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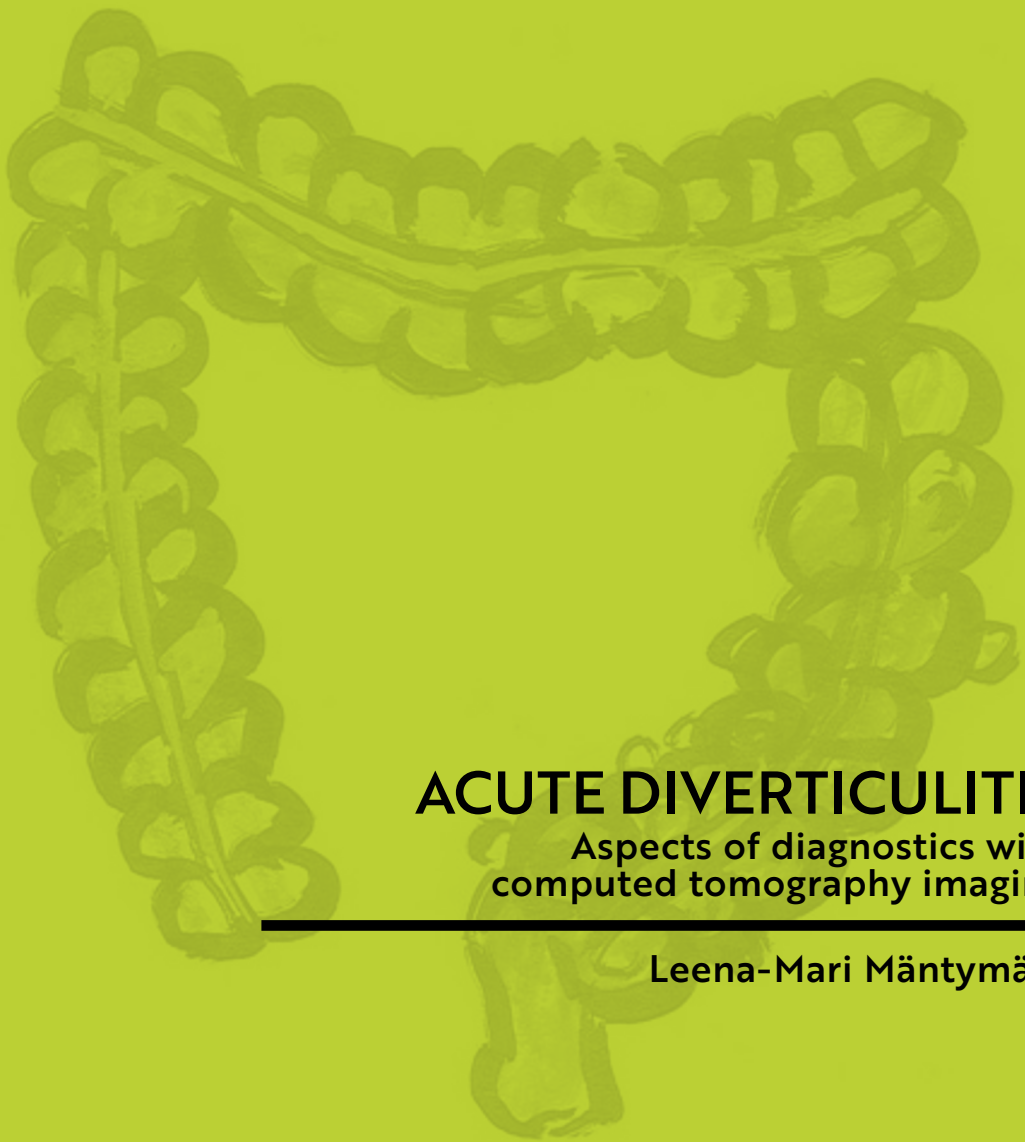

ACUTE DIVERTICULITIS

Aspects of diagnostics with computed tomography imaging

Leena-Mari Mäntymäki

TURUN YLIOPISTON JULKAISUJA – ANNALES UNIVERSITATIS TURKUENSIS
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To My Family

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ABSTRACT

The incidence of acute diverticulitis – common disease in Western countries – is increasing worldwide. Acute diverticulitis can be divided by its degree of severity into uncomplicated and complicated forms. Accurate diagnosis is a prerequisite for choosing optimal treatment and follow-up. Currently, the diagnosis is made using computed tomography imaging. Although the accuracy of computed tomography imaging in the diagnosis of acute diverticulitis is good, differential diagnostics can be challenging.

The purpose of this dissertation was to investigate the risk of colorectal cancer after computed tomography-verified acute diverticulitis with special interest in long-term follow-up. We also aimed to assess the usefulness of reassessment of computed tomography scans and the role of experience of radiologists in emergency settings in the diagnosis of acute diverticulitis. In addition, we aimed to create a risk score for acute diverticulitis to distinguish uncomplicated and complicated forms of the disease without using computed tomography imaging by evaluating risk factors for complicated acute diverticulitis.

We found that further colonic investigations were not needed after an attack of uncomplicated acute diverticulitis, as the risk of underlying colorectal cancer was low, although the risk was increased in the case of complicated disease in the short-term follow-up. No cases of colorectal cancer associated with acute diverticulitis were observed in the long-term follow-up. Reassessment of computed tomography reports in emergency settings changed the treatment or diagnosis in 5% of cases. The role of a radiologist's experience was not statistically significant, and reports given by residents were comparable to reports given by consultants. Based on statistically significant risk factors of complicated acute diverticulitis, we created a novel risk score for acute diverticulitis that, without computed tomography imaging, accurately separated patients with a potentially severe disease from those without.

KEYWORDS: acute diverticulitis, complicated acute diverticulitis, computed tomography imaging, diagnostics, follow-up, uncomplicated acute diverticulitis

TURUN YLIOPISTO
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TIIVISTELMÄ

Akuutti divertikuliitti on länsimaissa yleinen sairaus, jonka ilmaantuvuus on väestön ikääntymisen myötä kasvussa. Akuutti divertikuliitti voidaan jakaa vaikeusasteen mukaan komplisoitumattomaan ja komplisoituneeseen muotoon, joiden hoitolinjat eroavat toisistaan. Optimaalisen hoidon ja jatkohoidon valinnan edellytyksenä on tarkka diagnoosi, johon käytetään yleensä tietokonetomografiakuvausta. Vaikka tietokonetomografian tarkkuus divertikuliitin diagnostiikassa on hyvä, voi erotusdiagnostiikka olla haastavaa.

Tämän väitöskirjatyön tarkoituksena oli selvittää paksusuolen syövän riskiä tietokonekuvatun akuutin divertikuliitin jälkeen ja selvittää onko paksusuolen jatkotutkimuksista divertikuliitin jälkeisessä seurannassa hyötyä erityisesti pitkäaikaisseurannassa. Tutkimme myös, onko päivystysajalla tehdyn tietokonetomografiakuvauksen kaksoisluenta hyödyllistä, sekä radiologin kokemuksen merkitystä akuutin divertikuliitin diagnostiikassa. Lisäksi selvitimme komplisoituneen akuutin divertikuliitin riskitekijöitä, joiden perusteella tavoitteemme oli luoda pisteytyssysteemi erottamaan komplisoitumaton ja komplisoitunut tautimuoto toisistaan ilman tietokonetomografiakuvausta.

Akuutin, tietokonetomografialla diagnosoidun komplisoitumattoman divertikuliitiin jälkeen paksusuolen jatkotutkimuksista ei todettu olevan hyötyä, sillä syöpäriski oli hyvin matala. Komplisoituneeseen divertikulittiin sen sijaan liittyi korkeampi syöpäriski lyhyessä seurannassa. Pitkän aikavälin seurannassa ei havaittu paksusuolen syöpätapauksia akuuttiin divertikuliittiin liittyen. Päivystyspoliklinikalla tehtyjen tietokonetomografiakuvausten kaksoisluenta muutti hoitoa tai diagnoosia 5 %:ssa tapauksia. Radiologin kokeneisuudella ei ollut merkitystä diagnoosin osuvuudessa. Tilastollisesti merkittävien komplisoituneen akuutin divertikuliitin riskitekijöiden perusteella loimme pisteytyssysteemin, joka osoittautui hyödylliseksi taudin vaikeusasteen ennustamisessa.

AVAINSANAT: akuutti divertikuliitti, diagnostiikka, komplisoitumaton akuutti divertikuliitti, komplisoitunut akuutti divertikuliitti, seuranta, tietokonetomografiakuvantaminen

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Abbreviations

5-ASA	5-aminosalicylate
AUC	Area under curve
CAD	Complicated acute diverticulitis
CE	Contrast enema
CI	Confidence interval
CRC	Colorectal cancer
CRP	C-reactive protein
CT	Computed tomography
CTC	Computed tomography colonography
DCS	Damage control surgery
HP	Hartmann's procerude
ICD-10	International Classification of Diseases 10th Revision
IV	intravenous
MRI	Magnetic resonance imaging
OR	Odds ratio
QoL	Quality of life
RCT	Randomized controlled trial
ROC	Receiver operating characteristic
UAD	Uncomplicated acute diverticulitis
US	Ultrasound
WBC	White blood cell count

List of Original Publications

This dissertation is based on the following original publications, which are referred to in the text by their Roman numerals:

I Mäntymäki L-M, Grönroos J, Riskumäki M, Vahlberg T, Karvonen J. Risk for colorectal cancer after computed tomography verified acute diverticulitis—A retrospective cohort study with long-term follow-up. *Scandinavian Journal of Surgery*, 2023; 112(3): 157–163.

II Mäntymäki L-M, Grönroos J, Aronen A, Karvonen J, Ukkonen M. Is reassessment of computed tomography reports worthwhile in acute diverticulitis? *Digestive Surgery*, 2024; 41(1): 37–41.

III Mäntymäki L-M, Grönroos J, Karvonen J, Ukkonen M. A novel scoring system for predicting disease severity without CT imaging in acute diverticulitis. *International Journal of Colorectal Disease,* 2024; 39(1):164.

1 Introduction

Acute diverticulitis – prevalent disease in Western countries – is one of the most common causes of abdominal pain in emergency settings (Peery et al. 2019). The incidence of acute diverticulitis has increased worldwide in recent decades (Bharucha et al. 2015; Mizuki et al. 2017; Saren et al. 2023), with diverticular disease and its complications causing substantial economic burdens on healthcare (Mennini et al., 2017; Fialho et al., 2023).

After the recognition of diverticular disease and diverticulitis in the early twentieth century, an impressive number of studies on different aspects of acute diverticulitis enhanced our knowledge of the disease. Updates on the pathophysiology, diagnosis and treatment of acute diverticulitis have continued over the last decade. Stratification of the severity of this disease is crucial in determining the optimal treatment for patients. The diagnosis of uncomplicated acute diverticulitis (UAD) and complicated acute diverticulitis (CAD) is increasingly being made via computed tomography (CT) imaging (Bharucha et al. 2015). New treatment strategies have been suggested because more accurate diagnoses of the different stages of acute diverticulitis have become possible via CT imaging. For example, outpatient treatment and nonantibiotic treatment have proven safe and feasible in UAD and in some CAD cases (Chabok et al. 2012; Mali et al. 2016; Daniels et al. 2017; Isacson et al. 2018; Bolkenstein et al. 2019c). Debate on the best way to treat CAD with abscesses or perforation, as well as the need for further colonic evaluation and elective surgery after acute diverticulitis, is vivid and ongoing. Studies on the aetiology and pathogenesis of acute diverticulitis aim to develop solutions for prevention. Due to the increasing incidence and costs in healthcare, cost-effectiveness studies in the management of acute diverticulitis have recently been of interest to researchers and clinicians.

This thesis focused on aspects of diagnostics in patients with acute diverticulitis. Colorectal cancer (CRC) might mimic acute diverticulitis, and an increased prevalence of CRC has been found after an acute diverticulitis attack (Granlund et al. 2011). The increased use of CT imaging and colonoscopies, in addition to the increasing incidence of acute diverticulitis, increases the costs for healthcare systems (Fialho et al. 2023). However, CT imaging and further colonic investigations might

not be needed for every patient, which could save resources. Therefore, we wanted to evaluate whether colonic investigations were needed after CT-verified acute diverticulitis, particularly to ensure consistency of the initial CT diagnosis in long term follow-up. We also wanted to assess whether a diagnosis of UAD or CAD could be made with high certainty without CT imaging. Differential diagnostics between acute diverticulitis and CRC, as well as many other conditions, can be difficult. As the assessment of disease severity is crucial to finding optimal treatment, we wanted to evaluate whether reassessment of CT scans made in emergency department was beneficial, as well as whether radiologists' experience levels were of concern in this context.

2 Review of the Literature

2.1 History

The term diverticulum comes from Latin and means bypath (Quinn 1948). In the late 1700s, French surgeon Alexander Littre described the formation of diverticula, a saccular protrusion in the colon. The first descriptions of diverticulitis can be found in the 19th century, when the aetiology of diverticulosis was suspected due to inherent or congenital weakness of the bowel wall. In 1907, Mayo et al. described 27 cases of diverticulitis in which seven patients had carcinoma. It was believed that diverticulitis may result in the development of carcinoma (Douglas, 1913). In the mid-twentieth century, the incidence of diverticulosis and diverticulitis was considered low, and it was believed that diverticulosis mainly affected elderly people (Lockhart-Mummery 1926). Barium enema was the best choice for imaging to diagnose diverticular disease, and sigmoidoscopy was considered a promising diagnostic aid (Quinn 1948). Bowel resection in three stages was popular and considered the safest surgical procedure for acute diverticulitis (Welch, 1955; Ransom, 1956). In the 1970s, a low-fibre diet was suggested to cause diverticular disease (Painter and Burkitt 1971).

