." Br.J.Surg. 84.5 (1997): 599-602.
8. Bonjer, H.J.; Lange, J.F.; Kazemier, G.; De Herder, W.W.; Steyerberg, E.W.; Bruining, H.A."Comparison of three techniques for adrenalectomy." Br.J.Surg. 84.5 (1997): 679-82.
9. Giuffrida, M.C.; Marquet, R.L.; Kazemier, G.; Wittich, P.; Bouvy, N.D.; Bruining, H.A.; Bonjer, H.J. "Laparoscopic splenectomy and nephrectomy in a rat model. Description of a new technique." Surg.Endosc. 11.5 (1997): 491-94.
10. Kazemier, G.; Berends, F.J.; Bouvy, N.D.; Lange, J.F.; Bonjer, H.J. «The influence of pneumoperitoneum on the peritoneal implantation of free intraperitoneal cancer cells.» Surg.Endosc. 11.6 (1997): 698-99.
11. Kazemier, G.; de Zeeuw, G.R.; Lange, J.F.; Hop, W.C.; Bonjer, H.J."Laparoscopic vs open appendectomy. A randomized clinical trial.» Surg.Endosc. 11.4 (1997): 336-40.
12. Wittich, P.; Kazemier, G.; Schouten, W.R.; Jeekel, J.; Lange, J.F.; Bonjer, H.J. «The 'Colon cancer laparoscopic or open resection' (COLOR) trial.» Ned. Tijdschr. Geneeskd. 141.39 (1997): 1870-71.
13. Bonjer, H.J.; van der, Harst E.; Steyerberg, E.W.; De Herder, W.W.; Kazemier, G.; Mohammedamin, R.S.; Bruining, H.A. "Retroperitoneal adrenalectomy: open or endoscopic?" World J.Surg. 22.12 (1998): 1246-49.
14. Kazemier, G.; Hazebroek, E.J.; Lange, J.F.; Bonjer, H.J. "Vascular injuries during laparoscopy." J.Am. Coll.Surg. 186.5 (1998): 604-05.
15. Tseng, L.N.; Berends, F.J.; Wittich, P.; Bouvy, N.D.; Marquet, R.L.; Kazemier, G.; Bonjer, H.J. "Port-site metastases. Impact of local tissue trauma and gas leakage.» Surg.Endosc. 12.12 (1998): 1377-80.
16. den Hoed, P.T.; van Wessem, K.J.; Berends, F.J.; Kappers-Klunne, M.C.; Kazemier, G.; Bonjer, H.J. "Laparoscopic splenectomy for hematological diseases; results in 28 patients." Ned.Tijdschr. Geneeskd. 143.23 (1999): 1222-25.
17. Giraudo, G.; Kazemier, G.; van Eijck, C.H.; Bonjer, H.J. "Endoscopic palliative treatment of advanced pancreatic cancer: thoracoscopic splanchnicectomy and laparoscopic gastrojejunostomy." Ann. Oncol. 10 Suppl 4 (1999): 278-80.
18. Kazemier, G.; Hazebroek, E.J.; Lange, J.F.; Bonjer, H.J. «Needle and trocar injury during laparoscopic surgery in Japan.» Surg.Endosc. 13.2 (1999): 194.
19. Berends, F.J.; Cuesta, M.A.; Kazemier, G.; van Eijck, C.H.; De Herder, W.W.; van Muiswinkel, J.M.; Bruining, H.A.; Bonjer, H.J. "Laparoscopic detection and resection of insulinomas." Surgery 128.3 (2000): 386-91.
20. Bonjer, H.J.; Sorm, V.; Berends, F.J.; Kazemier, G.; Steyerberg, E.W.; De Herder, W.W.; Bruining, H.A. "Endoscopic retroperitoneal adrenalectomy: lessons learned from 111 consecutive cases." Ann. Surg. 232.6 (2000): 796-803.

