Acute Colonic Diverticulitis

The role of computed tomography in primary diagnosis, prediction of complications and surgical intervention

ARNAR THORISSON
Abstract

The overall aim of this thesis was to expand the current knowledge regarding the advantages and limitations of computed tomography (CT) for patients with acute diverticulitis and evaluate outpatient treatment for uncomplicated diverticulitis.

Paper I: A retrospective evaluation of 602 patients with reported uncomplicated diverticulitis. Scans were re-evaluated and the degree of inflammation was graded. Signs of complications or other diseases were also noted. No radiological findings on CT could predict the development of complications or recurrence in patients with uncomplicated diverticulitis. However, 44 patients (7.3%) had signs of complicated diverticulitis that had been overlooked on the initial assessment. Despite small complications and a non-antibiotic treatment, the majority of patients recovered without incident, further strengthening the non-antibiotic treatment strategy.

Paper II: A retrospective analysis of conservative treatment for perforated diverticulitis (n = 136) during a 5-year period. Twenty-nine of 136 patients were operated on within 24 h and not candidates for conservative management. Patients more than 75 years old, immunosuppressed patients, patients with free intraperitoneal air or free fluid in the abdominal cavity were at higher risk for emergency surgery within the first 24 h. Conservative treatment was successful in 101 of 107 patients (94%) when attempted. The presence of simultaneous abscess increased the risk for conservative treatment failure.

Paper III: The aim of this prospective study was to determine if a non-enhanced low-dose CT was as sensitive as standard CT with intravenous (IV) contrast for patients with suspected acute diverticulitis. The included patients underwent both types of CT examinations. CT images were graded by three independent radiologists for the presence of diverticulitis, complications or other findings that could explain the patient’s symptoms. Sensitivity, specificity and both intra- and inter-reader agreement for low-dose CT were very high. Therefore, we recommend this examination for suspected diverticulitis.

Paper IV: In this prospective study, 155 consecutive patients with CT-verified acute uncomplicated diverticulitis were treated as outpatients without antibiotics. Overall, only four patients (2.6%) returned to the hospital because of treatment failure, all of whom were hospitalized and received antibiotics. Outpatient treatment of uncomplicated diverticulitis is safe and recommended in selected patients.

Keywords: Colonic diverticulitis, complicated diverticulitis, computed tomography, low-dose CT

© Arnar Thorisson 2018

ISSN 1651-6206
ISBN 978-91-513-0397-0
urn:nbn:se:uu:diva-356710 (http://urn.kb.se/resolve?urn=nbn:se:uu:diva-356710)
"To be hopeful in bad times is not just foolishly romantic. It is based on the fact that human history is a history not only of cruelty, but also of compassion, sacrifice, courage, kindness. And if we do act, in however small a way, we don't have to wait for some grand Utopian future. The future is an infinite succession of presents, and to live now, as we think human beings should live, in defiance of all that is bad around us, is itself a marvelous victory."

-Howard Zinn
Illustrations
Page 14: Arnar Thorisson 2018, Figure 1: Diverticulosis of the sigmoid colon.
Page 21: Arnar Thorisson 2018, Figure 2: Diverticulitis with pericolic abscess.
Page 22: Arnar Thorisson 2018, Figure 3: Post-diverticulitis sigmoid stricture.
Page 23: Arnar Thorisson 2018, Figure 4: Postoperative status following sigma resection with anastomosis.
Page 24: Arnar Thorisson 2018, Figure 5: Pre- and postoperative Hartmann’s procedure.
This thesis is based on the following papers, which are referred to in the text by Roman numerals.


Table of contents

Introduction ................................................................................................... 11
  Background ................................................................................................ 11
  Definition ................................................................................................... 11
  Pathogenesis ............................................................................................ 12
  Classification ........................................................................................... 13
  Diagnostics ............................................................................................... 17
  Treatment ................................................................................................. 18
    Uncomplicated diverticulitis ................................................................. 18
    Complicated diverticulitis ..................................................................... 18
    Types of surgery (surgical procedures) .................................................. 20
  Follow-up ................................................................................................. 22
  Computed tomography ............................................................................. 23
    History .................................................................................................... 23
    Hounsfield units ................................................................................... 23
    Contrast media ..................................................................................... 24

Aims of the thesis.......................................................................................... 25

Materials and methods .................................................................................. 26
  Paper I ...................................................................................................... 26
  Paper II ..................................................................................................... 28
    Inclusion criteria .................................................................................. 28
    Exclusion criteria .................................................................................. 28
  Paper III .................................................................................................... 29
    Inclusion criteria .................................................................................. 30
    Exclusion criteria .................................................................................. 30
  Paper IV ................................................................................................... 30
    Inclusion criteria .................................................................................. 30
    Exclusion criteria .................................................................................. 31

Ethical considerations ................................................................................... 32

Statistical analyses ........................................................................................ 33

Results and discussion .................................................................................. 35
  Paper I ...................................................................................................... 35
  Paper II ..................................................................................................... 40
## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCR</td>
<td>American Society of Colon and Rectal Surgeons</td>
</tr>
<tr>
<td>AUD</td>
<td>Acute uncomplicated diverticulitis</td>
</tr>
<tr>
<td>AVOD</td>
<td>Antibiotika vid okomplicerad divertikulit (Swedish for “antibiotics in uncomplicated diverticulitis”)</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>CRP</td>
<td>C-reactive protein</td>
</tr>
<tr>
<td>CT</td>
<td>Computed tomography</td>
</tr>
<tr>
<td>ICD-10</td>
<td>International Classification of Diseases – 10th Revision</td>
</tr>
<tr>
<td>IV</td>
<td>Intravenous</td>
</tr>
<tr>
<td>LDCT</td>
<td>Non-enhanced low-dose computed tomography</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>mSv</td>
<td>millisievert</td>
</tr>
<tr>
<td>SDCT</td>
<td>Contrast-enhanced standard-dose computed tomography</td>
</tr>
<tr>
<td>SPSS</td>
<td>Statistical Package for the Social Sciences</td>
</tr>
<tr>
<td>VAS</td>
<td>Visual analogue scale</td>
</tr>
<tr>
<td>WBC</td>
<td>White blood cell</td>
</tr>
</tbody>
</table>
Introduction

Background
Acute diverticulitis is a common illness but diagnosing it correctly by clinical judgement alone can be difficult since patients commonly present with non-specific symptoms, such as lower abdominal pain or fever and elevated inflammatory blood markers, such as white blood cell (WBC) count and C-reactive protein (CRP) levels. Studies have shown that the diagnostic accuracy of a clinical assessment is only about 45–64% in cases of suspected diverticulitis (1–5). Therefore, patients with suspected acute diverticulitis should undergo some type of radiological examination to determine the diagnosis. A common examination method in Sweden for patients with suspected diverticulitis is computed tomography (CT) with intravenous (IV) contrast, but without per oral or rectal contrast. Ultrasound and magnetic resonance imaging (MRI) are used to a greater extent in other countries (6,7).

Radiological findings in patients with diverticulitis include colonic bowel wall thickening, diverticula in the colon and inflammation in the pericolic fat (5,8,9). Signs of complications include, but are not limited to, free air in the peritoneal cavity or presence of an abscess, fistula or rarely colonic obstruction (10).

The prevalence of diverticulitis is increasing and diverticulitis has been ranked as high as 5th or 6th in the total cost for gastrointestinal diseases (11–14).

Definition
A common finding in developed countries is colonic diverticula or small outpouchings through the colon wall (15). These diverticula are false diverticula because they do not contain all layers of the colon wall, but only the mucosal and serosa layers, in contrast to true diverticula, which contain all layers of the colon wall. This condition is called diverticulosis. Diverticulosis is a common condition and the incidence increases with age, and is seen in up to 70% of people over the age of 80 years (15–17).
In developed countries, the most common location for colonic diverticula is along the left colon; in most cases the sigmoid colon is primarily involved. Diverticulosis is less common in Asian countries where it affects the right side of the colon more frequently than the left (18).

The most frequent complication of diverticulosis is inflammation of a diverticulum, called diverticulitis, and was previously thought to affect up to 20% of patients with diverticulosis (19,20). However, more recent studies have shown that this may be overestimated. In total, only about 4–5% of patients with diverticulosis suffer from attacks of diverticulitis (21,22). Most commonly, patients suffering from acute diverticulitis have uncomplicated acute diverticulitis, as defined by the absence of abscess, free perforation, stenosis or fistula (10,23–25).

**Pathogenesis**

The colonic wall consists of an inner layer called the mucosa, followed by the submucosa, and an outer layer consisting of two layers of muscle. The inner muscle layer is circular and the outer muscle layer consists mainly of three longitudinal muscle bands along the colon, the taeniae coli. These three longitudinal bands become progressively thicker along the colon, down the sigmoid colon distally, and finally fuse in the proximal rectum.

The vasa recta are small vessels that penetrate the muscular wall to supply the underlying mucosa. These vessels penetrate the muscle layer, which causes a small area of weakness in the colon wall where colonic diverticula may form.

True diverticula of the colon involve all layers of the colon wall. However, are uncommon in white people of European ancestry, and are more common in the right colon in people of east Asian ancestry. The diverticula typically found in Western populations are false diverticula, only containing the mucosal and submucosal layers penetrating through the muscularis propria (muscle layer) at the site of the vasa recta (26), see Figure 1.
The cause of diverticulosis was thought to be increased intra-colonic pressure in the sigmoid colon secondary to hard stools and prolonged transit time (27), although this currently remains uncertain. Several studies have shown that low fibre diets, low physical activity, smoking, constipation and obesity are amongst the risk factors for the development of diverticular disease (28–30). Recent studies have not been able to confirm low fibre diet alone as a risk factor for developing diverticulosis; however, a low fibre diet along with a diet high in red meat and fat was found to be a significant risk factor by DiSiena et al. (31).