2.2 Anatomy

Diverticula, which are small pouch-like structures, are herniations of mucosa of the colon that develop in the lining of the colon between taenia coli (Stollman and Raskin 2004). Diverticula can be solitary or number in the hundreds and above, requiring the use of the term diverticulosis. The size of diverticula varies, but they are usually 5–10 mm in diameter (Stollman and Raskin 2004). Diverticula and diverticulosis are mostly found on the left side of the colon in the Western population, but they can also be found in all parts of the colon (Parks, 1969a; Meurs-Szojda et al., 2008; Peery et al., 2016). In the Asian population, diverticula are mainly found on the right side of the colon (Miura et al. 2000). In acute diverticulitis, diverticula become inflamed, with peri-diverticular inflammation of the bowel wall and the surrounding tissue found. An endoscopic picture of diverticula is shown in Figure 1.

Figure 1. Two diverticula in the mucosa of the colon.

2.3 Aetiology and pathogenesis of acute diverticulitis

The aetiology and pathophysiology of acute diverticulitis are not completely understood. A combination of genetic, dietary and many environmental factors may contribute to the development of acute diverticulitis.

It has been suggested that changes in colonic wall connective tissue and impaired motility causes herniation of mucosa and thus diverticulosis (Stollman and Raskin 2004). The traditional theory of acute diverticulitis is that inflammation occurs due to obstructed diverticulum causing ischemia and microperforation. Another explanation is that intestinal bacteria are translocated through the mucosa to the bowel wall when mucosal abrasions cause inflammation. It has also been suggested that diet-induced chronic inflammation is associated with the development of diverticulitis (Ma et al. 2020). Obesity and other lifestyle-related factors might also be related to an inflammatory response causing chronic inflammation, which could thus be associated with the development of acute diverticulitis (Strate and Morris

2019). The role of altered gut microbiota has also been discussed, although in a recent study by Alexandersson et al. (2023), no differences in microbiota were found between patients with and without diverticulitis.

2.3.1 Impact of environmental factors

Several environmental factors have been proposed as risk factors of acute diverticulitis. It has been suggested that diverticulosis is an acquired condition caused by a low-fibre diet that changes the colon's environment (Painter and Burkitt 1971). Observations of different incidences between industrialised and rural areas led to the conclusion that changed dietary habits, especially a low-fibre diet, influence the development of diverticular disease (Painter and Burkitt 1971). In a Swedish population-based study, the risk of hospital admissions due to diverticular disease and diverticulitis was lower in non-Western immigrants than in the native population (Hjern et al. 2006). Although the risk increased in non-Western immigrants after their settlement, the authors suggested that Western lifestyles influence the risk of symptomatic diverticular disease. Similarly, it has been shown that among Japanese immigrants and Japanese born in Hawaii, diverticulosis was more prevalent than in native Japanese people (Stemmermann and Yatani 1973). Additionally, diverticulosis was found to be more prevalent on the right side of the colon, but diverticulosis on the left side became more prevalent with increasing age (Stemmermann and Yatani 1973).

In a prospective cohort study of 46,295 men, a Western dietary pattern (i.e. high in red meat, refined grains and high-fat dairy) was associated with an increased risk of diverticulitis, and a prudent diet (i.e. high in fruits, vegetables and whole grains) was associated with a decreased risk (Strate et al. 2017). In two population-based studies, obesity increased the risk of acute diverticulitis (Hjern et al., 2012; Strate et al., 2009b). Increased abdominal visceral and subcutaneous fat are especially associated with the risk of acute diverticulitis (Yamada et al., 2013; Lee et al., 2018). In a cohort study of 104 patients, abdominal obesity was present in 82% of patients with CT-verified acute diverticulitis (Zaidi and Daly 2006). Additionally, the regular use of non-steroidal anti-inflammatory drugs, smoking and alcohol consumption are associated with an increased risk of acute diverticulitis (Liu et al., 2017; Gunby et al., 2024). A large prospective cohort study evaluated the combination of different lifestyle factors and the incidence of acute diverticulitis in men (Liu et al. 2017). High red meat intake and low dietary fibre intake, low physical exercise, overweight and smoking were independently associated with the risk of diverticulitis. In addition, the number of low-risk lifestyle factors (e.g. low red meat intake, high fibre intake, vigorous physical exercise, normal weight and not smoking) was inversely correlated with diverticulitis risk (Liu et al. 2017). The exact mechanisms by which

these environmental factors influence the development of acute diverticulitis are unclear.

2.3.2 Role of genetics

Population-based studies suggest that genetic factors appear to contribute to diverticular disease (Granlund et al. 2011; Strate et al. 2013). Granlund et al. (2011) found that twin similarity was higher in monozygotic twins than in dizygotic twins in developing diverticular disease. They reported that the OR of developing the disease, given that one's co-twin was affected, was 7.15 (95% CI: 4.82–10.61) for monozygotic twins and 3.20 (95% CI: 2.21–4.63) for same-gender dizygotic twins (Granlund et al. 2011). Strate et al. (2013) estimated that more than 50% of diverticular disease cases are due to genetic effects. They found that siblings had a higher relative risk of diverticular disease than the general population. They also investigated the relative risks in monozygotic and dizygotic twins and found that the relative risk of diverticular disease in one twin when the other had diverticular disease was 14.5 (95% CI, 8.9–23) for monozygotic twins compared with 5.5 (95% CI, 3.3–8.6) for dizygotic twins (Strate et al. 2013).

In a retrospective cohort study with prospective follow-up, the impact of family history on acute diverticulitis was investigated. The authors found that a positive family history was associated with a higher risk of recurrence and complicated recurrences (Almalki et al., 2020), although the risk could be due to similar environmental factors within the family. The different locations of diverticulosis between Western and Asian populations suggest that genetic factors are involved in diverticular disease. Stemmermann and Yatani (1973) found that Japanese immigrants living in Hawaii and eating a more Western diet had diverticulosis mainly on the right side of the colon, compared to the native population in whom the disease was found on the left side of the colon. Additionally, racial differences in the incidence of acute diverticulitis have been noted in the United States (Wheat and Strate 2016). These findings might indicate genetic differences rather than the influence of dietary factors on the development of diverticular disease.

2.4 Epidemiology

2.4.1 Incidence

Colonic diverticulosis is the most common incidental finding in colonoscopy (Everhart and Ruhl 2009). In a study on patients admitted for colonoscopy with different indications, the prevalence of diverticulosis was 25% (Meurs-Szojda et al. 2008). Additionally, the prevalence of diverticulosis and the incidence of

diverticulitis increase with age (Everhart & Ruhl, 2009; Bharucha et al., 2015). In the era of clinical diagnosis of acute diverticulitis, it was thought that 10%–25% of patients with diverticulosis suffered from acute diverticulitis. However, the use of colonoscopy and imaging techniques has shown that only 4%–7% of patients with diverticulosis develop diverticulitis (Shahedi et al., 2013; Loffeld, 2016). The true incidence of acute diverticulitis remains unclear, as studies on its incidence mainly reflect the number of emergency room visits or hospital admissions. Nevertheless, the incidence of acute diverticulitis has increased in Western countries (Bharucha et al. 2015; Saren et al. 2023). In Finland, the incidence of acute diverticulitis increased by 58% (from 262 to 413/100,000 inhabitants) between 2009 and 2018 (Saren et al. 2023). The population is ageing, and because diverticulosis is common in the elderly, it seems reasonable that the incidence of acute diverticulitis will also increase; however, an increased incidence has also been found among younger people (Bharucha et al. 2015; Fialho et al. 2023). The increased use of CT imaging might partially explain this increased incidence (Bharucha et al., 2015). Low-fibre diets and increased obesity among Western populations might also have impacted incidence rates (Fialho et al. 2023).

Diverticular disease and acute diverticulitis are more common in Western populations than in non-Western populations, but an increased incidence in low-prevalence countries has also been detected (Painter & Burkitt, 1971; Yamada et al., 2013; Mizuki et al., 2017; Imaeda & Hibi, 2018; Taah-Amoako et al., 2024). In the Asian population, acute diverticulitis mainly affects the right side of the colon (Yamada et al., 2013), although an increased incidence on the left side has been noted (Mizuki et al., 2017). In a large nationwide cohort study in the United States, the incidence of diverticulitis was highest among White Americans compared to other racial groups, although an increased incidence was found in every racial group (Wheat and Strate 2016).

2.4.2 Age and sex

The prevalence of diverticulosis is approximately 35% in people younger than 50 years old, 33%–40% in those 50–59 years old, 58% in those 60–79 years old and 71% in those older than 80 years old (Everhart and Ruhl 2009; Peery et al. 2016). Similarly, it has been found that the incidence of acute diverticulitis increases with age (Bharucha et al. 2015).

Controversies exist in studies on the gender distribution of diverticular disease. In a study evaluating the colonoscopy findings of more than 4,000 patients, no difference in the prevalence of diverticulosis between genders was found (Meurs-Szojda et al. 2008). In the early twentieth century, diverticular disease was thought to mainly affect men, but the reason for this was possibly the different

socioeconomic status of women at that time (Parks 1969a). More recent studies have suggested that acute diverticulitis seems to be more common in females than in males (Hjern et al. 2006; Wheat and Strate 2016). However, there are studies indicating no differences between the sexes (Loffeld 2016).

2.4.3 Economical aspects

Since diverticular disease and diverticulitis are highly prevalent, they cause a substantial burden to healthcare in terms of the utilisation of resources and the direct costs of their management. It was estimated that the annual hospital admission rate in Europe was 209/100,000 (approximately 800,000 admissions per year) at the beginning of the 21st century (Delvaux 2003). In the United States, there are more than 2.5 million clinic visits, 330,000 emergency department visits and 200,000 hospital admissions for diverticular disease annually (Peery et al. 2019). In Italy, it is estimated that the number of hospital admissions due to diverticular disease is 19,000 per year, and acute diverticulitis costs €63.5 million annually (Mennini et al. 2017). The mean hospital charges for diverticular disease increased over 100% between 1997 and 2018 in the United States (Fialho et al. 2023). Admissions due to diverticular disease increased 32% in 21 years, but at the same time, the length of hospital stays decreased. The increased costs were attributed to expensive investigations, such as CT imaging and colonoscopy (Fialho et al. 2023). Several cost-effectiveness studies have been conducted on different aspects of acute diverticulitis and its management (Gehrman et al., 2016; Isacson et al., 2018; Bolkenstein et al., 2019b; Lambrichts et al., 2020b).

2.4.4 Association with colorectal cancer

In the early twentieth century, diverticulitis was associated with the development of CRC (Douglas, 1913). Diverticulitis and CRC share similar epidemiological characteristics. For example, both are thought to be predisposed by Western lifestyles, a low-fibre diet, obesity and smoking (Kirkegaard et al. 2010; Strate and Morris 2019). Additionally, an increased incidence of CRC was found after an episode of acute diverticulitis compared to the general population (Meyer et al. 2015). It has been speculated that chronic inflammation could increase the risk of malignancy (Meurs-Szojda et al. 2008). Therefore, the association between diverticular disease and CRC has been debated. In population-based studies, a strong association between diverticulitis and CRC has been found, raising questions about a causal association (Stefánsson et al., 2004; Mortensen et al., 2017). However, current evidence shows that diverticulosis and diverticulitis are not associated with an increased risk of CRC (Meurs-Szojda et al., 2008; Tomaoglu, 2020; Mortensen

et al., 2022). In a systematic review and meta-analysis of 38,621 patients, the risk of CRC in long-term follow-up after an episode of acute diverticulitis was 0.6% (Mortensen et al. 2022). A population-based study with 41,037 patients showed an increased risk of CRC within 6 months after acute diverticulitis, but after 1 year, there was no increased risk (Granlund et al. 2011). A nationwide population-based cohort study of 7,473 patients showed similar results (Azhar et al. 2020). The risk of CRC at the 1-year follow-up on patients with acute diverticulitis was higher than in the general population, especially if diverticulitis was complicated (Azhar et al. 2020). In a systematic review and meta-analysis of observational studies comprising 505,445 patients, the pooled prevalence of CRC was 1.9% in all patients with acute diverticulitis (Meyer et al., 2019). The prevalence was much higher among patients with CAD than in patients with UAD, at 7.9% and 1.3%, respectively.

In studies with CT-verified acute diverticulitis, the prevalence of CRC varied from 0.25% to 3.2% (Brar et al., 2013; Lecleire et al., 2014; Sallinen et al., 2014b; Horesh et al., 2016; Andrade et al., 2017; Lau et al., 2022), although the risk was much lower (0%–0.5%) when the disease was uncomplicated (complicated 5.4%–16.3%) (Brar et al., 2013; Sallinen et al., 2014b; Andrade et al., 2017; Suhardja et al., 2017). In a meta-analysis of more than 3,000 patients with CT-proven acute diverticulitis and a follow-up colonoscopy within 1 year, the risk of CRC after UAD was only 0.5%, compared to CAD at 8.3% (Rottier et al. 2019).