21. Lange, J.F.; Koppert, S.; van Eyck, C.H.; Kazemier, G.; Kleinrensink, G.J.; Godschalk, M. "The gastrocolic trunk of Henle in pancreatic surgery: an anatomo-clinical study." J.Hepatobiliary.Pancreat.Surg. 7.4 (2000): 401-03.
22. van't Riet, M.; Burger, J.W.; van Muiswinkel, J.M.; Kazemier, G.; Schipperus, M.R.; Bonjer, H.J. "Diagnosis and treatment of portal vein thrombosis following splenectomy." Br.J.Surg. 87.9 (2000): 1229-33.
23. Wittich, P.; Marquet, R.L.; Kazemier, G.; Bonjer, H.J. "Port-site metastases after CO(2) laparoscopy. Is aerosolization of tumor cells a pivotal factor?" Surg.Endosc. 14.2 (2000): 189-92.
24. de Jonge, J.; Kazemier, G.; Metselaar, H.J.; Tilanus, H.W. «Partial liver transplantation.» Scand. J.Gastroenterol.Suppl.234 (2001): 98-102.
25. Riet, M.; Smet, A.A.; Kuiken, H.; Kazemier, G.; Bonjer, H.J. «Prevention of compensatory hyperhidrosis after thoracoscopic sympathectomy for hyperhidrosis.» Surg.Endosc. 15.10 (2001): 1159-62.
26. Berends, F.J.; den Hoed, P.T.; Bonjer, H.J.; Kazemier, G.; van, Riemsdijk, I; Weimar, W.; IJzermans, J.N. "Technical considerations and pitfalls in laparoscopic live donornephrectomy." Surg.Endosc. 16.6 (2002): 893-98.
27. Berends, F.J.; Harst, E.V.; Giraudo, G.; Terkivatan, T.; Kazemier, G.; Bruining, H.A.; De Herder, W.W.; Bonjer, H.J. «Safe retroperitoneal endoscopic resection of pheochromocytomas.» World J.Surg. 26.5 (2002): 527-31.
28. Konsten, J.L.; Kazemier, G.; Dees, J.; van Eijck, C.H. «Pancreas-preserving total duodenectomy due to familial adenomatous polyposis in 4 patients.» Ned.Tijdschr.Geneeskd. 146.13 (2002): 621-24.
29. Van Veelen, M.A.; Kazemier, G.; Koopman, J.; Goossens, R.H.; Meijer, D.W. "Assessment of the ergonomically optimal operating surface height for laparoscopic surgery." J.Laparoendosc.Adv. Surg.Tech.A 12.1 (2002): 47-52.
30. Vlot, J.; Kazemier, G.; Heijsterkamp, J.; Tilanus, H.W.; van, der Sijp, Jr.; IJzermans, J.N. "The treatment of colorectal liver metastases: good 5 year survival chance after partial liver resection at the Rotterdam University Hospital, 1984/1999." Ned. Tijdschr. Geneeskd. 146.5 (2002): 214-18.
31. Van Heek, N.T.; De Castro, S.M.; van Eijck, C.H.; van Geenen, R.C.; Hesselink, E.J.; Breslau, P.J.; Tran, T.C.; Kazemier, G.; Visser, M.R.; Busch, O.R.; Obertop, H.; Gouma, D.J."The need for a prophylactic gastrojejunostomy for unresectable periampullary cancer: a prospective randomized multicenter trial with special focus on assessment of quality of life." Ann.Surg. 238.6 (2003): 894-902.
32. Van Veelen, M.A.; Meijer, D.W.; Uijttewaal, I.; Goossens, R.H.; Snijders, C.J.; Kazemier, G. "Improvement of the laparoscopic needle holder based on new ergonomic guidelines." Surg.Endosc. 17.5 (2003): 699-703.
33. Van Veelen, M.A.; Snijders, C.J.; Van Leeuwen, E.; Goossens, R.H.; Kazemier, G. "Improvement of foot pedals used during surgery based on new ergonomic guidelines." Surg.Endosc. 17.7 (2003): 1086-91.
34. Veldkamp, R.; Gholghesaei, M.; Bouvy, N.D.; Kazemier, G.; Bonjer, H.J. "Laparoscopic resection of colonic cancer." Scand.J.Surg. 92.1 (2003): 97-103.
35. Berends, F. J.; Schep, N.; Cuesta, M.A.; Bonjer, H.J.; Kappers-Klunne, M.C.; Huijgens, P.; Kazemier, G. «Hematological long-term results of laparoscopic splenectomy for patients with idiopathic thrombocytopenic purpura: a case control study.» Surg.Endosc. 18.5 (2004): 766-70.
36. Tran K.T., Smeenk H.G, van Eijck C.H, Kazemier G, Hop W.C, Greve J.W, Terpstra O.T, Zijlstra J.A, Klinkert, P.; Jeekel, J. "Pylorus preserving pancreaticoduodenectomy versus standard whipple procedure: a prospective, randomized, multicenter analysis of 170 patients with pancreatic and periampullary tumors." Ann.Surg. 240.5 (2004): 738-45.
37. Albayrak A, Kazemier G, Meijer D.W, Bonjer H.J. Current state of ergonomics of operating rooms of dutch hospitals in the endoscopic era. Min Invas Ther & Allied Technol: 13.3: 156-160.
38. Gerbrands A, Albayrak A, Kazemier G. Ergonomic evaluation of the work area of the scrub nurse. Min Invas Ther & Allied Technol: 13.3: 142-146.
39. In't Hof, K. H.; van Lankeren, W.; Krestin, G.P.; Bonjer, H.J.; Lange, J.F.; Becking, W.B.; Kazemier, G. "Surgical validation of unenhanced helical computed tomography in acute appendicitis." Br.J.Surg. 91.12 (2004): 1641-45.
40. Slooff, M. J. and Kazemier G. "Living donor liver transplantation." Ned. Tijdschr. Geneeskd. 148.46 (2004): 2257-59.