Diverticulitis was believed to be an inflammatory response secondary to impacted stools in the diverticula, but recently there have been suggestions that alterations in the colonic bacterial flora adjacent to the diverticula may play a role in the disease process (32). However, the exact pathogenesis for diverticulitis remains uncertain, despite all the recent advances in the field.

**Classification**

Diverticulitis is commonly classified into subgroups based on the presence or absence of complications. Several different types of complications can accompany an episode of diverticulitis. The most commonly complicated disease consists of a perforation with air in the abdominal cavity or a diverticular abscess. Other types of complications include fistulas, strictures or bleeding. A
diverticular fistula is an abnormal connection between the colon and an adjacent organ, and they most commonly affect the bladder, forming colo-vesical fistulas. However, fistulas may involve other organs adjacent to the colon, such as the vagina or small bowel or even reach the skin surface, resulting in a colo-cutaneous fistula. A diverticular stricture is a late complication usually occurring months or years after the initial attack of diverticulitis.

Peritonitis is an inflammation or infection of the inner lining of the abdominal cavity and can be fatal. This is a rare additional complication to primarily perforated diverticulitis or diverticular abscess where the peritoneal lining becomes infected. Patients with this condition are very ill, have severe abdominal pain and irritation, and the condition is often connected to septicaemia. Septicaemia is the spread of the infection into the bloodstream and patients with septicaemia can deteriorate very quickly.

To our knowledge, no classification system has been described specifically dividing acute uncomplicated diverticulitis (AUD) into subgroups depending on the degree of inflammation. Classification systems are rather based on differentiating uncomplicated diverticulitis from complicated disease and the sub classification of complicated diverticulitis into subgroups. Three commonly used are the Hinchey, Ambrosetti and Dharmarajan classification systems (10,33,34).

The Hinchey classification system is based on severity and type of complication secondary to diverticulitis (see Table 1). The Hinchey classification system has good clinical correlation. However, it is based on surgical findings and it has been difficult to correctly correlate this classification system to CT findings (35,36).

**Table 1.** The original Hinchey classification system of complicated diverticulitis (33).

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Pericolic abscess</td>
</tr>
<tr>
<td>II</td>
<td>Distant abscess (pelvis or retroperitoneal abscess)</td>
</tr>
<tr>
<td>III</td>
<td>General purulent peritonitis</td>
</tr>
<tr>
<td>IV</td>
<td>Faecal peritonitis</td>
</tr>
</tbody>
</table>
Several modifications have been made to correlate the Hinchey classification system better with CT findings. The most well-known was described by Wasvary et al. and is referred to as the Modified Hinchey Classification system (37). This classification system is based on two groups of uncomplicated diverticulitis and four groups of complicated diverticulitis (see Table 2).

Table 2. The modified Hinchey classification system of complicated diverticulitis (37).

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Mild clinical diverticulitis. Colonic wall thickening and pericolic fat stranding</td>
</tr>
<tr>
<td>Ia</td>
<td>Confined pericolic inflammation—phlegmon</td>
</tr>
<tr>
<td>Ib</td>
<td>Confined pericolic abscess (within sigmoid mesocolon)</td>
</tr>
<tr>
<td>II</td>
<td>Pelvic, distant intra-abdominal or intraperitoneal abscess</td>
</tr>
<tr>
<td>III</td>
<td>Generalized purulent peritonitis</td>
</tr>
<tr>
<td>IV</td>
<td>Faecal peritonitis</td>
</tr>
</tbody>
</table>

Ambrosetti et al. described a classification system that divided patients into uncomplicated and complicated diverticulitis based on CT findings with IV and rectal contrast (10) (see Table 3).

Table 3. The Ambrosetti classification system for diverticulitis (10).

<table>
<thead>
<tr>
<th>Mild diverticulitis</th>
<th>Severe diverticulitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized sigmoid wall thickening (&gt;5 mm)</td>
<td>Abscess</td>
</tr>
<tr>
<td>Pericolic fat stranding</td>
<td>Extraluminal air</td>
</tr>
<tr>
<td></td>
<td>Extraluminal contrast</td>
</tr>
</tbody>
</table>
In 2016, Ambrosetti revised his classification system to the following for CT with IV contrast to include chronic complications such as fistula or stenosis (see Table 4).

**Table 4.** Ambrosetti—revised CT classification (38).

<table>
<thead>
<tr>
<th>Classification</th>
<th>CT performed with IV contrast and water-soluble rectal contrast</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Uncomplicated acute diverticulitis</td>
</tr>
<tr>
<td></td>
<td>Site: proximal or distal descending colon/proximal or distal sigmoid</td>
</tr>
<tr>
<td></td>
<td>Length of inflammation (cm)</td>
</tr>
<tr>
<td></td>
<td>Inflammation of pericolic fat—phlegmon</td>
</tr>
<tr>
<td>2</td>
<td>Complicated acute diverticulitis (classification 1 + one or more of the following findings):</td>
</tr>
<tr>
<td></td>
<td>Contrast extravasation: mesocolic/peritoneal</td>
</tr>
<tr>
<td></td>
<td>Free air: mesocolic/pericolic/at distance (maximum diameter in cm)</td>
</tr>
<tr>
<td></td>
<td>Free fluid: mesocolic/peritoneal (volume in mL)</td>
</tr>
<tr>
<td>3</td>
<td>Complicated chronic diverticulitis</td>
</tr>
<tr>
<td></td>
<td>Fistula</td>
</tr>
<tr>
<td></td>
<td>Stenosis</td>
</tr>
</tbody>
</table>

In 2011, Dharmarajan et al. described a CT classification system for complicated diverticulitis with strong correlation to the need for emergency surgery for stage 4 (34) (see Table 5).

**Table 5.** The Dharmarajan classification system of complicated diverticulitis (34)

<table>
<thead>
<tr>
<th>Stage 1</th>
<th>Localized free air (mesocolic) without abscess</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 2</td>
<td>Collection of free air (&lt;2 cm) or abscess (&lt;4 cm)</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Collection of free air (&gt;2 cm) or abscess (&gt;4 cm)</td>
</tr>
<tr>
<td>Stage 4</td>
<td>Free air with non-loculated free fluid in the peritoneal cavity</td>
</tr>
</tbody>
</table>

Thus, several classification systems have been described for acute diverticulitis. However, all focus on the differentiation of uncomplicated disease from complicated disease and the division of complicated diverticulitis into subgroups based on severity. Some complications, such as venous thrombosis, are not dealt with at all.
Studies have shown that the most reliable of the above, with regards to inter-observer differences, are the Ambrosetti, Dharmarajan and modified Hinchey classifications systems with inter-observer $\kappa$ values of 0.83, 0.76 and 0.72, respectively (39).

### Diagnostics

Commonly presented clinical symptoms for patients with acute diverticulitis are lower left abdominal pain, elevated WBC count, CRP and fever. However, these findings are not specific for diverticulitis. Toorenvliet et al. showed that the clinical assessment of patients with suspected AUD has low accuracy and is thus unreliable (40). Other studies have found the clinical diagnosis of acute diverticulitis to be correct in only 43–64% of the cases (3–5). Therefore, this patient group needs radiological evaluation to either confirm or exclude the diagnosis and stage the disease when present.

The radiological examinations that can be used to diagnose diverticulitis are barium or water-soluble contrast enema, CT, ultrasound and MRI. Contrast enema can be used in acute settings with water-soluble contrast instead of barium in case colon perforation is present. This method has a highly accurate diagnostic value, but has largely been replaced by CT. Early reports on the diagnostic accuracy of CT favoured barium enemas (41), but CT technology has since greatly evolved and studies have shown CT to have near 100% diagnostic accuracy for diverticulitis (4,5,42). The limitations of barium enemas are that the technique cannot show disease outside of the colon, is unpleasant for the patient and is considered an invasive procedure.

Ultrasound has been shown to be as sensitive as CT and is used as the first-line examination for patients with suspected diverticulitis in several countries, including Germany (6,7). The primary advantages of ultrasound are its low cost and no ionizing radiation to the patient. However, although ultrasound is readily available and inexpensive, it is largely operator-dependent. Therefore, its availability in experienced hands is often limited.

The examination of choice in Sweden is CT with IV contrast, but without per oral or rectal contrast, in part because of its accessibility and that CT has been shown to be extremely accurate for diagnosing diverticulitis (4,5).

CT findings in AUD include colon wall thickening >5 mm, visible colonic diverticula and adjacent pericolic inflammation (5,8,9). CT findings of complicated diverticulitis include signs of AUD plus one or more of the following: abscess, non-loculated free fluid, free air or rectal contrast material in the per-
itoneal cavity (10). Other complications include colonic stricture after a previous diverticulitis episode and fistula, which is a connection to other adjacent organs, most commonly the bladder, vagina or skin.

Treatment

Uncomplicated diverticulitis
The traditional treatment for AUD comprises hospitalization, bowel rest and IV antibiotics (43,44). However, this has slowly been changing in recent years. In a multicentre, randomized, controlled trial, Chabok et al. showed that antibiotic use in AUD did not decrease the complication rate or frequency of recurrence (45). Patients with uncomplicated diverticulitis can be treated as outpatients with antibiotics instead of being hospitalized (46–50) with a readmission rate of about 2.5% (51–53). A recent meta-analysis showed no difference in complication rate, hospital re-admission, duration of hospital stay, surgical intervention or disease relapse for patients with AUD regardless of antibiotic treatment (54).