In radiologically confirmed UAD, the risk of CRC is similar to the general asymptomatic population (Sharma et al., 2014; Rottier et al., 2019). The increased risk seems to be related to CAD. It has been suggested that the increased risk of CRC after acute diverticulitis, particularly after CAD, is associated with difficulties in interpreting CT scans and the misdiagnosis of CRC as acute diverticulitis (Granlund et al., 2011; Meyer et al., 2019; Rottier et al., 2019; Azhar et al., 2020).

2.5 Classification of acute diverticulitis

Acute diverticulitis can be divided into uncomplicated and complicated forms based on the severity of the disease. UAD and CAD have different prognoses and require different management. UAD poses a low risk of complications and may resolve without management (Chabok et al. 2012; Mali et al. 2016; Chabok et al. 2017). In contrast, CAD is more severe, with increased morbidity and mortality (Kaiser et al., 2005; Sallinen et al., 2015a). While most acute diverticulitis episodes are uncomplicated, approximately 12%–28% are complicated (Kaiser et al. 2005; Rezapour et al. 2018). Risk factors of having complicated disease include smoking, obesity, corticosteroid use and first attack of acute diverticulitis (Papagrigoriadis et al., 1999; Chapman et al., 2005; Turunen et al., 2010; Ritz et al., 2011).

Classification based on the severity of acute diverticulitis helps physicians predict prognosis and guide management. Although there are several different classifications of acute diverticulitis, there is no consensus on the best classification. The best known is Hinchey's classification, which was based on the operative findings of 98 patients (Hinchey et al. 1978). In this classification, perforated diverticulitis is divided into four stages, indicating the severity of the perforation (Hinchey et al. 1978). Since the majority of patients do not require surgery, more recent classifications are based on CT findings (Neff & vanSonnenberg, 1989; Sher et al., 1997; Wasvary et al., 1999; Ambrosetti et al., 2002; Kaiser et al., 2005; Sallinen et al., 2015a; Sartelli et al., 2015). One classification considers patients' clinical and physiological findings (Sallinen et al., 2015a). The Kaiser classification, which is modified from Waswarys classification, considers chronic manifestations of acute diverticulitis as well (Kaiser et al. 2005). The definitions of UAD and CAD and their stages vary in different classifications (

Table 1). For example, pericolic air bubbles can be classified in UAD or CAD, depending on the classification, but some classifications do not comment on pericolic air bubbles separately (Sallinen et al., 2015a; Sartelli et al., 2015).

Table 1. Classifications of acute diverticulitis by Hinchey et al. (1978), Neff & vonSonnenberg (1989), Sher et al. (1997), Waswary et al. (1999), Sallinen et al. (2015) and Sartelli et al. (2015).

STAGE	HINCHEY (1978)	NEFF (1989)	SHER (1997)	WASWARY (1999)	SALLINEN (2015)	SARTELLI (2015)
0		Uncomplicated diverticulitis		Mild clinical diverticulitis		
1	Pericolic abscess or phlegmon	Locally complicated with local abscess	Pericolic abscess		Uncomplicated diverticulitis	Uncomplicated diverticulitis
1A				Confined pericolic inflammation		
1B				Confined pericolic abscess		
2	Pelvic, intra-abdominal or retroperitoneal abscess	Complicated with pelvic abscess		Pelvic or distant intra-abdominal abscess	Complicated diverticulitis with small abscess (< 6 cm)	
2A			Distant abscess amendable for percutaneous drainage			Pericolic air bubbles or little pericolic fluid
2B			Complex abscess associated with fistula			abscess < 4 cm
3	Generalized purulent peritonitis	Complicated with distant abscess	Generalized purulent peritonitis	Generalized purulent peritonitis	Complicated diverticulitis with large abscess (> 6 cm) or distant intraperitoneal or retroperitoneal air	
3A						Abscess > 4 cm
3B						Distant air
4	Generalized fecal peritonitis	Complicated with other distant complications	Fecal peritonitis	Fecal peritonitis	Generalized peritonitis without organ dysfunction	Diffuse fluid without distant air
5					Generalized peritonitis with organ dysfunction	Diffuse fluid with distant air

2.6 Diagnosis of acute diverticulitis

The diagnosis of acute diverticulitis was previously determined by clinical evaluation based on signs, symptoms and laboratory tests. However, while clinical evaluation of patients with suspected acute diverticulitis is needed, clinical symptoms are highly unspecific, and the accuracy of the clinical diagnosis of acute diverticulitis is low (Barksdale et al. 2015). Toorenvlient et al. (2010) compared initial diagnoses to final diagnoses after imaging and found that the clinical diagnosis of acute diverticulitis had high specificity (98%) but poor sensitivity (68%) (Toorenvliet et al. 2010). The clinical diagnosis of acute diverticulitis is considered inadequate; therefore, imaging is usually required to achieve an accurate diagnosis.

2.6.1 Clinical signs and symptoms

Left lower quadrant pain and fever have been considered the classic symptoms of acute left-sided diverticulitis (Hinchey et al., 1978; Eggesbø et al., 1998). However, patients with acute diverticulitis may present with pain in different parts of the abdomen, diffuse abdominal pain, abdominal guarding or no pain at all (Parks, 1969b; Toorenvliet et al., 2010). In a study evaluating the clinical features of 521 patients, only 30% had pain in the lower abdomen affecting both the left and right quadrants and 15% had lower left quadrant pain (Parks 1969b). Although many patients with acute diverticulitis present with left lower abdomen pain, patients with CAD tend to have more diffuse abdominal pain than patients with UAD (Laméris et al. 2010; Longstreth et al. 2012; van de Wall et al. 2013).

Fever is typically present in patients with acute diverticulitis. van de Wall et al. (2013) studied the value of fever in discriminating UAD from CAD, and no significant difference was found. The median body temperatures for UAD and CAD were 37.5 °C and 37.6 °C, respectively (van de Wall et al. 2013). Some studies have shown that patients with UAD have a normal body temperature compared to CAD patients, who present with fever more frequently (Tursi et al. 2008).

Patients with acute diverticulitis may also present with nausea, vomiting, urinary tract symptoms, anorexia, constipation or diarrhoea (Toorenvliet et al. 2010; van de Wall et al. 2013).

2.6.2 Laboratory tests

C-reactive protein (CRP) and white blood cell count (WBC) are used as serological markers for inflammation and infection. WBCs react to inflammation more rapidly than CRP does. Leucocytosis and elevated levels of CRP are common in acute diverticulitis (Hinchey et al., 1978; Eggesbø et al., 1998). It has been shown that in acute diverticulitis, WBC levels significantly decrease after 24 hours in

conservatively treated patients, while CRP levels increase after the first 24 hours (Kechagias et al. 2016).

CRP and WBC levels have been studied as potential predictors of disease severity. In a study by van de Wall et al. (2013), the optimal threshold to discriminate UAD from CAD was a CRP level of 175 mg/L with an area under curve (AUC) of 0.715 (van de Wall et al. 2013). Patients with a CRP level of 25mg/l had only a 15% chance of having CAD. Even though very high CRP levels may indicate CAD, lower levels cannot safely exclude complicated diseases. In the same study, WBC was significantly higher in patients with CAD, but it had no value in discriminating disease severity (AUC 0.578) (van de Wall et al. 2013). Mäkelä et al. (2016) found that CRP levels between 100 and 150 mg/l predicted complicated disease, but low CRP values did not reliably predict UAD (Mäkelä et al. 2016). Käser et al. compared patients with and without diverticular perforation and found that CRP (but not WBC) was a significant predictor of perforation. Perforation seemed to be unlikely with a CRP level < 50 mg/L, but a CRP > 200 mg/L was associated with a high risk of perforation (Käser et al. 2010).

2.6.3 Diagnostic imaging

2.6.3.1 Contrast enema

Before advancements in CT technology became available, contrast enema (CE) was commonly used to diagnose diverticulosis (Parks 1969a). The contrast medium (water-soluble or barium) is instilled in the rectum, and a plain X-ray of the abdomen is taken (Figure 2). The major limitations of CE in emergency settings are that CE cannot find differential causes of abdominal pain and is time consuming. In addition, barium enema is contraindicated if colonic perforation is suspected. CT imaging in the diagnosis of acute diverticulitis has been shown to be superior to CE (Hulnick et al., 1984; Ambrosetti et al., 2002). Therefore, at present, there is no role for CE in diagnosing acute diverticulitis.

Figure 2. X-ray image with barium enema examination of diverticulosis.

2.6.3.2 CT imaging

At present, CT imaging is the gold standard and the suggested modality for diagnosing acute diverticulitis (Francis et al., 2019; Hall et al., 2020; Sartelli et al., 2020; Schultz et al., 2020). CT imaging in diagnosing acute diverticulitis has many advantages, and it is currently widely available at referral centres. CT imaging facilitates determining the severity of the disease and consequently helps guide the management of acute diverticulitis. CT imaging may reveal alternative diagnoses that mimic acute diverticulitis with similar symptoms. If the diagnosis of diverticulitis is made by CT imaging, further colonic investigations are not needed in certain cases (Sallinen et al. 2014a). Given its advantages, CT's role in diagnosing acute diverticulitis has increased remarkably in recent decades (Bharucha et al. 2015).

CT is usually performed with a contrast-enhanced method. Contrast medium is mainly given intravenously (IV), and the scan is usually performed from the diaphragm to the symphysis pubis in the noncontrast and portovenous phases. Oral contrast medium can be used, but it does not provide diagnostic benefits in cases of

acute diverticulitis. Rectal contrast medium can be beneficial in cases of fistula suspicion. Technical parameters are adjusted based on a patient's size to optimise image quality and radiation dose (Tiralongo et al. 2023). The most sensitive findings for acute diverticulitis in CT imaging are bowel wall thickening and fat stranding (Kircher et al. 2002). Other findings can include inflamed diverticula, the arrowhead sign, free air or fluid, abscess, phlegmon and fascial thickening (Hulnick et al., 1984; Rao & Rhea, 1998; Kircher et al., 2002). CT images of UAD are shown in Figure 3 and CAD images are shown in Figure 4 and 5.

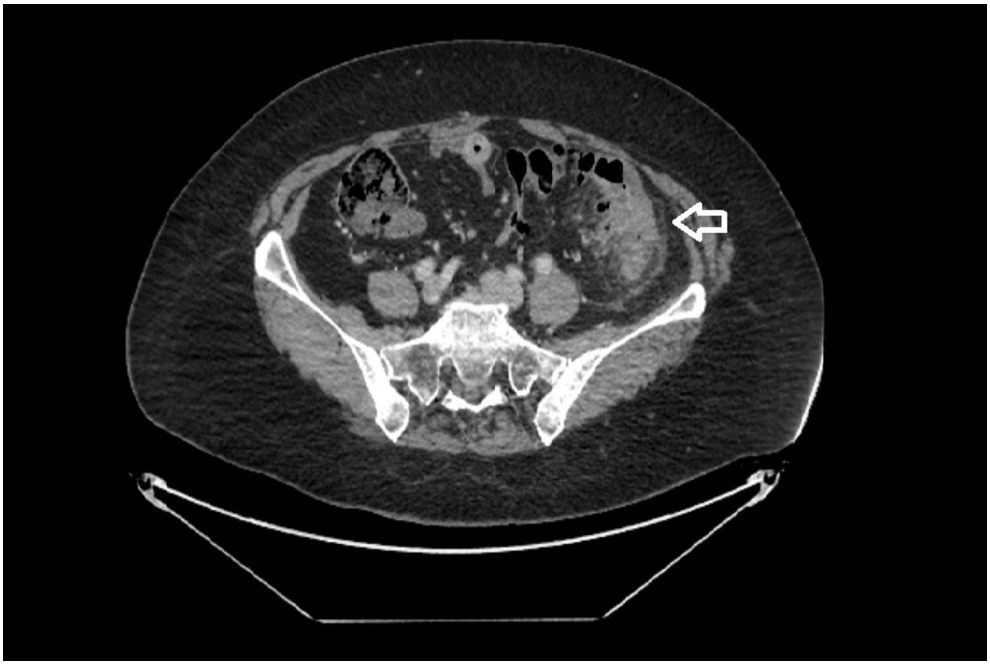

Figure 3. Uncomplicated acute diverticulitis.

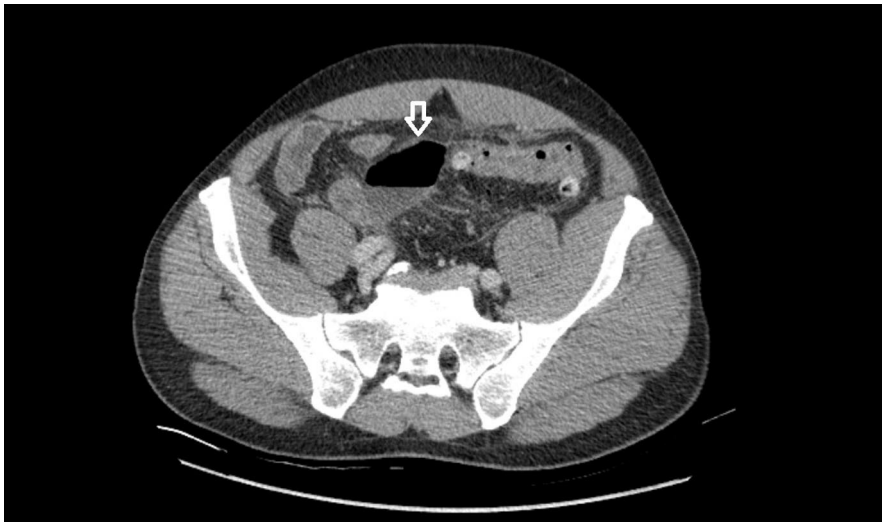

Figure 4. A large abscess (arrow) in the CT image of complicated acute diverticulitis.