CHAPTERS

Bonjer HJ, Kazemier G, Lange JF, van Erp WFM., Cuesta MA. Laparoscopic Appendectomy in The Netherlands. In *Acute Appendicitis: Standard Treatment or Laparoscopic Surgery,* Krähenbühl L, Frei E, Klaiber Ch, Büchler MW (eds), vol. 25, Karger: Basel 1998; 135-137.

Kazemier G and Lange JF. Anatomy of the Liver. In *Split Liver Transplantation*, Rogiers X, Bismuth H, Busuttil RW, Broering DC, Azoulay D (eds). Steinkopff Verlag: Darmstadt 2002; 35-45.

Bonjer HJ, Kazemier G, de Herder WW. Retroperitoneal Endoscopic Adrenalectomy. In *Minimally Invasive Endocrine Surgery*, Gagner M and Inabnet WB (eds). Lippincott Williams & Wilkins: Philadelphia 2002; 193-203.

Lange JF and Kazemier G. The Portosystemic Connections. In *Surgical Anatomy of the Abdomen*, Lange JF and Kleinrensink G-J (eds). Elsevier: Maarssen 2002; 101-106.

Kazemier G and Lange JF. Surgical Anatomy of the Liver. In *Diagnostic and Interventional Radiology in Liver Transplantation*, Bücheler E, Nicolas V, Broelsch CE, Rogiers X, Krupski G (eds). Springer-Verlag: Berlin 2003; 2-8.

Kazemier G, Steyerberg EW, Bonjer HJ. Meta-analysis of Trials Comparing Laparoscopic and Open Appendectomy. In *Laparoscopic Surgery*, Cueto-Garcia J, Jacobs M, Gagner M (eds.), McGraw-Hill Companies 2003; 295-230.

Kazemier G, Bijnen AB, Schilthuis MS. Appendicitis and Pelvic Inflammatory Disease. In *Integrated Medical and Surgical Gastroenterology*, van Lanschot JJB, Gouma DJ, Jansen PLM, Jones EA, Pinedo HM, Schouten WR, and Tytgat GNJ (eds). Bohn Stafleu Van Pochum: Houten 2004; 338-345.

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Chirurgen en assistenten heelkunde van het Erasmus MC en het MCRZ, dank voor jullie inzet om de patiënten warm te maken en te houden voor de studies en voor de operaties die jullie bij nacht en ontij moesten doen.

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Lieve Inger, jij brengt orde in mijn vaak chaotische hoofd. Zonder jou had ik dit nooit afgemaakt. En als het gips op is..... dan kom je toch gewoon lekker thuis!

CURRICULUM VITAE

Geert Kazemier werd geboren op 6 maart 1964 te Rotterdam. Na het behalen van zijn VWO diploma op het 'Eerste Vrijzinnig Christelijk Lyceum' te 's-Gravenhage in 1982, studeerde hij een jaar Civiele Techniek aan de Technische Universiteit te Delft. In 1983 begon hij zijn medische studie aan de Erasmus Universiteit te Rotterdam, waar hij in 1989 zijn artsexamen haalde. In dat jaar deed hij onderzoek onder leiding van prof. dr O.T. Terpstra en dr J.F. Lange naar het ideale sneevlak in de lever bij levende donor levertransplantatie. In 1990 werd hij AGNIO op de afdeling Heelkunde van het toenmalige Academisch Ziekenhuis Rotterdam-Dijkzigt (afdelingshoofd prof. dr J. Jeekel). In 1992 startte hij zijn opleiding tot chirurg in het toenmalige St. Clara Ziekenhuis te Rotterdam (opleider dr T.I. Yo). De opleiding zette hij vanaf 1995 voort in het toenmalige Academisch Ziekenhuis Rotterdam-Dijkzigt (opleider prof. dr H.A. Bruining, afdelingshoofd prof. dr J. Jeekel). Vanaf 1998, toen hij zijn opleiding had afgerond, werkte hij eerst als chirurg en vanaf 1999 tot heden als staflid in het inmiddels tot Erasmus MC omgedoopte Academisch Ziekenhuis Rotterdam-Dijkzigt te Rotterdam (afdelingshoofden prof. dr J. Jeekel en prof. dr H.J. Bonjer). In 1999 was hij eveneens werkzaam in de Universitätsklinikum Hamburg-Eppendorf te Hamburg in Duitsland op de afdeling Leverchirurgie (afdelingshoofd prof. dr X. Rogiers) om zich verder te bekwamen in de leverchirurgie en levertransplantaties. Sinds 2002 is hij naast chirurg ook afdelingshoofd van de afdeling OK H-gebouw van het Erasmus MC.