Despite evidence that the outpatient management of patients with uncomplicated diverticulitis is safe, the majority of patients hospitalized for diverticulitis have AUD (12,15,25,55) and antibiotic use for uncomplicated diverticulitis remains widespread, both in the United States and Europe (56,57). However, this may be slowly changing, as recent guidelines for treatment of diverticulitis no longer recommend antibiotics for uncomplicated diverticulitis, but rather that antibiotic treatment should be evaluated on an individual basis (58).

Complicated diverticulitis
The preferred treatment for complicated diverticulitis is also somewhat controversial, although surgical intervention is often required. However, the type of surgery performed depends on the severity of complications and loco-regional practices. Perforated diverticulitis with free air and free fluid requires a more aggressive treatment. In most cases, an operation with the removal of the diseased colon segment, if possible.

Guidelines from the American Society of Colon and Rectal Surgeons (ASCR) for complicated diverticulitis recommend drainage and antibiotic treatment with elective surgery for Hinchey grades I and II (59). However, other guidelines recommend resection surgery only in cases with Hinchey grade II (33). The common theory is that the elective surgical removal of the involved colon segment will reduce the risk for recurrent disease with abdominal or pelvic
sepsis by more than 40% (9,60). However, this theory is based on small retrospective studies.

Attempts have been made to classify diverticular abscesses based on size. A commonly used cut-off is 5 cm, that is, abscesses in patients without severe clinical status and an abscess of <5 cm can be managed medically, while abscesses ≥5 cm should be drained either percutaneously or surgically (61), see Figure 2. Late complications consist of fistulas and strictures, see Figure 3. The most common fistulas to occur after diverticulitis are colo-vesical (to the urine bladder), colo-ental (to another bowel segment), colo-cutaneous (to the skin), and in women, colo-vaginal fistulas can occur.

**Figure 2:** Sigmoid diverticulitis with a pericolic abscess and enlarged mesenteric lymph nodes.
Figure 3: A late complication of diverticulitis, post-inflammation colonic stricture of the sigmoid colon with lumen narrowing, muscle wall hypertrophy and scarring of the colonic wall and mesocolon.

Types of surgery (surgical procedures)

In patients with complicated diverticulitis, the four most common types of surgery are: Hartmann’s procedure, laparoscopic lavage, segmental colonic resection with primary anastomosis and proximal colostomy with a secondary segmental resection performed later.

Sigmoid resection consists of removing the diseased segment of the colon and connecting the proximal part to the top of the rectum with or without a diverting stoma (see Figure 4). Hartmann’s procedure involves the removal of the diseased sigmoid segment, a left colostomy (often permanent) and closure of the rectal stump (see Figure 5). Laparoscopic lavage involves gaining access to the peritoneal cavity via laparoscopy and then cleaning the peritoneal cavity with large amounts of saline until all visual faecal/infected material has been removed (59,62–64). The fourth type of surgical procedure is to suture the perforation combined with abscess drainage and a diverting proximal colostomy. This can be performed when resection of the involved colonic segment is assessed to be difficult technically or contraindicated because of the patient’s general condition.
Optimal emergency surgical procedure is still debated as recent randomized studies have given conflicting results; a study by Thornell et al. (65) favoured laparoscopic lavage over Hartmann’s operation because of fewer complications, while Schultz et al. found fewer complications for Hartmann’s operation (63). A more recent multicentre study in Scandinavia evaluated laparoscopic lavage versus sigma resection in patients with perforated diverticulitis, with no significant differences in disease-related 1-year mortality or severe complications (66).

A conservative approach without surgical intervention has been proven to be safe in the majority of patients with complicated diverticulitis because of pericolic extraluminal air (67,68). However, this approach should only be considered in otherwise healthy patients with mild clinical status.
Recurrence of diverticulitis is common and seen in 5–20% of cases, with most recurrences within the first year (69,70). However, recent research has shown the likelihood of disease relapse decreases with each new episode of diverticulitis. This has in turn led to the disregard of previous recommendations for elective colonic segmental resection after two episodes (71).

Based on previous reports by Stefansson et al., a follow-up colonoscopy or CT-colon is routinely performed within three months after the initial case of diverticulitis to exclude colon adenocarcinoma (72,73). This recommendation remains uncertain as some more recent studies have shown that it is only safe to investigate further patients seen with complicated disease on CT or with uncertain inflammatory findings (74–76). De Vries et al. found that the incidence of colon adenocarcinoma in patients with previously uncomplicated diverticulitis was about 1%, the same as the frequency found during routine screening in asymptomatic individuals (74). The radiologist can be a factor determining the selection of patients who need to have further follow-up (77). However, other studies have shown that further investigation in this patient group is needed as both Granlund et al. and Grahnat et al. found a high incidence of colon cancer during the first year of follow-up after an episode of diverticulitis.
diverticulitis (78,79). This may be the result of a primary misdiagnosis because differentiation between diverticulitis and colonic adenocarcinoma is often difficult using CT, with a known considerable overlap between the CT findings for these two conditions instead of a causative link between diverticulitis and colonic carcinoma.

Computed tomography

History

CT was developed in the late 1960s and early 1970s with the first CT being installed at the Atkinson Morley Hospital (Wimbledon, London, United Kingdom) in September of 1971 (80). This scanner was only able to scan heads and was unable to examine the thorax or abdomen. The first patient ever to have their head examined by CT was imaged on 1st October 1971, at Atkinson Morley Hospital and this imaging was reported in Radiology by Hounsfield et al. (81). Using the first CT scanner, one slice with a resolution of $50 \times 50$ pixels took about 5 min to acquire; however, using current scanners a $512 \times 512$ resolution matrix of the entire head volume can be completed in a couple of seconds. Despite never having collaborated together and not knowing each other, Dr Godfrey Hounsfield and physicist Allan M. Cormack (University of South Africa) received the Nobel prize in medicine 1979 for the invention of CT (82,83). Cormack had developed mathematical calculations that allowed for the computation of data required for the development of CT, while Hounsfield had done work in developing the first CT scanner.

Hounsfield units

A CT image is a grey-scale image that ranges from pitch black to bright white. All CT scanners have scales with assigned values in which pure air is black on CT and measures –1000 Hounsfield units (HU), water is grey and measures 0 HU, while sclerotic cortical bone is very white and measures +1000 HU. Other organs are scaled in between and most parenchymal organs measure from about +30 to + 100 HU depending on water content and tissue density (84). In simplified terms, one can think of the darkness of an image as directly related to the density of the tissue or substance imaged. Air allows all radiation to pass without any absorption, which results in a dark pixel on the image. The denser a tissue is, the more radiation it absorbs, leaving less radiation to get through to the detector and thus less radiation to “turn the film from white to black”. In other words, the denser an item is, the whiter it will be on CT.
Contrast media

IV: CT for parenchymal organs is greatly assisted by IV contrast medium and is needed to evaluate parenchymal lesions. IV contrast is iodine based and works by increasing the radiation absorption of organs in a manner consistent with blood perfusion. IV contrast is necessary for evaluation, detection and characterization of intraparenchymal lesions, such as liver lesions, because these lesions are often of similar density to normal liver parenchyma and thus cannot be detected on non-enhanced CT. Contrast medium helps to detect these lesions by exploiting the difference in contrast uptake compared with normal liver parenchyma. Some lesions are hypervascular, that is, they take up contrast faster than normal parenchyma and are brighter on arterial and often venous phase contrast-enhanced CT than the surrounding liver tissue. Other lesions may be hypovascular, taking up less contrast than liver parenchyma, or avascular, taking up no contrast at all. These lesion characteristics help differentiate different types of parenchymal lesions. IV contrast is also useful in differentiating abscesses from adjacent small bowel or otherwise free fluid in the peritoneal cavity. Here, the contrast medium is concentrated in the abscess capsule, which shows often vivid contrast enhancement.

Per oral: A diluted iodine-based contrast medium can be used orally, usually consisting of intake of 1000 mL solution over 2 h. This is done to opacify the lumen of primarily the small intestine, helping to detect intraluminal lesions and to help differentiate small bowel from, for example, an abscess. This is now seldom used in the acute setting at our hospital as it delays scanning time by 2 h and is seldom required to make acute diagnoses.

Rectal contrast can be used for specific examination of the large bowel, primarily looking for fistulas to adjacent organs. This is seldom done at our hospital, but when required, the same diluted iodine-based solution is infused rectally at an amount of about 500 mL. This is usually sufficient to distend the large bowel lumen and help diagnose strictures, fistulas and occasionally malignancy.
Aims of the thesis

The overall aim of this thesis is to improve knowledge of the benefits and limitations of CT in patients with acute diverticulitis, and to evaluate outpatient treatment for patients with CT-verified uncomplicated diverticulitis without antibiotics.

**Paper I**
The aim of the first study was to evaluate whether CT findings in patients with uncomplicated diverticulitis could predict development of complications or recurrence of disease, and to evaluate the accuracy of previous CT findings.

**Paper II**
The aim of the second study was to describe characteristics and results for non-operative management of patients with perforated diverticulitis.

**Paper III**
The aim of the third study was to evaluate diagnostic accuracy for a non-enhanced low-dose CT protocol as a method for primary investigation of patients with suspected acute diverticulitis.