Figure 5. CT image of perforated acute diverticulitis with free extra-luminal air next to an inflamedsigmoid colon and in the left upper quadrant (arrows).

The accuracy of CT in diagnosing acute diverticulitis is 98%–99%, and sensitivity and specificity are excellent, at 97%–99% and 98%–99%, respectively (Kircher et al. 2002; Werner et al. 2003). CT also has high accuracy in detecting perforations and abscesses (Ambrosetti et al. 2002; Werner et al. 2003). CT imaging has been found to be superior to CE and ultrasound (US) methods (Ambrosetti et al. 2002; van Randen et al. 2011). Ambosetti et al. (2002) compared CE and CT in 452 patients with acute diverticulitis and found CT to be superior in sensitivity to contrast enema. CT also significantly detected the severity of the disease, especially abscesses (Ambrosetti et al. 2002). In a study comparing the accuracy of CT and US, the sensitivity of CT in diagnosing acute diverticulitis was 81%, compared to US at 61%, and the difference was statistically significant (van Randen et al. 2011). However, the positive predictive values were comparable among the imaging modalities (van Randen et al. 2011). In two meta-analyses, the accuracy of US and CT showed no statistically significant difference in diagnosing acute diverticulitis (Laméris et al., 2008; Andeweg et al., 2014). However, both meta-analyses found that CT had a better ability to identify alternative diagnoses than US. In Andeweg et al.'s (2014) meta-analysis, other modalities were also investigated, and CT and US were found to be superior in diagnosing acute diverticulitis.

Unenhanced low-dose CT is an option when contrast medium is contraindicated. Since the radiation dose is much lower, it might also be an option for younger patients requiring repeated CT imaging. Thorisson et al. (2020) showed that diagnostic performance in detecting acute diverticulitis was similar with low-dose CT compared to contrast-enhanced standard CT; however, some complications of acute diverticulitis or differential diagnoses may be missed. Sensitivity and specificity were similar with contrast-enhanced CT, at 99% and 98%, respectively (Thorisson et al., 2020).

2.6.3.3 Ultrasound

US is also used to detect acute diverticulitis. A step-up approach using US first, followed by CT for inconclusive or negative findings, is recommended in some guidelines (Andeweg et al. 2011; Sartelli et al. 2020).

Abdominal US is performed with graded compression. Faeces-filled diverticula can be easily identified with US, unless the sigmoid colon is filled with faeces. In US examination, hyperechoic, noncompressible tissue represents inflamed fat, and it is always present in acute diverticulitis. The inflamed diverticulum usually corresponds to the spot of maximum tenderness (Puylaert, 2012).

The advantages of US are that it does not predispose patients to radiation, and it can be used when intravenous contrast medium is contraindicated in patients with suspected acute diverticulitis (Hall et al., 2020). Limitations of the use of US are that

it is operator-dependent, and assessment of obese patients may be difficult (Puylaert 2012). The specificity and sensitivity of US in diagnosing acute diverticulitis have been shown to be 85%–99% and 61%–89%, respectively (Zielke et al., 1997; van Randen et al., 2011; Ripollés et al., 2021; Perysinakis et al., 2024). It has been suggested that US is not reliable for finding alternative diagnoses or determining the severity of acute diverticulitis. In a study by Nielsen et al. (2014), US misdiagnosed 17% of patients with UAD and 79% with CAD compared to CT imaging (Nielsen et al. 2014). However, some studies have indicated better results. In a prospective study of 132 patients with clinically suspected acute diverticulitis, US performed by an experienced radiologist was compared to CT imaging (Perysinakis et al. 2024). In that study, the sensitivity and specificity of US were 88.6% and 84.9%, respectively, using CT as a reference standard. The severity of acute diverticulitis could be determined effectively, with an AUC of 88.9%. The authors also suggested that US could effectively exclude acute diverticulitis and confirm an alternative diagnosis in patients with left lower quadrant pain (Perysinakis et al. 2024). In a prospective study of 240 patients that evaluated the usefulness of US in differentiating UAD from CAD, the sensitivity of US for diagnosing CAD was 84% and specificity was 95.8% (Ripollés et al. 2021). US correctly classified CAD in 87.5% of patients (Ripollés et al., 2021).

US can be performed quickly and is widely available in emergency departments. Recently, point-of-care US performed by surgeons or emergency physicians has been proposed as an alternative to CT imaging to save time and resources. Point-of-care US has shown good levels of sensitivity and specificity, at 92%–98% and 88%–97%, respectively (Cohen et al., 2020; Zago et al., 2021).

2.6.3.4 Magnetic resonance imaging

Magnetic resonance imaging (MRI) has been shown to be as good as CT in diagnosing acute diverticulitis, with a sensitivity of 94%–96% and a specificity of 88% (Heverhagen et al. 2008; Lurz et al. 2022). It has been shown that MRI could be better at diagnosing small abscesses and CRC than CT (Heverhagen et al. 2008; Öistämö et al. 2013). However, the use of MRI in emergency settings is limited by its availability and higher costs compared to CT. In addition, claustrophobia and difficulty fitting into the scanner due to its small and enclosed space may restrict the use of MRI. MRI is a feasible option when ionising radiation needs to be avoided (e.g. during pregnancy).

2.6.4 Diagnostic scoring

Clinical diagnosis alone is insufficient to diagnose acute diverticulitis (Parks 1969a; Toorenvliet et al. 2010). Scoring systems have been developed to aid in the clinical diagnosis of acute diverticulitis (Laméris et al., 2010; Andeweg et al., 2011; Bolkenstein et al., 2018; Covino et al., 2021; Sigurdardottir et al., 2022). Laméris et al. (2010) suggested a clinical decision rule to identify patients with suspected acute diverticulitis. A combination of three features—the absence of vomiting, left lower quadrant pain and elevated CRP levels—could predict the probability of acute diverticulitis, with a positive predictive value of 88% (Laméris et al. 2010). In a study by Andeweg et al. (2011), previous episodes, the absence of vomiting, left lower quadrant pain, aggravation of pain on movement and CRP > 50 mg/L were found to be independent predictors of acute diverticulitis and were used to create a nomogram to predict the risk of the disease (Andeweg et al. 2011). Sigurdardottir et al. (2022) formulated a risk score with several predictors of acute diverticulitis that could predict its occurrence, with an AUC of 0.852 (Sigurdardottir et al. 2022). These scoring systems were developed to help clinicians differentiate acute diverticulitis patients from those with abdominal pain.

Bolkenstein et al. (2018) and Covino et al. (2021) developed and validated risk scores to predict the severity of acute diverticulitis. Bolkenstein et al. (2018) created a scoring system that can estimate the risk of CAD by using abdominal guarding, CRP and WBC levels as variables in the score. CRP and WBC were given zero to seven points depending on the value, and abdominal guarding was given four points. Risk was then stratified according to the combined points. For example, the risk for CAD is only 4% with a CRP < 100 mg/L, WBC < 15.0 x 10^9/L and no signs of abdominal guarding (total points 0). In the PACO-D score, variables associated with CAD were male sex, obesity, constipation, no proton pump inhibitor medication, anaemia and elevated CRP (each worth one point) (Covino et al. 2021). The risk of CAD was then stratified to low, moderate and high risk according to the total points. Patients with low risk in their validation cohort had an OR of 2.5 compared to patients with a high-risk OR of 5.3 (Covino et al. 2021).

2.6.5 Differential diagnosis

Several other conditions may present similar symptoms as those of acute diverticulitis, such as non-specific abdominal pain, appendicitis, colitis, bowel obstruction, gynaecological diseases, colon cancer and nephrolithiasis (Hinchey et al. 1978; Laurell et al. 2007; Wilkins et al. 2013). In a study of 287 patients with clinically suspected acute diverticulitis, only 43% had it based on a CT evaluation (Andeweg et al. 2011). The most frequent differential diagnoses found in CT were no abnormal findings, gynaecological disorders and diverticulosis without

inflammation. Laméris et al. (2010) found that 63% of patients with clinically suspected diverticulitis had acute diverticulitis confirmed by imaging. The most frequent differential diagnoses were acute appendicitis and nonspecific abdominal pain (Laméris et al. 2010).

2.7 Management of acute diverticulitis

2.7.1 Nonoperative management of UAD

Antibiotics were long the cornerstone of treatment for acute diverticulitis because diverticulitis was considered an infectious process (Hinchey et al. 1978). Contrary to recent guidelines, bed rest, nil per os and IV fluids were also recommended until recovery (Hinchey et al. 1978). At present, physical activity and an unrestricted diet are preferred if a patient's general condition allows them (Schultz et al. 2020).

Current guidelines do not recommend antibiotic treatment for UAD in immunocompetent patients (Hall et al., 2020; Sartelli et al., 2020). Four randomised controlled trials (RCT) have shown that UAD can be safely managed without antibiotics (Chabok et al. 2012; Daniels et al. 2017; Jaung et al. 2021; Mora-López et al. 2021). These trials placed randomised patients in the observation group without antibiotics or in the group receiving antibiotic therapy (Table 2). In the AVOD (Antibiotika Vid Okomplicerad Divertikulit) trial, no statistically significant difference was found between the groups for recovery, recurrence or complications at the 1-year follow-up (Chabok et al. 2012). The outcomes of the DIABOLO (Diverticulitis: antibiotics or close observation?) trial were similar at the 6-month follow-up (Daniels et al. 2017). Morbidity, time to recovery from the initial episode, occurrence rates of CAD and recurrent diverticulitis were similar between the groups (Daniels et al. 2017). Additionally, readmission/intervention rates and the need for surgery were comparable. Patients without antibiotic treatment had shorter hospital stays because they were mainly treated as outpatients, while patients receiving antibiotics were admitted (Daniels et al. 2017). The STAND (Selective treatment with antibiotics for non-complicated diverticulitis) trial was placebo controlled and found no difference in adverse events, readmission rates and need for interventions between the groups (Jaung et al. 2021). In DINAMO (Nonantibiotic outpatient treatment of mild acute diverticulitis) study in which patients were treated in outpatient protocol no statistically significant difference was found in hospital admissions nor in revisits, pain control, recovery or complications (Mora-López et al. 2021). Non-antibiotic treatment in selected UAD patients is supported by several systematic reviews and meta-analyses (Tandon et al. 2018; Mocanu et al. 2018; Desai et al. 2019; Au and Aly 2019; Poh et al. 2023).

Table 2. RCTs comparing antibiotic treatment to observation in uncomplicated acute diverticulitis(Chabok et al. 2012, Daniels et al. 2017, Jaung et al. 2021, Mora-López et al 2021).

RCT	Imaging criteria	Patients	Antibiotics used in the study	Patients admitted	Follow-up time, months	Primary outcomes (p-value)	Secondary outcomes
AVOD (Chabok et al 2012)	CT (Ambrosetti classification mild)	Antibiotics n= 314 Symptomatic treatment n=309	IV cefalosporin & metronidazole or carbapenem or piperacillin-tazobactam followed by pociprofloxacin or cefadroxil + metronidazole (at least 7 days treatment)	Yes	12	Complications (p=0.3) and emergency surgery (p=0.54)	Length of hospital stay, recurrent diverticulitis
DIABOLO (Daniels et al 2017)	CT (Wasvary classification Hinchey 1 or Ambrosetti classification mild)	Antibiotics n = 266 Symptomatic treatment n= 262	IV amoxicillin-clavulanic acid at least 48 h followed by po treatment (total of 10 days treatment)	Yes (35 patients treated outpatient)	6	Time to recovery (p=0.15)	Readmissions, complicated, ongoing or recurrent diverticulitis, sigmoid resection, mortality
STAND (Jaugn et al 2021)	CT (Wasvary classification Hinchey 1a)	Antibiotics n = 85 Plasebo n= 95	IV cefuroxime & metronidazole max 48 h followed by po amoxicillin/clavulanic acid (max 7 days treatment)	Yes	1	Length of hospital stay (p=0.2)	Adverse events, readmissions, interventions, change in inflammation markers, pain scores
DINAMO (Mora-Lopez et al 2021)	CT (Neff classification 0)	Antibiotics n = 242 Symptomatic treatment n = 238	IV amoxicillin-clavulanic acid max 24 h followed by po treatment (max 7 days treatment)	No	3	Hospital admission (p=0.19)	Number of emergency department visits, pain control, emergency surgery

It has been shown that outpatient management of patients with UAD is feasible and does not increase the risk of complications (Biondo et al. 2014; Isacson et al. 2015; Mali et al. 2016; Joliat et al. 2017; Mora-López et al. 2021). A RCT comparing admitted and outpatient treated patients receiving antibiotic therapy found no difference in treatment failure, readmissions, need for surgery and morbidity (Biondo et al. 2014). In a study of 155 patients with first-time UAD, 97.4% were managed successfully as outpatients without antibiotics, admissions or complications (Isacson et al. 2015). Disease management failed for four patients, but they did not require surgery (Isacson et al. 2015). Similar results were found by Mali et al. (2016). In their prospective cohort study, only 3% of outpatients had readmissions within 30 days, and none of these patients had complications or surgery (Mali et al., 2016). Outpatient management of patients with UAD also reduces healthcare costs (Isacson et al. 2018). For example, healthcare costs were reduced by nearly 50% between 2011 and 2014, when patients were increasingly treated as outpatients (Isacson et al. 2018). In a study by Biondo et al. (2014) outpatient treatment reduced healthcare costs by 67%.