**Paper IV**
The aim of the fourth study was to evaluate the safety and feasibility of outpatient management without antibiotics in patients with CT-verified AUD.
Materials and methods

Paper I

The AVOD study (Antibiotika vid okomplicerad divertikulit, Swedish for “antibiotics in uncomplicated diverticulitis”) was a multicentre, randomized study involving 10 centres in Sweden and one centre in Iceland, which was conducted between 2003 and 2010 (45). In short, 623 patients that had received a diagnosis of left-sided AUD based upon clinical or CT findings, or both, were included. The patients were randomized to treatment with (314 patients) or without (309 patients) antibiotics (45).

In 2012, CT images were retrieved from the participating hospitals and re-evaluated by two independent radiologists. The radiologists were blinded to the CT assessments conducted by their colleague, as well as patient outcome and previous CT findings. Several different types of CT examinations had been conducted in the study population, presumably because of different hospital routines, the various ages of patients and use of contrast material. Most commonly, a portal venous phase CT with IV and per oral contrast reformatted to a 5-mm slice thickness was performed.

All CT images were re-evaluated and all measurements were conducted with a Sectra RIS and PACS system (IDS7 RIS, version 14.2) and PACS (version 4.3.1; Sectra Imtec AB, Linköping, Sweden).

The CT images were reviewed and assessed for signs of diverticulitis (diverticula, colonic wall thickening >5 mm, pericolic fat stranding (5,8,9)) and several factors related to the degree of inflammation (see Table 6 and Figure 6).
Table 6. Study I CT checklist

- **Contrast:**
  - IV or per oral

- **Diverticula:**
  - Location, size and presence of faecoliths

- **Colon wall at site of inflammation**
  - Length of segment involved, wall thickness and symmetry
  - Lumen narrowing at site of inflammation
  - Involved colon segment

- **Pericolic inflammation**
  - Size of pericolic inflammation in cm² and mean density measured in HU.
  - Length of inflammation from colon wall

- **Abscess or extraluminal air**
  - Presence, size and location

- **Local or paraaortic lymphadenopathy**

- **Other findings**
  - Free fluid
  - Secondary inflammation such as inflammation of adjacent small bowel
  - Secondary findings

![CT image](image)

**Figure 6:** CT of colonic diverticulitis in the sigmoid colon, the picture on right showing measurement of pericolic fat inflammation. Both area of inflammation in cm² and mean HU were measured.

Data from CT images were then correlated to clinical data such as complications, recurrence of disease, temperature, CRP, WBC, age and gender for statistical analysis.
Paper II

Paper II was a retrospective study, which involved examination of medical records for all patients treated for diverticulitis at Västmanland Hospital Sweden during a 5-year period from 1st January, 2010 through to 31st December 2014. Medical records were evaluated for clinical signs of complications, CT reports describing complicated diverticulitis or annotations classifying the patient as having complicated diverticulitis according to International Classification of Diseases, 10th Revision (ICD-10). All patients with medical records indicating they had suffered from a case of complicated diverticulitis during the period involved were included for CT re-evaluation regardless of type of complication specified in the medical records. All CT examinations were re-evaluated for signs of complicated diverticulitis and classified according to the severity and type of complication present. Patients with diverticular abscess only, signs of perforation, but no definitive signs of diverticulitis, and complicated diverticulitis because of fistulas or strictures were excluded. Patients with a primary diagnosis of diverticulitis, later found to have colonic adenocarcinoma at follow up were excluded.

Inclusion criteria

• Hospitalization for diverticulitis (ICD-10 K57) from 1st January 2010 to 31st December 2014.

Exclusion criteria

• Uncomplicated diverticulitis.
• Free intraabdominal air, pericolic air and/or abscess without definitive findings of diverticulitis.
• Diverticular abscess without perforation.
• Fistula or stricture secondary to diverticulitis.

Medical records were reviewed and the patient’s sex, age, WBC, CRP levels, temperature, duration of presenting symptoms and episodes of previous diverticulitis were registered. Also, what type of treatment the patient received, if surgical intervention was required and what type of surgical intervention was performed.

Emergency surgical intervention was defined as surgery during the first hospital stay. Elective surgery was also noted and registered separately. Patients operated on within 24 h were treated as a separate group and analysis was conducted using patients that were treated primarily using a conservative treatment approach.
CT images were re-evaluated and assessed for signs of diverticulitis; diverticula, colonic wall thickening >5 mm and pericolic fat stranding (5,8,9). The length of the involved colonic segment was measured, the part of the colon involved was noted, and the presence, amount and localization of free air noted. Signs of other complications were also assessed.

Median follow up was 58 months ranging from 0 to 92 months and disease recurrence was noted.

**Paper III**

Paper III was a multicentre, prospective study in which patients with suspected acute diverticulitis were examined using two types of CT protocols. Patients from two hospitals were included in the study: that is, Region Västmanland Hospital in Västerås and Mora Lasarett in Mora, Northern Dalarna County Sweden.

Patients seeking medical attention at the emergency room with clinical symptoms suspicious for diverticulitis and were scheduled to undergo CT for confirmation were asked to participate in the study. If the patient accepted, they first underwent a non-enhanced low-dose CT (LDCT) protocol followed by a contrast-enhanced standard-dose CT (SDCT) protocol. Both CT protocols were conducted without per oral or rectal contrast.

In this study, even though prospective, it was not possible to randomize the patients to undergo one or other of the two CT examinations. The reason for this is that the accuracy of the clinical diagnosis in suspected acute diverticulitis is low, which would result in an unknown number of true cases in the study group examined by the LDCT protocol.

Three independent radiologists blinded to clinical data reviewed and analysed both CT examinations from all participants (two abdominally-oriented consulting specialists and a fourth-year radiology resident). First, each radiologist graded and classified all LDCT examinations for signs of diverticulitis, complications or other reasons for the patient’s symptoms if no signs of diverticulitis were present. At a later date, to reduce recall bias, all SDCT examinations were reviewed and graded using the same protocol. All radiologists were blinded to patient outcome, previous CT findings and each other’s findings. Abscess size cut-off was placed at 15 mm because of the inability to differentiate on standard CT between small abscesses and an inflamed fluid filled diverticulum in selected cases, as well as the reasoning that abscesses of this size are seldom clinically relevant (34,50,85).
Inclusion criteria

- Clinical suspicion of acute colonic diverticulitis.
- CRP level above 25 mg/L and/or WBC count above $10 \times 10^9$ g/L.
- Age >50 years.

Exclusion criteria

- Pregnancy.
- Renal failure, allergy or other cause of not being able to receive contrast medium.
- Language barrier, dementia or other reason why informed consent was not possible.

All CT examinations were conducted using 64 slice General Electric Optima CT660 systems. Participants received individualized doses of IV contrast medium based on height, weight and age using contrast dosage calculations performed in OmniVis software (General Electric), and all patients received Omnipaque (General Electric) contrast medium. Scan delay time after contrast injection was also individualized using a smart preparation technique with a region of interest in the abdominal aorta.

Radiation doses were registered and calculated for both CT protocols using the dose length product (DLP) given on the CT report multiplied by 0.015 to approximate the patients’ dosage in mSv (86).

Paper IV

Paper IV was a prospective, observational study involving two Swedish hospitals, Västmanlands Hospital in Västerås and Mora Hospital in Northern Dalarna County. Patients presenting at the emergency department with suspected acute diverticulitis were screened for potential eligibility.

Inclusion criteria

- Adult 18 years or older.
- Acute lower abdominal pain with duration of less than 3 days.
- Elevated CRP or WBC.
- Signs of uncomplicated acute diverticulitis on CT.
- Informed written consent.
Exclusion criteria

- High fever, affected general condition, peritonitis or septicaemia,
- Pain requiring IV or subcutaneous pain medication.
- Immunologically compromised patient.
- Ongoing antibiotic therapy for another disease.
- Pregnancy, dementia or language barrier.
- Unable to take care of themselves at home.

Diverticulitis was classified radiologically as uncomplicated when there were no signs of perforation, abscess, fistula or colonic obstruction (10). Outpatient management was defined as being discharged directly from the emergency department or within 24 h if patients were admitted while waiting for a CT examination to be performed.

Participants completed a day journal questionnaire including pain score on a visual analogue scale (VAS), body temperature, oral intake of food and liquids, bowel habits and use of pain medication with the recommendation of paracetamol. Fluid intake for the first 48 h was recommended, followed by a liquid diet before moving on to a solid diet when tolerated. This information was explained to participants both orally and in written form. Participants were contacted daily by a nurse by telephone to assess patient well-being and all participants had physician visits after 3 months. Blood samples were taken for evaluation on day 1 and day 7. All patients underwent colonoscopy or CT colonography three months after the initial diverticulitis episode to exclude colonic malignancy as is standard practice with diverticulitis at our centre.

All CT images of patients included in the study were re-evaluated later and graded with the same protocol as in Study I, which focuses on the presence/grade of diverticulitis, signs of complications and other causes of abdominal pain.
Ethical considerations

**Paper I**
The study protocol was approved by the local ethics committee in Uppsala and followed the Declaration of Helsinki guidelines (Dnr 02-180), ClinicalTrials.gov registration number NCT01008488.

**Paper II**
The study protocol was approved by the local ethics committee in Uppsala and followed the Declaration of Helsinki guidelines (Dnr 2015/213).