Notably, studies on outpatient management and non-antibiotic treatment have mainly included immunocompetent and otherwise generally healthy individuals. It has been shown that immunocompromised diverticulitis patients have an increased risk of morbidity and mortality (Tartaglia et al. 2023). Therefore, it is recommended that immunocompromised patients and patients with other comorbidities be treated with antibiotics (Sartelli et al. 2020).

2.7.2 Nonoperative management of CAD

It has been shown that the nonoperative management of perforated diverticulitis is also safe in selected patients. Sallinen et al. (2014a) showed that patients with a small amount of distant extraluminal or pericolic air can be treated conservatively if there are no signs of clinical peritonitis. Only 15% of the patients needed emergency surgery. Of those with pericolic air, the success rate of conservative management was 99%, with a 0% mortality rate. If patients showed distant intra- or retroperitoneal air, the success rates were 62% and 44%, respectively (Sallinen et al., 2014a). A retrospective cohort study of patients with Hinchey 1A diverticulitis with isolated pericolic air on CT evaluated the failure rates of conservative treatment (Bolkenstein et al., 2019c). Only 8% of patients (9/109) showed treatment failure, which was defined as the need for percutaneous abscess drainage or emergency surgery within 30 days. In addition, almost 50% of patients were treated without antibiotics, and the treatment failure between patients with or without antibiotic treatment was not statistically significant (Bolkenstein et al., 2019c). A cohort study by Adiamah et al. (2021) evaluated the outcomes of 880 patients treated conservatively after a

diagnosis of CAD (Adiamah et al. 2021). They recorded readmissions, mortality rates and the need for surgery at short- and long-term follow-up. The readmission rate was 18.2%, and 3% required emergency surgery at their one-year follow-up. The mortality rate was low in younger age groups but significantly higher in the older population, indicating that older patients were likely unsuitable for surgery. They concluded that conservative treatment of locally perforated diverticulitis is safe in patients under 65 years of age (Adiamah et al. 2021). A prospective study of 810 patients with pericolic air bubbles showed a low failure rate of 6.3% in conservatively treated patients during index admission and 16.5% of patients were readmitted within one-year follow-up requiring antibiotics, percutaneous drainage or surgery (Tejedor et al. 2023).

Furthermore, outpatient management of mild complicated diverticulitis is suggested to be safe (Joliat et al., 2017; Bolkenstein et al., 2019c). A retrospective study compared inpatient and outpatient treatment of patients with uncomplicated or mild complicated diverticulitis, which was defined as an abscess < 4 cm or pneumoperitoneum < 2 cm (Joliat et al. 2017). All patients were treated with antibiotics, and treatment failure was defined as readmission or the need for drainage or surgery. Treatment failure was found in 10% of the outpatient management group and 32% of the inpatient management group. The difference was statistically significant in favour of outpatient treatment (Joliat et al. 2017). Although they could not identify the risk factors of early treatment failure for admitted patients, treatment was chosen by a physician on a case-by-case basis, which might have biased the results (Joliat et al. 2017).

2.7.3 Interventional radiology

Percutaneous drainage of abscesses associated with diverticulitis was found to be feasible in the 1980s (Saini et al., 1986; Neff et al., 1987). It has been suggested that, in many cases, with the drainage of abscesses, emergency surgery can be avoided (Durmishi et al. 2006; Elagili et al. 2014). Abscesses over 3 cm are usually suitable for drainage, depending on the location. Either US- or CT-assisted percutaneous drainage can be used (Clark and Towbin 1983). Small abscesses can be treated with antibiotics alone (Siewert et al., 2006; Mali et al., 2019). The drainage of large abscesses is the current clinical practice and is recommended in international guidelines (Hall et al., 2020; Sartelli et al., 2020; Schultz et al., 2020). However, several studies have shown that in patients with diverticular abscesses, percutaneous drainage is not superior to antibiotic treatment alone (Brandt et al., 2006; Elagili et al., 2015; Mali et al., 2019; Podda et al., 2024).

2.7.4 Emergency surgery

Surgical management is needed in critically ill patients with acute diverticulitis. In a large cohort study, 20% of all patients admitted due to diverticular disease required emergency surgery (Anaya 2005). It has been shown that free perforation requiring emergency surgery occurs more frequently with the first presentation of the disease than after recurrent episodes (Nylamo, 1990; Issa et al., 2009; Carmona Agúndez et al., 2024). Patients in older age groups, those who are immunocompromised and patients with respiratory disease have a greater risk of perforated disease (Carmona Agúndez et al. 2024).

Different surgical procedures have been used to manage perforated diverticulitis over the decades, but which is the best procedure is still under debate (Cirocchi et al. 2017). Hartmann's procedure (HP), in which sigmoid resection and proximal end colostomy are performed, with the rectal stump then closed, was introduced in 1921 by Henri Hartmann (Hotouras 2008). It is still recommended for critically ill patients with peritonitis and unstable haemodynamics (Sartelli et al. 2020).

Primary resection with anastomosis, with or without diverting stoma, has been suggested as the preferred procedure for selected patients requiring operative treatment (Lambrichts et al., 2020a; Ryan et al., 2020). Four RCTs compared HP and primary anastomosis in haemodynamically stable patients with Hinchey III and IV diverticulitis (Binda et al., 2012; Oberkofler et al., 2012; Bridoux et al., 2017; Lambrichts et al., 2020a). No significant difference was found in mortality, morbidity or complication rates after short-term follow-up between the groups, but the permanent stoma rate was significantly higher in the HP group (Oberkofler et al., 2012; Bridoux et al., 2017; Lambrichts et al., 2020a). Due to recruitment difficulties, all four RCTS were terminated before the planned sample size was reached, and the sample sizes were relatively small (n = 62–133). A meta-analysis of 12 studies, including the four RCTs, compared primary resection with anastomosis to HP in acute diverticulitis with generalised peritonitis (Ryan et al. 2020). There was no difference in 30-day mortality or overall morbidity rates. However, primary anastomosis showed less severe complications, unplanned reoperations and permanent stoma rates compared to those of HP. The meta-analysis was in favour of primary resection with anastomosis in selected patients, but in patients with Hinchey IV peritonitis, more HP was performed than primary anastomosis (Ryan et al. 2020). Whether a protective stoma is essential after resection and primary anastomosis is still unclear and of interest for future studies (Pinson et al. 2022). Emergency surgery is traditionally performed as open surgery, but it can be performed with the laparoscopic approach. It has been shown that less experienced surgeons perform more HP procedures with open surgery than with laparoscopic procedures and primary anastomosis compared to more experienced surgeons (Perrone et al. 2024). In addition, robotic surgery has shown promising results and advantages over

laparoscopic approach in terms of anastomotic leakage, intensive care unit admissions and conversion rates (Curfman et al. 2023).

A decade ago, laparoscopic lavage was considered a promising procedure to avoid emergency resection. Three RCTs evaluated its feasibility in CAD patients. Laparoscopic lavage was compared to HP in the DILALA (Diverticulitis laparoscopic lavage vs. resection) trial, to primary resection in the SCANDIV (Scandinavian Diverticulitis) trial and to HP and primary resection in the LOLA (LaparOscopic Lavage) trial (Schultz et al., 2015; Vennix et al., 2015; Angenete et al., 2016). With primary endpoints of morbidity and mortality at 12 months in the DILALA trial, no difference was found between the HP and laparoscopic lavage groups (Angenete et al. 2016). The conclusion of the SCANDIV trial was that laparoscopic lavage was not recommended due to higher complications and reoperation rates (Schultz et al. 2015). The LOLA trial was terminated early due to safety concerns with the lavage group (Vennix et al. 2015). Currently, laparoscopic lavage is not recommended as the first-line method in patients requiring surgery.

Damage control surgery (DCS), which is used to treat unstable trauma patients, has been suggested in select cases for critically ill patients with perforated diverticulitis (Sartelli et al. 2020). A systematic review and meta-analysis by Cirocchi et al. (2021) evaluated the outcomes of DCS in patients with Hinchey II–IV acute diverticulitis. The meta-analysis showed promising results: approximately 62% of patients had no stoma, major leaks were found in 4.7% of patients and mortality was 9.2% (Cirocchi et al. 2021). Further studies are needed to evaluate the benefits of DCS in patients with perforated acute diverticulitis. A multicentre RCT is currently recruiting patients with complicated peritonitis and septic shock to evaluate the DCS approach (Kirkpatrick et al. 2018).

2.7.5 Follow-up investigations after acute diverticulitis

Colonic evaluation has been suggested after an episode of acute diverticulitis to verify the diagnosis if it was made based on clinical findings and to rule out CRC. Colonoscopy is usually performed four to six weeks after the acute phase of diverticulitis. CE and CT colonography (CTC) investigations have also been used to evaluate the colon after acute diverticulitis (Hjern et al. 2007). Since colonoscopy has been shown to be significantly more sensitive than CE or CTC in the detection of colonic polyps and CRC, the roles of CE and CTC have diminished (Rockey et al. 2005).

In the last decade, the need for colonic evaluation after an episode of diverticulitis has been questioned because the diagnosis is more often made with CT imaging. In a recent meta-analysis, the risk of CRC after CT-verified acute diverticulitis was 0.5% in UAD and 8.3% in CAD (Rottier et al. 2019). Differential

diagnosis between CRC and CAD can be difficult, and an increased risk of CRC, especially after CAD with abscesses, has been found (Sallinen et al., 2014b; Andrade et al., 2017). Therefore, after CT-verified CAD, the need for colonoscopy is widely acknowledged in national and international guidelines and in clinical practice (Hall et al., 2020; Sartelli et al., 2020; Schultz et al., 2020; Qaseem et al., 2022). However, routine colonic evaluation after UAD may not be necessary. Several studies have shown a very low risk of CRC after CT-verified UAD (Westwood et al., 2011; Brar et al., 2013; Sallinen et al., 2014b; Andrade et al., 2017; Suhardja et al., 2017). It has been shown in Hinchey 0 and I patients that the risk of CRC increases if alarming symptoms (e.g. weight loss, rectal bleeding, change in bowel habits or ongoing or persistent symptoms) are present (Ramphal et al. 2016). A large cross-sectional study compared the prevalence of CRC on colonoscopy in patients with diverticulitis and to those undergoing CRC screening (Redd et al. 2024). In colonoscopies performed solely for the follow-up of diverticulitis, with no other indications, the prevalence of CRC was lower (0.17%) compared to screening colonoscopies (0.33%) (Redd et al. 2024). However, patients with CAD showed an increased prevalence of CRC (1.43%). Many recent guidelines recommend not routinely performing colonoscopy after a conservatively treated episode of UAD with an uneventful recovery or without alarming symptoms (Hall et al., 2020; Sartelli et al., 2020; Schultz et al., 2020; Qaseem et al., 2022). Some older guidelines recommend colonoscopy after the recovery of conservatively managed CT-verified acute diverticulitis, regardless of severity (Andersen et al. 2012; Stollman et al. 2015). The Dutch guidelines do not recommend routine colonoscopy after an episode of acute diverticulitis in asymptomatic patients, regardless of whether the disease is uncomplicated or complicated on CT (Andeweg et al. 2013).

2.8 Recurrent acute diverticulitis

The recurrence of acute diverticulitis after its first presentation is common. In a population-based cohort study of 65,162 patients with first-time diverticulitis, the recurrence rate was 11.5%, with a minimum of a 4-year follow-up (El-Sayed et al. 2018). Similar findings were made in a prospective observational study in which the recurrence rate was 19.8% after the first CT-verified diagnosis of acute diverticulitis (Pastor-Mora et al. 2024). In a cohort study of 672 patients, the recurrence rate was 36% at the 5-year follow-up, and complicated recurrence was found in 3.9% of the cases (Hall et al., 2011). It has been shown that the risk of recurrence increases with subsequent episodes (Bharucha et al. 2015). The cumulative incidence of the first recurrent episode of acute diverticulitis was 8% at 1 year, 17% at 5 years and 22% at 10 years. The cumulative incidence after the second recurrence was 19% at 1 year, 44% at 5 years and 55% at 10 years. Finally, after the third recurrence, the cumulative

incidence was 24% at 1 year and 40% at 3 years (Bharucha et al. 2015). Recurrences seem to occur similarly in younger and older age groups (Kaiser et al. 2005).