**Paper III**
In this study, the participant was exposed to an extra radiation dose compared with non-participants in the study. This extra radiation dose was because of the extra CT examination with the non-enhanced LDCT protocol. This radiation dose was estimated to be about 3 mSv per participant, which is slightly higher than the background radiation exposure during a 1-year period for a person living in Sweden, which amounts to approximately 2.1 mSv (87). Because of this extra radiation, patients <50 years old were excluded. The study protocol was approved by the local ethics committee in Uppsala and the local Swedish Radiation Safety Authority. This study followed the Declaration of Helsinki guidelines (Dnr 2016/411), ClinicalTrials.gov registration number NTC03443011.

**Paper IV**
The study protocol was approved by the local ethics committee in Uppsala and followed the Declaration of Helsinki guidelines (Dnr 2013/433), ClinicalTrials.gov registration number NCT01515150.
Statistical analyses

Paper I
A Pearson chi-squared ($\chi^2$) test was used for categorical variables and a Mann–Whitney $U$ test was used for ordinal data and for data without normal distribution. A Student $t$ test was used for data with normal distribution. Statistical significance was set at $P < 0.05$, two-sided tests. All statistical analyses were performed using IBM SPSS (Statistical Package for the Social Sciences) Statistics for Windows (version 20.0; IBM Corp., Armonk, NY, USA).

Weighted $\kappa$ statistics were used to evaluate the rate of agreement between radiologists. Agreement was regarded as poor if $\kappa \leq 0.2$, fair if $\kappa = 0.21–0.4$, moderate if $\kappa = 0.41–0.60$, good if $\kappa = 0.61–0.80$ and excellent if $\kappa \geq 0.80$ (88).

Paper II
Pearson’s $\chi^2$ test was used for discrete variables and a Student $t$ test was used for data with normal distribution. A Mann–Whitney $U$ test was used for ordinal data and for data without normal distribution. Statistical significance was set at $P < 0.05$, two-sided tests (StatXact version 7; Cytel). Statistical analyses were conducted using IBM SPSS Statistics for Windows (version 24.0; IBM Corp., Armonk, NY, USA).

Paper III
Power calculations were based on the confidence interval (CI) width for sensitivity without consideration for specificity. Using an anticipated sensitivity of 0.95 for the non-enhanced low-dose CT protocol and a half CI of 0.03 a total of 104 patients with diverticulitis were needed. Presuming a clinical accuracy of 65% and 10% drop out revised the total required to 176 patients. However, admission protocols noted presence of diverticulitis on admission CT and these numbers were followed regularly, and study inclusion was discontinued when a sufficient number of patients with diverticulitis had been included. Inter- and intra-observer correlation was assessed using weighted $\kappa$ calculations. $\kappa$ values were graded according to same criteria as used in Paper I (88).
A two-sided $P < 0.05$ was considered statistically significant. All statistical analyses were conducted using IBM SPSS Statistics for Windows (version 24.0; IBM Corp., Armonk, NY, USA).

**Paper IV**

A re-admission rate of 2.5% is expected for patients with AUD treated with antibiotics and managed as outpatients (51-53). Without antibiotic therapy and outpatient management, we predicted a re-admission rate of 7.5%. A sample size of 134 patients was calculated with an $\alpha$ of 5% and power of 80%. A total sample size of 161 patients would be needed with an anticipated drop-out rate of 20%.

Data were analysed using IBM SPSS for Windows (version 19; IBM Corp., Armonk, NY, USA). Differences in proportions were calculated using a $\chi^2$ test or a Student $t$ test for independent samples. Unpaired numerical data were analysed using a Mann–Whitney $U$ test. A Fisher exact test was used for low numbers. $P < 0.05$ was considered significant.
Results and discussion

Paper I

Of the 623 patients included in the AVOD study, 602 CT images could be obtained for re-evaluation. Findings consistent with acute diverticulitis were found in 574 patients (95%). During the early part of the AVOD study, some patients that had no conclusive CT findings for diverticulitis were included as this was not an initial inclusion criterion (only clinical suspicion). However, CT-confirmed uncomplicated diverticulitis as an inclusion criterion was added quickly. This may explain, at least in part, why not all CT images had findings consistent with diverticulitis.

After re-evaluation of the CT images, 44 patients were found to have signs of complications on their admission CT that had been overlooked. Twenty-seven had varying amounts of extraluminal pericolic or free air and seventeen had an abscess (see Figure 7). Inter-observer reliability between radiologists was very good ($\kappa = 0.84$) with regards to the presence or absence of complications.

![Figure 7: Perforated diverticulitis in the descending colon. Extraluminal pericolic air (arrow) is seen medical to the inflamed colon segment.](image-url)
Patients with acute complicated diverticulitis had higher levels of WBC, CRP and inflammatory parameters on CT compared with patients without complications (see Table 7).

**Table 7.** Comparison of clinical, laboratory and radiological data in acute uncomplicated vs acute complicated diverticulitis

<table>
<thead>
<tr>
<th></th>
<th>Uncomplicated diverticulitis n = 530</th>
<th>Complicated diverticulitis n = 44</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum CRP (mg/L)</td>
<td>93 (57)</td>
<td>128 (75)</td>
<td>0.001</td>
</tr>
<tr>
<td>WBC ($\times 10^9$/L)</td>
<td>12.3 (2.9)</td>
<td>13.6 (4.1)</td>
<td>0.009</td>
</tr>
<tr>
<td>Pericolic inflammation (ROI average greater than 0 HU)</td>
<td>60 (11.4%)</td>
<td>10 (22.7%)</td>
<td>0.025</td>
</tr>
<tr>
<td>Maximal colonic wall thickness (mm)</td>
<td>9.5 (2.3)</td>
<td>9.7 (1.9)</td>
<td>0.409</td>
</tr>
<tr>
<td>Size of inflammation in pericolic fat (cm²)</td>
<td>10.9 (5.9)</td>
<td>14.8 (8.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Length of pericolic inflammation (cm)</td>
<td>5.8 (1.8)</td>
<td>7.0 (1.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Operation during primary hospital stay</td>
<td>2 (0.37%)</td>
<td>2 (4.5%)</td>
<td>0.001</td>
</tr>
<tr>
<td>All operations</td>
<td>7(1.3%)</td>
<td>4(9.1%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>VAS pain score</td>
<td>6 (4–8)</td>
<td>7 (5–8)</td>
<td>0.192</td>
</tr>
<tr>
<td>Palpation tenderness</td>
<td>3 (2–3)</td>
<td>3 (2–3)</td>
<td>0.217</td>
</tr>
<tr>
<td>Recurrent diverticulitis</td>
<td>80 (16.0%)</td>
<td>5 (12.8%)</td>
<td>0.600</td>
</tr>
</tbody>
</table>
Late complications were classified as recurrence of diverticulitis within 1 year and/or the need for elective or emergency surgery. Of the 574 patients with confirmed diverticulitis on re-evaluation, 500 remained at the 1-year follow-up. Within the 1-year follow-up, 80 had a recurrent episode of diverticulitis (16%). Comparisons of clinical and radiological parameters between these two patient groups showed no significant differences (see Table 8).

**Table 8.** Comparison of clinical, laboratory and radiological data for patients with acute diverticulitis at 1-year follow-up.

<table>
<thead>
<tr>
<th></th>
<th>No recurrent diverticulitis</th>
<th>Recurrent diverticulitis</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 420</td>
<td>n = 80</td>
<td></td>
</tr>
<tr>
<td>Serum CRP (mg/L)</td>
<td>94 (58)</td>
<td>86 (52)</td>
<td>0.257</td>
</tr>
<tr>
<td>WBC ($\times 10^9$/L)</td>
<td>12.3 (2.9)</td>
<td>12.3 (2.6)</td>
<td>0.932</td>
</tr>
<tr>
<td>Pericolic inflammation (ROI average greater than 0 HU)</td>
<td>48 (11%)</td>
<td>10 (13%)</td>
<td>0.431</td>
</tr>
<tr>
<td>Presence of free fluid</td>
<td>158 (38%)</td>
<td>36 (45%)</td>
<td>0.220</td>
</tr>
<tr>
<td>Maximal colonic wall thickness (mm)</td>
<td>9 (2.2)</td>
<td>10 (2.5)</td>
<td>0.245</td>
</tr>
<tr>
<td>Size of inflammation in pericolic fat (cm²)</td>
<td>10.8 (5.8)</td>
<td>11.0 (6.8)</td>
<td>0.802</td>
</tr>
<tr>
<td>VAS</td>
<td>6 (4–8)</td>
<td>6 (4–8)</td>
<td>0.385</td>
</tr>
<tr>
<td>Palpation tenderness</td>
<td>2 (2–3)</td>
<td>2 (2–3)</td>
<td>0.636</td>
</tr>
<tr>
<td>Temperature C°</td>
<td>38.1 (0.60)</td>
<td>38.1 (0.69)</td>
<td>0.712</td>
</tr>
</tbody>
</table>
There were no specific CT findings that could predict complications or recurrence in AUD. However, a limiting factor is the small number of patients that progressed from uncomplicated diverticulitis to complicated disease. Of the 623 patients included in the AVOD study, only nine patients developed clinically apparent complications, of which four had signs of complication overlooked on admission CT. Four of these patients had uncomplicated disease on admission CT and one CT examination was not available for re-evaluation. Thus, only a confirmable four of 602 (0.7%) patients progressed from AUD to complicated disease, resulting in low statistical power.