Most recurrent acute diverticulitis episodes are uncomplicated (Hall et al., 2011; Sallinen et al., 2015b). The first attack of acute diverticulitis is usually the most severe (Nylamo 1990; Chapman et al., 2006; Issa et al., 2009). It has been suggested that recurrent diverticulitis is not associated with an increased risk of complications or mortality (Ambrosetti et al., 2002; Chapman et al., 2006; Bharucha et al., 2015; Sallinen et al., 2015b; El-Sayed et al., 2018). Conversely, it has been shown that a history of three or more previous episodes is a risk factor for UAD but not for CAD (Sallinen et al., 2015b). Additionally, patients with complicated recurrences after one or two episodes of acute diverticulitis had more perforations compared to those with more than two episodes (Chapman et al., 2006).

Several risk factors of recurrence have been suggested, including younger age, dyslipidemia, history of CAD and family history of diverticulitis (Hall et al., 2011; El-Sayed et al., 2018; Pastor-Mora et al., 2024). Obesity, smoking and female sex were found to be risk factors of recurrence in a study by El-Sayed et al. (2018) and a long segment of associated colon in a study by Hall et al. (2011), but in a study by Pastor-Mora et al. (2024), they were not statistically significant factors for recurrence. Earlier diverticulitis, abscess and corticosteroid use have been found to be risk factors of complicated recurrence (Sallinen et al., 2015b). Based on these risk factors, Sallinen et al. (2015b) proposed a risk score to predict the complicated recurrence of acute diverticulitis. Earlier diverticulitis is one point, abscess is two points and corticosteroid use is three points. A low risk of recurrence is one to two points and a high risk is more than two points. Notably, 43% of patients with high risk developed complicated recurrences, while only 3% of the low-risk group did (Sallinen et al., 2015b). This score might help surgeons and patients determine the need for elective surgery.

2.9 Prevention of acute diverticulitis

Acute diverticulitis is common and prone to recurrence; therefore, studies addressing the prevention of diverticulitis have been conducted. Since the aetiology of acute diverticulitis is linked to several lifestyle factors, it has been suggested that modifying these factors could prevent diverticulitis. The number of low-risk lifestyle factors (e.g. low red meat intake, high fibre intake, vigorous physical exercise, normal weight and not smoking) has been shown to inversely correlate with diverticulitis risk (Liu et al. 2017). It has been suggested that physical exercise could reduce the development of acute diverticulitis (Strate et al., 2009a). Maintaining a normal weight might be an important factor in preventing acute diverticulitis (Ma et al., 2018; Strate et al., 2009). Strate et al (2009b) found that men who gained 45

pounds or more since age 21 had higher risk for acute diverticulitis than those who gained less than 5 pounds. Women who gained > 20 kg had 80% increased risk compared to those without weight gain or with loss or gain of maximum of 2 kg [Ma et al., 2018]. A high fibre diet seems to decrease the need for hospital admission for diverticular disease (Mahmood et al., 2019). Previously, patients with diverticulosis were advised to avoid nuts, seeds and corn to prevent obstruction of the diverticulum. However, the intake of nuts, corn and popcorn does not increase the risk of acute diverticulitis (Strate et al., 2008). Some medications, such as rifaximin and 5-aminosalicylate (5-ASA), have been proposed to reduce the recurrence of acute diverticulitis, although the evidence is not convincing. Rifaximin might lower the risk of a first episode of diverticulitis, but the cost–benefit ratio is high, and the value for preventing recurrences is unclear (Koch et al., 2023). In a 2017 Cochrane review, no beneficial effect on 5-ASA was found in terms of preventing recurrent diverticulitis (Carter et al., 2017).

2.9.1 Elective surgery

Elective surgery is needed when diverticulitis causes complications, such as fistulas or obstructions. Laparoscopic surgery has been widely accepted as the standard care for elective surgery for diverticular disease. Robotic approach is gaining more and more interest and may offer advantages in terms of conversion rates and shortened hospital stay (Giuliani et al. 2022).

Previously, sigmoid resection was also indicated after two episodes of acute diverticulitis or one episode of nonoperatively treated CAD. Several studies have shown that a history of several episodes of acute diverticulitis is not associated with an increased rate of complications or mortality (Chapman et al., 2006; Sallinen et al., 2015b; El-Sayed et al., 2018). Therefore, current guidelines recommend a more individual approach that considers patients' related risk factors and preferences (Stollman et al., 2015; Sartelli et al., 2020; Schultz et al., 2020). Even though elective surgery does not eliminate the risk of recurrent acute diverticulitis, it can improve the quality of life (QoL) and reduce further diverticulitis episodes (Santos et al., 2023). In a systematic review, the risk of recurrence after sigmoid resection was 0%–15% at long-term follow-up (Waser et al., 2023). When the recurrent episode was diagnosed with CT imaging, the risk was between 2.1% and 8.6% (Giulio et al., 2022; Waser et al., 2023). Most recurrences after surgery are uncomplicated (Giulio et al., 2022; Waser et al., 2023). Two RCTs comparing sigmoid resection to conservative treatment of patients with multiple recurrences or persistent symptoms of diverticulitis have been conducted (Bolkenstein et al., 2019a; Santos et al., 2023). The LASER (Laparoscopic Elective Sigmoid Resection Following Diverticulitis) trial, a multicentre RCT, compared sigmoid resection to conservative treatment in

patients with multiple recurrences or persistent symptoms. The patients' QoL improved after resection at the two-year follow-up compared to patients in the conservative treatment group (Santos et al., 2023). Similar findings resulted from the DIRECT (Diverticulitis Recurrences or Continuing Symptoms Treatment) trial at the five-year follow-up (Bolkenstein et al., 2019a). The patients' QoL improved after six months, and the results lasted through a five-year follow-up period (Bolkenstein et al., 2019a). In both trials, the risk of recurrent diverticulitis was 11% in the surgery group but significantly higher (30 % and 61%) in the conservative treatment group. Major complications in the surgery group were present in 10% of the patients in the LASER trial and 11% in the DIRECT trial, while 27% and 34% of the patients had minor complications, respectively.

3 Aims

This thesis focused on aspects of the diagnostics of patients with acute diverticulitis. The specific aims were as follows:

I To investigate the risk of CRC after CT-verified acute diverticulitis, with a special interest in long-term follow up and whether colonic examination is needed.

II To assess the usefulness of reassessment of CT imaging reports and the role the radiologists' experience in emergency settings.

III To investigate risk factors for CAD and create a risk score for predicting disease severity without CT imaging.

4 Patients and Methods

4.1 Patients

4.1.1 Study I

The study population was obtained from the Register of Primary Health Care Visits (HILMO). The cohort included 1,694 patients with an International Classification of Disease, 10th revision (ICD-10) diagnosis of K57.0–K57.9 who were treated at Turku University Hospital between 2003 and 2012. Patients with ICD-10 codes C18–C20, indicating CRC, in addition to ICD-10 codes K57.0–K57.9, were identified from the same register. For the study purposes, patients with CT-verified acute diverticulitis were identified from the hospital electronic patient records. Patients with only clinical diagnosis of acute diverticulitis or with unenhanced low-dose CT or US were excluded from the analysis. In addition, 77 patients with diagnosis other than acute diverticulitis in CT, 62 patients with no real evidence of acute diverticulitis despite of ICD code K57, and 57 patients eventually presenting with diagnosis other than acute diverticulitis after further investigations during hospitalization were excluded. Overall, 270 patients with CT-verified acute diverticulitis were included in Study I. Information on the patient data used in Study I is shown in Figure 6.

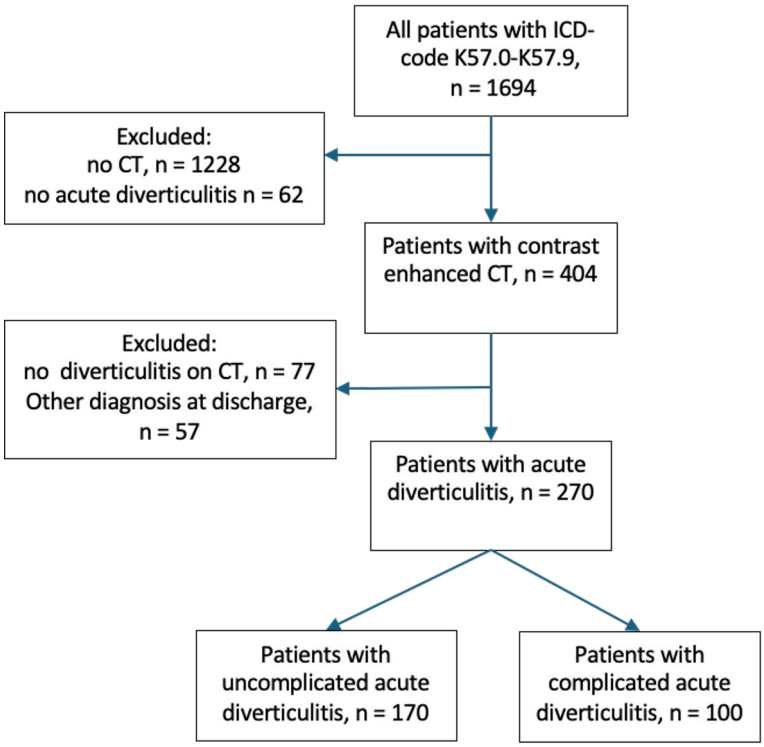

Figure 6. Flowchart of the Study I (Modified from Study I with the permission of the copyright holder).

4.1.2 Studies II and III

All patients treated in the emergency department of Tampere University Hospital with ICD-10 codes K57.0–K57.9 from 2015 to 2017 were identified from the hospital records. A patient flowchart is shown in Figure 7. Overall, 606 patients were identified. For Study II, patients with another diagnosis, despite having ICD-10 codes K57.0–K57.9, were excluded, as well as patients who did not undergo contrast-enhanced CT. The final population of Study II comprised 562 patients with CT imaging and ICD-10 codes K57.0-K57.9. In Study III, patients with a final diagnosis other than AD (n = 8) were excluded from the analysis. Additionally, patients with incomplete data on the variables used in Study III (n = 41) were not included in the formulation of the scores.

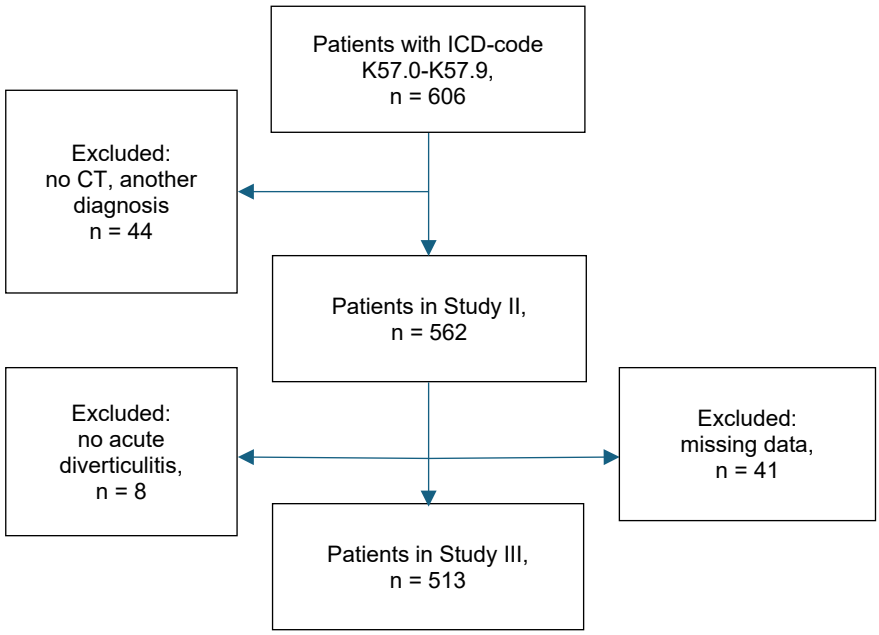

Figure 7. Flowchart of Studies II and III.

4.2 Data collection and methods

All patients included in Studies I–III underwent IV contrast-enhanced CT imaging. All abdominal CT scans were performed from the diaphragm to the symphysis pubis using helical data acquisition in the portovenous phase, according to the standard imaging protocol of the hospital. In all studies, CT scans were initially analysed by an on-call radiologist in an emergency setting. The electronic patient records of patients were retrospectively scrutinised for the studies' purposes.

4.2.1 Study I

The data collected from electronic patient records included age, sex, clinical and initial laboratory findings on admission, findings in CT reports, information on further colonic evaluation, history of previous diverticulitis and occurrence of CRC. For the purposes of long-term follow-up, the patient data were re-evaluated, and the possible occurrence of CRC was detected. The study hospital is responsible for all CRC patients in the district, and therefore, all patients with CRC can be found in our electronic patient records. Follow-up until 1 year was considered short-term follow-up. Long-term follow-up times varied between 9 and 17 years. The patients were divided into two groups based on their CT reports. One group comprised patients with UAD (a CT report of acute diverticulitis without signs of complications). In the

other group, acute diverticulitis was considered complicated if CT scans showed a suspicion of perforation, abscess, fistula, bowel obstruction or stricture.

4.2.2 Studies II and III

Study II examined the data on patients' age, sex, history of previous diverticulitis, treatment and final diagnosis on hospital discharge. The mean follow-up time was 64 months after an episode of acute diverticulitis. The experience of the radiologist was noted. CT images were analysed in the emergency department by either a consultant with six or more years of experience or a resident radiologist with a minimum of two years of experience. Reassessment of CTs was completed by consultant abdominal radiologists during normal working hours. The severity of acute diverticulitis was determined based on CT reports, according to the classification by Ambrosetti et al. (2002) in Study II. Acute diverticulitis was considered uncomplicated (moderate diverticulitis) with evidence of inflammation of pericolic fat or moderate bowel wall thickening and with no signs of complication. Severe diverticulitis (i.e. CAD) was considered when signs of abscess or perforation were detected.

The same retrospectively collected data were used in Studies II and III. In addition, in Study III, patients' clinical findings and duration of symptoms were examined, along with patients' comorbidities and the use of immunosuppressive medication. In Study III, the severity of acute diverticulitis was classified according to Sallinen et al. (2015a) after reviewing electronic patient charts. Stage 1 was defined as UAD and Stages 2-5 as CAD in Study III.

In Study III, the Acute Diverticulitis Severity Score was formulated by logistic regression analysis. Variables associated with a higher risk of CAD, as identified through univariate analysis, were selected for multivariate analysis. Then variables independently related to CAD were incorporated into the score. Although cardiac comorbidities were linked to CAD in the univariate analysis, their lack of association in the multivariate analysis led to their exclusion. Instead, we used a new variable that incorporated any significant comorbidity. Continuous laboratory values and body temperature were categorised according to cut-off points, which were determined using receiver operating characteristic (ROC) analysis. The cut-off points were 1) the value corresponding to 80% sensitivity, 2) the value corresponding to 80% specificity and 3) the mean of these two values. The cut-off values for the CRP level were rounded to the nearest five units. Two cut-off points were used for CRP because the distribution of the CRP values differed in patients with symptoms lasting < 24 hours and > 24 hours. The score points were obtained from regression coefficients rounded to the nearest integer. Since patients with peritonitis or sepsis and those with worsening symptoms despite of ongoing wide-spectrum antibiotic

therapy usually require radiological investigations, they were given the maximum number of points, reflecting the necessity of CT imaging in these patients.

4.3 Statistical analyses

Statistical analyses were performed using the SAS System for Windows version 9.4 in Study I and SPSS Statistics version 22 for Windows in Studies II and III.

In Study I, descriptive statistics for categorical variables were reported as percentages and for continuous variables as means (standard deviations). Mean differences in continuous variables between the uncomplicated and complicated diverticulitis groups were tested using a two-sample t-test. A chi-squared test or Fisher's exact tests were used to compare differences in categorical variables between the groups.

In Study II, descriptive statistics for categorical variables were reported as percentages and for continuous variables as medians (along with minimum and maximum values). Categorical variables were compared using $\chi 2$ or Fisher's exact test (when the expected cells' values were five or lower). Cohen's Kappa analysis was used to analyse interobserver reliability. Values ≤ 0 indicated no agreement, while 0.01–0.20 indicated none to slight, 0.21–0.40 indicated fair, 0.41– 0.60 indicated moderate, 0.61–0.80 indicated substantial and 0.81–1.00 indicated almost perfect agreement.

The χ^2 test or Fisher's exact test was performed to compare categorical variables, and the Mann–Whitney U-test was employed for continuous variables in Study III. Continuous variables were presented as means (and standard deviations) or medians (along with the minimum and maximum values or the interquartile range), depending on the value distribution. Regression analysis was used to identify independently associated risk factors. The cut-off points of the continuous variables were determined through ROC analysis. The Kruskal–Wallis test was applied to estimate the statistical significance of the categorised variables. The regression coefficients were calculated using logistic regression analysis employing the enter method.

A p-value < 0.05 was considered statistically significant in all studies.

4.4 Study approval

Study I was approved by the Turku Clinical Research Centre. Studies II and III were approved by the Regional Ethics Committee of the Expert Responsibility Area of Tampere University Hospital (permission number R21587).

5 Results

5.1 Risk for CRC after CT verified acute diverticulitis

UAD was found in 170 patients, and CAD was found in 100 patients. A comparison of both groups' baseline characteristics is shown in Table . In the UAD and CAD groups, the mean ages were 61 and 64 years, and 59% and 57% were female, respectively. The characteristics of the patients in both groups were otherwise similar but the CRP levels were higher in the CAD group ($p < 0.001$).

Table 3. Demographic data of patients in Study I (modified from study I with the permission of the copyright holder).

	UAD n=170 mean (SD) or %	**CAD n=100 mean (SD) or %**	**p-value**
Female, %	59	57	0.70
Age, years	61 (15)	64 (14)	0.07
No previous diverticulitis, %	88	85	0.55
Temperature, °c	37.6 (0.8)	37.8 (0.8)	0.19
CRP, mg/l	120 (80)	158 (87)	0.0003
Haemoglobin, g/l	134 (16)	131 (15)	0.14
WBC, x10^9/l	12.3 (4.9)	12.6 (5.6)	0.58

In the short term, CRC was found in 1.5% (n = 4) of all patients. When the risk of CRC was stratified according to disease severity, there was no statistically significant difference between the study groups ($p = 0.15$). In the UAD group, CRC was found in 0.6% (n = 1) of the patients, compared to 3% (n = 3) in the CAD group. Patient with CRC in the UAD group underwent emergency surgery during the same admission due to obstruction of the sigmoid colon. In the CAD group, CRC was found after further colonic evaluation. The electronic patient charts of the study participants were reviewed for 9 to 17 years after the initial episode of acute diverticulitis, which revealed an additional 3 cases of CRC in patients with UAD at the initial presentation. No CRC was found in CAD patients in the long run. In long-

term follow-up all CRC cases were found in parts of the colon other than where diverticulitis had occurred. The CRC findings of the Study I are summarised in Table

Table 4. CRC findings in short-term and long-term follow-up (modified from Study I with permission of the copyright holder).

CRC finding	All n=270	UAD n=170	CAD n=100
Short-Term Follow-Up	4 (1.5 %)	1 (0.6 %)	3 (3.0 %)
Emergency Surgery	1 (0.4 %)	1 (0.6 %)	0 (0 %)
Follow-Up Investigation	3 (1.1 %)	0 (0 %)	3 (3.0 %)
Long-Term Follow-Up	3 (1.1 %)	3 (1.8 %)	0 (0 %)
Total	7 (2.6 %)	4 (2.4 %)	3 (3.0 %)

Overall, 227 patients were treated conservatively (164 UAD patients and 63 CAD patients). Of these, 146 patients underwent further colonic evaluation by colonoscopy (n = 65), barium enema (n = 66), CTC (n = 26) or additional abdominal CT scan (n = 5). Notably, 16 patients underwent more than one investigation due to an incomplete or inadequate first examination. Diverticulosis was present in 92 (95%) UAD and 43 (88%) CAD patients. One fistula was found in the CAD group, and one stricture was found in each group. Low-grade adenomas were found in four patients in the UAD group and one patient in the CAD group. In both groups, three patients had no findings, and three patients had other findings. Further investigations were recommended to all conservatively treated CAD patients, unless the patient was too frail or elderly or colonoscopy was performed < 5 years earlier. In patients with conservatively treated UAD, further colonic evaluation was recommended for 76% (n = 128) of the patients. The features of the follow-up investigations are listed in Table 5.

Table 5. Proportion of patients with and without follow-up investigations and reasons for not to perform follow-up investigations (modified from Study I with permission of the copyright holder).

	All (n=270)	UAD n=170	CAD n=100
Patients with follow-up investigations	146 (54 %)	97 (57%)	49 (49 %)
No follow-up due to:	124 (46 %)	73 (43 %)	51 (51 %)
Surgery	43 (16 %)	6 (3.5 %)	37 (37 %)
Patient declined	4 (1.5 %)	3 (1.8 %)	1 (1 %)
Patient too old/frail	11 (4.1 %)	7 (4.1 %)	4 (4 %)
Recent colonoscopy	21 (7.8 %)	16 (9.4 %)	5 (5 %)
Recommended, data not found	32 (12 %)	28 (17 %)	4 (4 %)
Not recommended	13 (4.8 %)	13 (7.6 %)	0 (0 %)

5.2 Reassesment of CT reports in acute diverticulitis

Study II included 438 patients with UAD and 124 patients with CAD. Abscess was found in 56 (10%) patients, and 6 (1.1%) patients had peritonitis. The median age of the patients was 59 (26–96) years, and 63% were female. The patients' demographics are shown in Table . In 439 cases (78%), CT images were re-analysed by consultant abdominal radiologists. The initial CT reports were written by residents in 274 (62%) cases and by a consultant in 165 (38%) cases. When comparing the initial and final reports, in 22 reports (5.0%), the final report differed from the initial report. Reanalysis changed the initial assessment in 4.0% of UAD cases and 9.1% if the disease was complicated. Disease management changed due to the reassessment of CT images in 20 cases: colonoscopy could be omitted in 5 cases, and for 11 patients, colonoscopy was recommended due to changes in the final report. In five cases, the additional report stated other diagnoses that required different management. The reasons for changes in the reports are listed in Table . The final report differed in 5.1% of the reports made by residents and in 4.8% of the reports made by consultants. There was no significant difference between the resident and consultant radiologists compared to consultant abdominal radiologists. Cohen's Kappa values for residents and consultants were 0.95 ($p < 0.001$) and 0.94 ($p < 0.001$), respectively, showing almost perfect agreement.

Table 6. Patient characteristics in study II (modified from Study II with the permission of the copyright holder).

Variable	All patients N =562
Age, median (min-max)	59 (26-96) years
Sex, female	356 (63 %)
Uncomplicated acute diverticulitis	438 (78 %)
Complicated acute diverticulitis	124 (22 %)
Abscess	56 (10 %)
Abscess size, median (min-max)	4 (2-12) cm
Peritonitis	6 (1.1 %)
Conservative management	546 (97%)
Previous diverticulitis	143 (25 %)

Table 7. The explanations for changed reports (modified from Study II with the permission of the copyright holder).

Change in report	Resident N=14	Consultant N=8
UAD → CAD	4 (29 %)	3 (38%)
UAD → additional diagnosis[1]	2 (14%)	0 (0%)
UAD → other diagnosis[2]	3 (21%)	0 (0%)
CAD → UAD	3 (21%)	2 (25%)
CAD → other perforation	0 (0%)	1 (13%)
CAD → CRC suspicion	1 (7%)	1 (13%)
Unspecific findings → UAD	0 (0%)	1 (13%)
Epiploic appendagitis → CAD	1 (7%)	0 (0%)

[1] suspicion of CRC in addition to UAD (cancer was not found in colonoscopy)
[2] colitis

5.3 A novel scoring system for predicting the severity of acute diverticulitis

Of the 513 patients included in this study, 449 (88%) had UAD and 64 (12%) had CAD. Clinical peritonitis occurred in 6 (1.1%) patients, and abscesses occurred in 47 (9.2%) patients. The median age of the patients was 59 (28–96) years, and 64% of the patients were female. A comparison of patients' characteristics is shown in Table . The univariate analysis of patient-related characteristics revealed that only chronic cardiovascular disease ($p = 0.011$), any significant pre-existing comorbidity ($p = 0.007$) and older age ($p < 0.001$) were predictors of CAD risk.

Table 8. Patient characteristics in Study III (modified from Study III with the permission of the copyright holder).

Variable	UAD n=449	CAD n=64	P-value
Age, years, range	58 (28-94)	67 (34-96)	<0.001
Age 60 years or over	202 (45%)	46 (69%)	<0.001
Sex, female	284(63 %)	43 (67%)	0.540
Comorbidities			
Cardiac disease	164 (37%)	34 (53%)	0.011
Pulmonary disease	41 (9%)	8 (13%)	0.391
Diabetes	36 (80%)	9 (14%)	0.110
Rheumatoid disease	15 (3%)	3 (5%)	0.394
Neurological disease	12 (3%)	3 (5%)	0.285
Kidney disease	7 (2%)	0 (0%)	0.391
Inflammatory bowel disease	7 (2%)	0 (0%)	0.391
Liver disease	2 (1%)	1 (2%)	0.330
Malignancy	8 (2%)	1 (2%)	0.688
Any significant comorbidity	221 (49%)	43 (67%)	0.007
Corticosteroid medication	21 (5%)	4 (6%)	0.382
Earlier diverticulitis	112 (25%)	20 (31%)	0.280
CRP, mg/L, IQR	101 (61-150)	166 (99-221)	<0.001
WBC x10^{9}mg/L, IQR	10.8 (8.9-13.0)	12.5 (9.6-15.2)	0.002
Mean arterial pressure, IQR	104 (96-114)	103 (92-111)	0.239
Body temperature, °C, IQR	37.1 (36.6-37.5)	37.2 (36.8-37.6)	0.046
≥37.0 °C	253 (56%)	46 (72%)	0.018
≥38.5 °C	20 (5%)	3 (5%)	0.565
Vomiting	14 (3%)	9 (14%)	<0.001
Peritonitis	0 (0.0%)	6 (9%)	<0.001
Localization of the pain			
Left lower abdomen	63 (14%)	13 (20%)	0.285
Lower abdomen	229 (51%)	31 (49%)	
Other/diffuse	157 (35%)	20 (31%)	

In multivariate analysis, six factors were independently associated with increased CAD risk: older age ($p < 0.001$, OR 1.054, 95% CI 1.027–1.081), significant pre-existing comorbidity ($p = 0.043$, OR 1.066, 95% CI 0.543–2.092), increased WBC ($p = 0.018$, OR 1.104, 95% CI 1.017–1.198), increased CRP levels ($p < 0.001$, OR 1.008, 95% CI 1.004–1.011), body temperature ($p = 0.046$, OR 1.686, 95% CI 0.880–3.224) and vomiting ($p = 0.026$, OR 3.151, 95% CI 1.151–8.627).