A total of 44 patients (7.6%) had CT signs of either an abscess or extraluminal air. An explanation for the high rate of missed complications is that the AVOD study started in 2003, and, at that time, CT of the abdomen in patients with suspected diverticulitis was not routine. Therefore, the radiologists may have had less experience in assessing and grading diverticulitis than radiologists currently do when CT is routinely performed in this patient group.

Despite having complicated diverticulitis and regardless of antibiotic therapy, the clear majority of patients recovered without further treatment (see Figure 8). Only four of these 44 patients with unobserved complications on CT developed clinically apparent complications (9.1%). These findings further support the non-antibiotic strategy for treating AUD.
Since publication of this study, van Dijk et al. similarly reported a retrospective evaluation of all CT of patients from a previous prospective, multicentre study to find predictive factors for development of complications. That study was conducted including the measurements suggested in our report (89). van Dijk et al. found that patients that progressed to complicated disease after an initial uncomplicated diverticulitis did have a longer inflamed colon segment and were more likely to have free fluid in the peritoneal cavity. However, as with our study, the limitations were that very few patients with uncomplicated diverticulitis progress to complicated disease. van Dijk et al. evaluated all 528 patients from the DIABOLO study and only a total of 16 (3%) progressed from uncomplicated diverticulitis to complicated disease.

In conclusion, our findings support previous studies suggesting less invasive treatment of acute complicated diverticulitis is safe (67,90).
Paper II

During the 5-year period in question, 1188 patients had been treated for a total of 1353 episodes of diverticulitis at our hospital. Examination of medical records for this group found a total of 223 patients had been treated for complicated diverticulitis, of which 143 had been treated for perforated diverticulitis according to medical records. Two duplicate cases were identified and the later hospitalization for each patient was excluded (see Figure 9).

![Flowchart showing study population for Study II](image)

**Figure 9.** Flowchart showing study population for Study II

A total of 141 patients was found with medical records indicating hospitalization for perforated diverticulitis during the period involved. CT for all 223 patients with complicated disease according to medical records was re-evaluated regardless of type of complication stated. On re-evaluation of CT examinations, a total of 136 were confirmed as cases of perforated diverticulitis with or without a simultaneous abscess.

The patients’ median age was 60 years, ranging from 20 to 92 years with a male-to-female ratio of 1.4:1. A total of 80 men and 56 women were included.
The incidence of perforated diverticulitis found in our study was 10.4 per 100,000 population per annum, a number significantly higher than previously reported, which commonly has been reported between 3.0 and 4.0 per 100,000 population per annum (91–93). This difference may be explained by the fact that at our hospital almost all patients with suspected diverticulitis undergo CT examination, which allows for patients with subtle complicated disease on CT, but no clinical signs of complications to be detected, who might not undergo radiology at other centres.

Twenty-nine patients required surgical intervention within 24 h and were not candidates for conservative treatment. Non-operative management was attempted in 107 cases and successful in 101 (94%). Eight patients later underwent elective surgery, bringing the total of patients requiring surgical intervention to 43 (32%).

Univariate analysis comparing patients that underwent direct surgery with those who were treated using a conservative approach showed that patients whom required acute surgical intervention were more commonly >75 years, immunosuppressed, more likely to have free fluid in the abdominal cavity, and more often had free intraperitoneal air than extraluminal pericolic air only. Neither sex, CRP levels, WBC nor temperature varied between the groups.

Patients that attempted conservative management but required surgical intervention were more likely to have a simultaneous abscess compared to patients whom were treated successfully non-operatively (see Table 9).

Four patients died in hospital (mortality 3%) of whom three (2%) had underwent acute surgical intervention and one patient was not considered a candidate for surgery because of comorbidity secondary to cardiovascular disease. Thirty-day mortality was 4% (five patients) and 90-day mortality was 6% (eight patients). Three of these eight patients had end-stage cancer not related to the gastrointestinal tract.

In our study, only about one in four patients (26%) required emergency surgical intervention, which reflects the conservative approach to surgical intervention often practiced in Sweden. When attempted, a conservative approach was successful in 94% of cases, which is consistent with other recent studies where the majority of patients with pericolic gas only can be managed conservatively.

Out of the 32 patients with free air in the abdominal cavity, 11 (34%) were treated conservatively without any surgical intervention. These patients were managed successfully with hospitalization and antibiotics.
In conclusion, perforated diverticulitis is often a surgical emergency. However, when appropriate, conservative management is possible in the majority of patients. However, immunocompromised patients, and patients with a simultaneous abscess should be monitored closely as they have a higher incidence of conservative treatment failure.

**Table 9.** Comparison of clinical, laboratory, radiological and follow-up data in patients treated conservatively for perforated diverticulitis in Västmanland between 2010 and 2014.

<table>
<thead>
<tr>
<th></th>
<th>Conservative treatment failure n = 6</th>
<th>Successful conservative treatment n = 101</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>60 (50–86)</td>
<td>56 (20–92)</td>
<td>0.168</td>
</tr>
<tr>
<td>Male sex</td>
<td>1 (17%)</td>
<td>60 (59%)</td>
<td>0.082</td>
</tr>
<tr>
<td>Serum CRP (mg/L)</td>
<td>129 (7–288)</td>
<td>134 (2–392)</td>
<td>0.567</td>
</tr>
<tr>
<td>WBC (× 10^9/L)</td>
<td>11.6 (6.3–19.2)</td>
<td>13.2 (5.3–25.5)</td>
<td>0.301</td>
</tr>
<tr>
<td>Immunosuppressive therapy</td>
<td>0 (0%)</td>
<td>8 (8%)</td>
<td>1.000</td>
</tr>
<tr>
<td><strong>Radiological parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximal colonic wall thickness (mm)</td>
<td>9.8 (6.5–14.0)</td>
<td>9.6 (5.0–22.5)</td>
<td>0.797</td>
</tr>
<tr>
<td>Length of inflamed colon segment (cm)</td>
<td>7.6 (3.0–15.0)</td>
<td>7.6 (3.5–16.0)</td>
<td>0.459</td>
</tr>
<tr>
<td>Free intraperitoneal air</td>
<td>1 (17%)</td>
<td>11 (11%)</td>
<td>0.519</td>
</tr>
<tr>
<td>Presence of free fluid</td>
<td>2 (33%)</td>
<td>32 (32%)</td>
<td>1.000</td>
</tr>
<tr>
<td>------------------------</td>
<td>---------</td>
<td>----------</td>
<td>-------</td>
</tr>
<tr>
<td>Presence of simultaneous abscess</td>
<td>4 (67%)</td>
<td>17 (17%)</td>
<td>0.013</td>
</tr>
</tbody>
</table>

**Follow-up**

| 30-day mortality | 0 (0%) | 2 (2%) | 1.000 |

**Paper III**

A total of 149 patients were included in the study, 107 women and 42 men, of which 42 were included at Mora Hospital and 107 in Västerås. Patients median age was 68 years ranging from 39 to 94 years. Three patients <50 years were included in the study despite exclusion criteria; however, it was our opinion that because these patients had already received the extra radiation dose, to include them in the study, as this exclusions criterion was only included to minimize radiation doses to younger patients and does not have any effect on study outcome or findings. Patient body mass index (BMI) ranged from 19.5–47.8 kg/m² with a median BMI of 28.8 kg/m².

One hundred and seven cases were confirmed as acute colonic diverticulitis by consensus of consultants on a standard CT protocol.

Sensitivity for acute diverticulitis on LDCT was 100% and 99% for the abdominally orientated consulting radiologists with respective κ of 1.000 and 0.983. For the radiology resident, sensitivity was 92% with a κ of 0.742. In all cases for the resident, the pathology was seen, but was described as unclear whether it was the result of diverticulitis or colonic malignancy.

Sensitivity for complications because of diverticulitis on LDCT was 73% and 60% for the consultants and 54% for the radiology resident, while specificity was 96%, 100% and 86%, respectively. κ values for presence of any complications were 0.778, 0.580 and 0.342, respectively.

As expected, small abscesses were difficult to visualize; however, these were only seen in 10 cases where both consultants agreed on the standard CT protocol (SDCT). Specificity for abscess was 56% and 17% for the consultants, and 33% for the resident on LDCT. This discrepancy may be explained, at least in part, by describing the complication as extraluminal air or a pericolic...
abscess on one of the CT protocols. In a few cases the findings were described as a fluid filled inflamed diverticulum rather than an abscess. Specificity for abscess was 100%, 99% and 100%, respectively (see Table 10 and Figure 10). Abscesses were small and ranged 1.6–3.7 cm at largest with a median size of 2.2 cm, this small size may also partially explain why abscesses were difficult to detect on LDCT.

Table 10: Frequency of findings for LDCT and SDCT, respectively, sensitivity and specificity for consultants. Presence of diverticulitis was calculated for all included patients (n = 149), while complications were calculated for patients with diverticulitis only (n = 107). For information on resident, see Paper III.

<table>
<thead>
<tr>
<th></th>
<th>Consultant 1</th>
<th>Consultant 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LDCT</td>
<td>SDCT</td>
</tr>
<tr>
<td>Diverticulitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extraluminal or free air</td>
<td>18</td>
<td>24</td>
</tr>
<tr>
<td>Abscess</td>
<td>5</td>
<td>9</td>
</tr>
</tbody>
</table>
Figure 10: Weighted $\kappa$ values with asymptotic error for LDCT using SDCT as reference test for respective readers. For presence of diverticulitis 149 patients were included, but for other variables only patients with diverticulitis ($n = 107$) were included. Reader 1 (●), reader 2 (▲) and reader 3 (■). The variable “Overall signs of complications” included extraluminal or free air and abscess. Free fluid was not considered a complication.

Free intraperitoneal air was seen in three patients for which all readers agreed for two patients regardless of CT protocol. For the third patient, two readers agreed on both CT methods while one described the findings as extraluminal air only using either examination method.

Sensitivity for extraluminal air only rather than free intraperitoneal air was 75% and 74% for the specialists and 53% for the resident, while specificity was 100%, 96% and 81%, respectively.

Inter-observer agreement for presence of diverticulitis on LDCT was excellent between consultants and good between consultants and the resident (see Figure 11).
Figure 11: Comparison of inter-observer agreement. Agreement between readers 1 and 2 (●), between reader 1 and reader 3 (▲) and between reader 2 and reader 3 (■). All LDCT comparisons are in non-filled blue and SDCT is in filled red. For comparison of presence of diverticulitis 149 patients were included, for all other variables only diverticulitis patients were included (n = 107).

Not all included patients had findings consistent with acute colonic diverticulitis, overall 26 patients had other findings explaining abdominal symptoms seen on standard CT. Of these 26 patients, the correct diagnosis could be made using the LDCT protocol for 23 (88%) patients. The diagnoses that were missed on low-dose CT were one case of splenic infarction and two cases of subtle segmental colitis. The most common other reasons for abdominal pain were colitis (n = 8) and appendicitis (n = 7) (see Table 11). Sixteen patients had no consensus of diagnosis or no visible cause of abdominal symptoms on either CT method.
Table 11: Frequency of other diagnoses than diverticulitis for all readers with both CT methods.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Consultant 1</th>
<th>Consultant 2</th>
<th>Resident</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LDCT</td>
<td>SDCT</td>
<td>LDCT</td>
</tr>
<tr>
<td>Appendicitis</td>
<td>7</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Colitis</td>
<td>7</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Small bowel ileus</td>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Cholecystitis</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Basal pneumonia</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Kidney stone/pyelonephritis</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Small bowel perforation</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Colon malignancy</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Gynaecological</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Splenic infarction</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Radiation doses were monitored as the study resulted in participants receiving extra radiation compared to non-participants. On average, participants received an extra 3.3 mSv compared with non-participants, which is because of the additional low-dose CT protocol. The standard deviation for LDCT radiation dose was 1.9 mSv. This radiation dose is variable because of patient size and body configuration and ranged from 0.8 to 9.8 mSv. The standard CT protocol resulted in a mean radiation dose equivalent to 10.9 mSv (SD ± 4.8 mSv). The LDCT was equivalent to about 29% of the standard protocol for each respective participant.
The low-dose CT protocol was shown to be a highly sensitive and specific for diagnosing suspected diverticulitis; therefore, we recommend this protocol as a primary CT examination method for patients with suspected acute diverticulitis.

**Paper IV**

A total of 161 patients were included in the study of which six were excluded for various reasons. Thus, the study population consisted of 155 patients (101 women and 54 men) with CT-verified uncomplicated diverticulitis. All included patients were sent home from the emergency department and treated on an outpatient basis without antibiotics.

Four patients (2.6%) developed treatment failure and required hospitalization because of exacerbation of symptoms. Three of these patients had complicated diverticulitis at the time of treatment failure, although a small pericolic abscess was overlooked in one of these patients on the initial CT report. All four patients were treated successfully with antibiotics and no patient in the study group required surgery.

After 1 week, the CRP and WBC had normalized in 84% of patients, and, after 3 days, the median VAS score had dropped to 1.8 and 70% of patients had stopped using pain medication.

Three patients had signs of complicated diverticulitis on the admission CT that had been overlooked, two with an abscess and one patient with localized extraluminal air. Two of these three patients recovered without further incident or antibiotic treatment.

Three patients were flagged as having cases suspicious for malignancy, of whom two turned out to have sigmoid adenocarcinoma at the routine colonoscopy follow-up at 3 months. Two additional patients had benign colonic polyps on the follow-up colonoscopy.

To our knowledge, this was the first study that managed CT-verified AUD on an outpatient basis without antibiotics. As antibiotic resistance has become a major health problem, and antibiotic use is being increasingly recognized as the main causative factor for this resistance, it is necessary to minimize antibiotic usage as much as possible. Our study results further strengthen the previous conclusion that the routine use of antibiotics in AUD should be avoided in common practice. It should also be kept in mind that diverticulitis affects a
heterogeneous group of patients, some of whom present with contraindications for outpatient treatment without antibiotics according to their symptoms, general condition and associated medical diseases.

Since this study was published, the results have been confirmed in a few other studies, most notably a recent meta-analysis by van Dijk et al., which found it both to be safe for the majority of patients and reduce medical costs substantially (97). However, this meta-analysis included patients both treated with and without antibiotics as outpatients. Nevertheless, to our knowledge at least two studies by Estrada Ferrer et al. and Mali et al. have confirmed our conclusion that outpatient treatment without antibiotics is safe for selected patients and does not increase the risk for complications (98,99).

A follow up study by Isacson et al. regarding healthcare costs for diverticulitis at our hospital showed that with a higher number of patients being treated as outpatients the overall cost for treating diverticulitis in our region was reduced almost by half (100). In the meta-analysis by van Dijk et al., the healthcare costs by treating patients as outpatients were reduced between 42% to 82% depending on the participating centre (97).
General discussion

CT is the first-line radiology examination for suspected diverticulitis in Sweden. This method is fast and relatively inexpensive; however, it does have a few limitations, such as the use of ionizing radiation and the potential adverse effects of contrast medium. In trying to limit these adverse effects, we found that the radiation dosage can be lowered and contrast medium skipped. CT is efficient in helping to guide clinicians as to which patients require surgery and can assist in selecting patients that may be treated conservatively.

In recent years, the management of diverticulitis has changed and is still changing. Patients with uncomplicated diverticulitis have gone from hospital admission and IV antibiotics to more of an outpatient-based treatment regimen without antibiotics. These changes have and will reduce the cost of treating this condition. However, to our knowledge hospitalization and antibiotics are still the standard treatment in most parts of the world. This leaves us with the great and inspiring challenge, to spread our knowledge and the benefits of outpatient treatment as far as possible.

Overall, our studies have changed the management of diverticulitis at our hospital. Most patients are now treated as outpatients without antibiotics, benefitting both the patient and the healthcare system. Soon to be implemented, is a change in first-line radiology examination, which will be the LDCT protocol as this was shown to be equally sensitive and specific for patients with suspected acute diverticulitis while drastically reducing radiation exposure.

These changes have already saved the healthcare system considerable costs as well as saving patients unnecessary hospital admission with all the infection risks that may complicate hospital admissions and finally contributing to the fight against antibiotic resistance (100).

The planned further studies include evaluation of the need for CT colonoscopy or routine colonoscopy after acute diverticulitis, as the need for these procedures remains unclear with previous studies showing conflicting results. It is the authors’ opinion that they are unnecessary in the majority of cases, and selection could probably reduce the number requiring follow-up to about 10%.
Second, we have planned a study to investigate whether MRI can help differentiate between patients with diverticulitis during the early disease phase, which facilitates immediate cancer treatment when necessary rather than after 8–12 weeks, which is the time needed for the inflammatory changes to regress and allow malignancy to be distinguished from diverticulitis on CT of the colon.

Further studies planned include evaluation of ultrasound and its advantages as a first-line examination for suspected diverticulitis.

We are participating in a multicentre ongoing research project to evaluate CT findings in regard to preoperative staging of peritoneal contamination in perforated diverticulitis, and a follow up study of patients included in the SCAN-DIV study (66).
Conclusions

Paper I
Very few patients with uncomplicated diverticulitis progress to have complicated disease. However, we did find a limitation in the initial CT report with 44 overlooked complications. Despite having small complications, the majority of patients recovered even without antibiotic treatment. Additionally, patients with complicated diverticulitis were found to have higher levels of inflammatory markers, both haematological (CRP and WBC) and CT findings compared to patients with uncomplicated disease.

Paper II
Non-surgical treatment of patients with perforated diverticulitis is feasible in the majority of patients. However, patients with simultaneous abscess have a higher rate of conservative treatment failure. Patients operated on within 24 h and who are not candidates for conservative treatment were more commonly older, on immunosuppression therapy, had free fluid in the peritoneal cavity or free air rather than pericolic air only.

Paper III
Non-enhanced low-dose CT is as sensitive in detecting acute diverticulitis as the standard contrast-enhanced full radiation dose CT used in general practice today. Using this protocol would reduce the radiation to this patient group by up to two thirds, eliminate the risk for nephrotoxicity, while being both faster and less expensive. We therefore recommend this type of CT examination as the first-line examination for patients with suspected diverticulitis. Small abscesses can be missed, but the clinical significance of this is uncertain.
Paper IV

Outpatient non-antibiotic treatment for uncomplicated diverticulitis is safe and does not increase complication rates or hospitalization. This treatment regimen is therefore recommended in selected patients.

Divertikelsjukdomen är en kostsam sjukdom för hälsosjukvården och beräknas vara den femte mest kostsamma mag-tarmsjukdomen som drabbar befolkningen (11–14).

Det finns flera olika klassificeringssystem för att beskriva divertikulit men alla dessa syftar till att urskilja okompllicerad från komplicerad divertikulit och skilja mellan olika grader av komplikation (10,34,37). Det finns idag inget system för att differentiera mellan olika grader av okompllicerad divertikulit.

Behandling av akut okomplicerad divertikulit bestod tidigare av tarmvila, intravenöst dropp samt antibiotika (43,44). AVOD-studien (antibiotika vid okomplicerad divertikulit) var en multicentrisk randomiserad studie där patienter med okomplicerad divertikulit randomiserades till behandling med eller utan antibiotika. AVOD-studien visade att antibiotikabehandling vid detta tillstånd varken förkortar vårdtiden eller minskar risken för komplikationer. Dessa slutsatser har även verifierats i flera studier (102).

Målsättningen med avhandlingen är att med utgångspunkt från kliniska studier belysa följande:

I Undersöka om datortomografi (DT) kan förutsäga komplikationer eller recidiv hos patienter med primärt okomplicerad divertikulit.

II Att beskriva konservativ behandling av patienter med perforerad divertikulit och om DT kan förutsäga för vilka patienter med
perforerat divertikulit konservativ behandling misslyckas i högre utsträckning.

III Utvärdera om lågdos Datortomografi utan intravenös kontrast är tillräckligt känslig metod för att användas för diagnostik vid misstänkt akut divertikulit.

IV Utvärdera om patienter med DT-verifierad okomplicerad divertikulit kan skötas polikliniskt utan antibiotika.

**Delstudie I:** I denna delstudien eftergranskades alla DT-undersökningar av patienter inkluderade i AVOD studien. Förekomst och grad av divertikulit samt eventuella tecken på komplikationer bedömdes. Sammanlagt eftergranskades 602 DT undersökningar av vilka 574 patienter (95%) hade bilde för- enlig med akut divertikulit.

Inga DT fynd kunde förutsäga utveckling av komplikation eller recidiv. Där- emot upptäcktes brister i den primära röntgenbedömningen då 44 patienter med missad komplikation upptäcktes vid eftergranskningen. Dessa patienter med komplicerad sjukdom hade signifikant högre CRP, LPK och inflammationsparametrar på DT jämfört med patienter utan komplikation, se tabell 7 (sida 39).

**Delstudie II:** Retrospektiv granskning av alla patienter behandlade för perforerad divertikulit mellan januari 2010 och december 2014. 141 patient hade enligt journalanteckningar blivit behandlat för perforerad divertikulit under tidsperioden. Vid eftergranskning av DT undersökningar inkluderades 136 patienter i studien.

Tjugonio patienter (21%) blev opererade akut inom ett dygn från ankomsten till sjukhus. Äldre patienter, immunsupprimerade patienter och patienter med fri gas eller fri vätska i buken hade ökat risk för att behöva genomgå kirurgi inom första dygnet.

107 patienter erhåll konservativ behandling och denna behandlingen lyckades hos 101 (94%). Sex patienter försämrades med infektion av bukhinnan eller sepsis och krävde operativ åtgärd.

I vårt material var incidensen 10.4 fall per 100,000 invånare varje år men tidigare studier har visat en incidens på mellan 3.0 – 4.0 fall per 100,000 och år (91–93). Skillnaderna kan dock åtminstone delvis förklaras av att i Västmanland undersöks alla patienter med misstänkt divertikulit med datortomografi och andra studier är oftast baserade på operationsdata och alla patienter opereras ej.
Slutsatsen med delstudie II var att flesta patienter med perforerat divertikulit går att behandla konservativt men konservativ behandling misslyckas i högre utsträckning för patienter med samtidig abscess.

**Delstudie III** var en prospektiv studie där patienter med misstänkt akut divertikulit undersöktes för med lågdos DT utan intravenös kontrast (DT Bös) innan den standard metoden, dvs en full dos DT buk med intravenös kontrast. Målsättningen med denna studien var att utvärdera om DT Bös är tillräckligt känslig metod för att använda vid misstänkt divertikulit. Tre röntgenläkare (två överläkare och en 4de års ST-läkare) bedömdes första alla DT Bös undersökningar enligt protokoll. Vid ett senare tillfälle bedömdes alla standard DT undersökningar enligt samma protokoll. Anledningen till att dessa inte bedömdes samtidigt var att försöka minska minnesfel (recall bias).

Sammanlagt blev 149 patienter inkluderade varav 107 kvinnor. Medianålder var 68 år och median BMI var 28.8 kg/m². Sensitivitet för akut divertikulit med DT Bös var 100% och 99% för specialisterna och 92% för ST läkaren. Specificitet var 100% för specialisterna och 86% för ST läkaren. De flesta komplikationer hittades med lågdos DT metoden även om ibland dessa beskrivs som en annan typ av komplikation jämfört med standard DT metoden. DT Bös visar sig ha vissa svagheter för att upptäcka små abscesser men detta har en begränsad klinisk betydelse.

Vår slutsats med denna studien är att lågdos DT utan iv kontrast är tillräckligt känslig metod för diagnostik av patienter med misstänkt akut divertikulit och borde användas som första hands bildagnostik. Detta skulle minska strålningen till denna patientgrupp avsevärt, utesluta njurskada som är en sällsynt komplikation till intravenöst kontrastmedel och minska kostnaden för undersökningar av denna patientgruppen.

**Delstudie IV:** En prospektiv öppen observationsstudie där vi utvärderade huruvida patienter med akut okomplicerad divertikulit kunde behandlas polikliniskt utan antibiotika. Studien bedrevs vid sjukhusen i Västerås och Mora där sammanlagt 161 patienter inkluderades i studien. Sex patienter exkluderas. DT buk undersökningar av de inkluderade patienter eftergranskades och graderades på samma sätt som i Delstudie 1, se tabell 6 (sida 29).

Av 155 inkluderade patienter var det endast fyra patienter (2.6%) som återkom på grund av behandlingssvikt. Tre av dessa hade utvecklat komplikationer och den fjärde hade feber. Samtliga fyra lades in och erhöll antibiotikabehandling. Ingen patient genomgick operation. En av dessa fyra patienter hade missat komplikation från början.
Slutsatsen av delstudie II blev att patienter med okomplicerad divertikulit kan skötas polikliniskt utan antibiotika, med bevarad medicinsk säkerhet.
Acknowledgements

First of all, I would like to thank my beautiful wife, Johanna, for introducing me to her colleagues, and thus opening up the world of research to me. For standing by me through the long nights and weekends and giving me the chance to see my work through to the end. For always standing by my side and offering support and often a much-needed pep talk when things were looking grim. For being an inspiration on how one can achieve a successful career and making me a better overall person in every way.

To my beautiful children, Nonni, Siggi, Laufey and Ragnar: You guys are my world. It has been my greatest honour to see you grow up and I love every minute of being around you. You guys are everything to me and I am so proud of you every single day.

Abbas Chabok: For being my main tutor, but also being such a good friend and a true inspiration. I’ve probably never met anyone during my lifetime that has the energy levels you have and the love for research quite as passionately as you do. Thank you for showing me how to thrive in the world of research and guiding me through a maze of obstacles along the way. I love how you could send an email on a weekday after midnight and then ask my wife at 8 o’clock the next morning what my thoughts were on the subject and be surprised when she had no idea.

Maziar Nikberg: I have the greatest respect for you as I do your colo-rectal colleagues. Your energy levels and love for research is second to none and I have often wondered if you or Abbas ever sleep. Thanks for all the patience you have shown me during this long journey. I hope you and your colleagues realize how much it means to me how you all have taken my wife under your wing and been like a small family away from home, not just for me, but especially for her.

Kenneth Smedh: for giving much needed guidance and setting the bar so high. For inspiring the surgical unit to be the incredible group of researchers they have become and for all the support and wisdom during the last few years.
Michael Torkzad: for showing me how to improve my radiology skills along with research. And for always being there when needed for discussion or a late-night Skype conversation.

My radiology colleagues: for not being, at least noticeably, annoyed at the fact that I have been away part time for research this past year. And for showing me the ropes in radiology even when I couldn’t understand a word in Swedish.

Centre for Clinical Research Västerås: to all the wonderful personal at CKF in Västerås, first and foremost Maria Petterson, Maria Dell’Uva Karlsson and Mariana Ehn for helping so eagerly with the day-to-day troubleshooting. Mats Enlund and Kent Nilsson for all the support and helpful discussions. Jerzy Leppert for inspiration and insightful thoughts on my research and how it could be taken to another level. And finally, a special thanks to Phillipe Wagner and John Öhrvik, for their statistical assistance.

My older brother Hjalti: for suggesting to me to try out radiology at a point when I had pretty much decided to quit medicine and find another career. For being an inspiration on how things should be done and always being there when questions arose. For showing me that anything is possible and setting the bar high as to what would be expected of me.

My parents: Þórir and Sirrý, for believing in me and supporting me though all the years. Without you I would definitely not have achieved as much as I have during my life or medical career.

Finally, my beloved younger brother Ragnar, who is no longer with us. Of all the people I have known in my life, few have had as big of an impact on me. You were always such an inspiration on how to live one’s life. Without a doubt one of the smartest and best hearted persons I have had the privilege to meet and learn from. I still think of you every day and miss you so dearly. Hope to see you again one day, until then I hope I make you proud.
References

8. Kircher MF, Rhea JT, Kihiczak D, Novelline RA. Frequency, sensitivity, and specificity of individual signs of diverticulitis on thin-section helical CT with colonic contrast material: experience with 312 cases. AJR Am J Roentgenol. 2002;178(6):1313-1318.


A doctoral dissertation from the Faculty of Medicine, Uppsala University, is usually a summary of a number of papers. A few copies of the complete dissertation are kept at major Swedish research libraries, while the summary alone is distributed internationally through the series Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine. (Prior to January, 2005, the series was published under the title “Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine”.)