The optimal cut-off values for the score were determined through ROC analysis. The cut-off values and corresponding CAD risk estimates are presented in Table .

Table 9. The Acute Diverticulitis Severity Score with cut-off values and risk estimates for CAD (modified from Study III with the permission of the copyright holder).

	Regression coefficient	Score points
Age ≥ 60 years	3.043	3
Any significant comorbidity	1.452	1
CRP, mg/L (symptoms less than 1 day)		
>150 (150)	5.031	5
125–149 (80–149)	3.279	3
100–124 (10–79)	1.265	1
<100 (<10)	-	0
Body temperature, ≥ 37.0 °c	1.516	2
WBC, x10^9 mg/L		
≥13.3	1.942	2
11.3–13.29	0.996	1
9.3–11.29	0.896	1
≤9.3	-	0
Vomiting	3.106	3
Peritonitis or sepsis	-	max value
Worsening symptoms despite of ongoing wide spectrum antibiotics	-	max value

Proportion of patients with UAD and CAD with calculated score points are shown in Table 10. Patients with a score value ≤ 5 had a very low risk of CAD, as shown in Table 11. However, a significant increase in risk was observed when the score exceeded 10 points. One patient with CAD had a low score. In the CT report of this patient, differentiation between a small abscess or an inflamed diverticulum was difficult. This patient was classified as Stage 2 CAD in our study and was treated with antibiotic therapy without the need for interventions. The patient's recovery was uneventful.

Table 10. Proportion of patients with UAD and CAD according to calculated score points (modified from Study III with the permission of the copyright holder).

Score points	UAD	CAD
	n=449	n=64
0	12 (100%)	0 (0.0%)
1	29 (100%)	0 (0.0%)
2	31 (100%)	0 (0.0%)
3	36 (100%)	0 (0.0%)
4	61 (100%)	0 (0.0%)
5	52 (98%)	1 (1.9%)
6	57 (90%)	6 (9.5%)
7	50 (91%)	5 (9.1%)
8	35 (83%)	7 (17%)
9	32 (76%)	10 (24%)
10	18 (82%)	4 (18%)
>10	36 (54%)	31 (46%)

Table 11. Risk for UAD and CAD according to points (modified from Study III with the permission of the copyright holder).

Total points	UAD	CAD
0-5	221 (99.5%)	1[1] (0.5%)
6-10	192 (86%)	32 (14%)
>10	36 (54%)	31 (46%)

[1] Either small abscess or inflamed diverticula

Score was subjected to ROC analysis, yielding an excellent discrimination level (AUC 0.856, $p < 0.001$). While patients with scores > 5 had a risk of CAD, ranging from 9.1% to 46%, the score effectively identified low-risk patients, eliminating the need for further examinations, as shown in Figure 8.

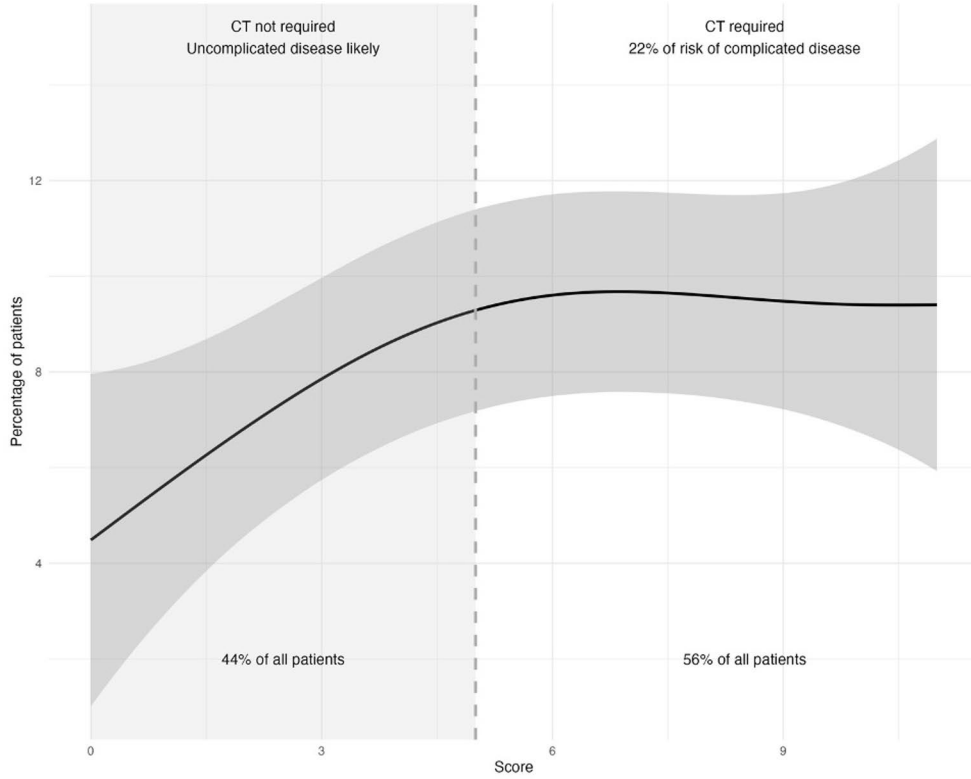

Figure 8. Share of patients with different risks for CAD (reproduced with the permission of the copyright holder).

6 Discussion

6.1 Risk of CRC in short-term follow-up

Only four cases of CRC were found at the short-term follow-up in our study, constituting a 1.5% overall risk of CRC after CT-verified acute diverticulitis. When the patients were divided into UAD or CAD, CRC was found in 0.6% and 3.0% of the patients, respectively. The difference was not statistically significant ($p = 0.15$). A recent meta-analysis of observational studies on patients with acute diverticulitis showed similar findings: the pooled prevalence of CRC was 1.9% (Meyer et al., 2019).

Previous retrospective cohort studies have reported an increased risk of CRC after CT-verified acute diverticulitis, with the risk varying between 0.25% and 3.2% (Brar et al., 2013; Lecleire et al., 2014; Sallinen et al., 2014b; Horesh et al., 2016; Andrade et al., 2017; Lau et al., 2022). However, the risk was much lower in patients with UAD compared to CAD, at 0%–0.5% and 5.4%–16.3%, respectively (Brar et al., 2013; Sallinen et al., 2014b; Andrade et al., 2017; Suhardja et al., 2017; Díaz et al., 2020). In a meta-analysis of more than 3,000 patients with CT-verified acute diverticulitis and a follow-up colonoscopy within 1 year, the risk of CRC after UAD was only 0.5%, compared to 8.3% in patients with CAD (Rottier et al., 2019). A meta-analysis by Meyer et al. (2019) showed that patients with CAD had a higher prevalence of CRC (7.9%) compared to patients with UAD (1.3%). Thus, the results of the present study align with earlier findings.

6.2 Risk for CRC in long-term follow-up

In a meta-analysis by Mortensen et al. (2022), no long-term risk of CRC was found after an attack of acute diverticulitis. The meta-analysis included 12 studies in which the follow-up time ranged between 6 months and 27 years (Mortensen et al., 2022). The present results of the long-term follow-up in Study I were in accordance with the meta-analysis. It has also been suggested that acute diverticulitis increases the long-term risk of CRC (Stefánsson et al., 2004; Mortensen et al., 2017). However, these studies were not conducted on patients with CT-verified acute diverticulitis, and there are no data available on follow-up investigations after acute diverticulitis.

In their population-based study, Granlund et al. (2011) reported that the risk of CRC increased after admission due to diverticular disease only within the first 12 months but not in the long-term follow-up up to 25 months. The risk of CRC increased within the first 12 months after diverticulitis, especially if a colonoscopy was not performed afterwards (Granlund et al., 2011).

Few studies have assessed the long-term risk of CRC in patients with CT-verified acute diverticulitis. Two retrospective cohort studies found no risk of CRC within a 1-year follow-up (Kim et al., 2014; Díaz et al., 2020). Only one study performed on patients with CT-verified acute diverticulitis reported a longer follow-up period (Elmi et al., 2013). In that study, 402 patients with CT-verified acute diverticulitis with subsequent colonoscopy were included, and they reported no increased risk of CRC in the long-term follow-up. However, the follow-up time (i.e. time to colonoscopy) ranged from 1 month to 5 years, and most of the patients had their colonoscopy within 1 year (Elmi et al., 2013). The study included only patients with subsequent colonoscopies (Elmi et al., 2013). In our study, patients without follow-up investigations were also included. Because all CRCs in the district are treated at our institution, we can assume that no additional cancers were found in patients still living in the same hospital district within the follow-up period. To our knowledge, our study is the first report of long-term follow-up from 9 to 17 years on patients with CT-verified acute diverticulitis.

6.3 Is colonoscopy mandatory after an episode of acute diverticulitis?

Many studies have reported a very low and even 0% risk of CRC after CT-verified UAD (Schmilovitz-Weiss et al., 2012; Brar et al., 2013; Kim et al., 2014; Sallinen et al., 2014b; Díaz et al., 2020). In a retrospective view of the CT scan of the only patient with UAD with CRC in Study I, obstruction of the sigmoid colon was found, and the patient underwent emergency surgery during the same hospital admission. This patient was misdiagnosed with UAD in our study. Similar findings were noted by Westwood et al. (2011). In their study, only 1 patient with CT-verified UAD had CRC and was found to be misdiagnosed when the CT scan was retrospectively re-evaluated (Westwood et al., 2011). No CRC cases were found in conservatively treated patients with UAD in Study I. Therefore, it is safe to say that there is no benefit of performing colonoscopy after conservatively managed CT-verified UAD. However, given the possibility of misdiagnosis on CT evaluation, conservatively treated patients with ongoing symptoms deserve further evaluation. In addition, our long-term follow-up also suggests that the risk of CRC is not increased in patients with UAD, regardless of whether colonic evaluation is conducted. As shown in Study I and several previous studies (Brar et al., 2013; Sallinen et al., 2014b;

Andrade et al., 2017; Suhardja et al., 2017), the risk of CRC is increased after CT-verified CAD, warranting colonoscopy for these patients.

6.4 Usefulness of reassessment of CT reports

In the present study, due to changes in reports, disease management changed in 5% of the patients. Thorisson et al. (2016) reported similar results. The CT reports of the AVOD RCT comparing antibiotic and non-antibiotic treatments in UAD were re-evaluated by two experienced radiologists (Thorisson et al., 2016). They found that 7% of the reports initially reported as UAD showed signs of complications. In emergency departments, surgeons and emergency department physicians must decide whether a patient is eligible for outpatient management based on clinical and radiological evaluations. Currently, patients with UAD and some patients with CAD can be treated conservatively without antibiotics, making outpatient treatment an option (Chabok et al., 2012; Daniels et al., 2017; Bolkenstein et al., 2019c). In Study II, all patients received antibiotic treatment, but if current guidelines were followed, most patients with UAD should avoid antibiotic treatment and could be managed in outpatient settings. The optimal treatment is based on the severity assessment of acute diverticulitis, which emphasises that the reliability of CT reports during on-call hours is important.

Since the recommendations for further investigations after UAD and CAD are different, the reliability of the appropriate assessment of disease severity made in emergency departments according to CT reports is vital. As recommended in the guidelines, including in the study hospital, colonoscopy is performed after an episode of CAD if it has not been performed recently (Sartelli et al., 2020; Schultz et al., 2020). In Study II, the changed reports led to further investigations in 11 patients, with the final diagnosis being CAD. Since the risk of CRC is increased in patients with CAD, it is important to identify patients who need further evaluation to avoid possible delays in diagnosis and treatment. In addition, five patients with a final diagnosis of UAD could avoid unnecessary colonoscopy, since it is not recommended for conservatively treated patients with uneventfully resolved UAD.

It has been shown that CT examinations reported within normal working hours have a higher strength of agreement than CTs reported during on-call hours (Perry et al., 2016). Although the level of agreement between the reports given during on-call hours and normal working hours was not assessed in Study II, we found that the reassessment of CT scans by more experienced radiologists was feasible, since the change in reports affected 5% of patients, leading to more precise management.

6.5 Inter-observer agreement

Few studies have assessed the interobserver agreement of CT reports in acute diverticulitis. CT scans in the emergency department performed during on-call hours are mainly evaluated by less experienced radiologists (i.e. residents or consultants with no further specialisation), which might influence the reliability of the CT reports. Our study showed no statistically significant difference in the experience of the radiologist, and interobserver agreement was excellent among both residents and consultants. Perry et al. (2016) demonstrated similar findings for CT examinations conducted due to abdominal pain; the seniority of the reporter was not associated with improved diagnostic accuracy. Van Randen et al. (2009) showed excellent interobserver agreement (median Kappa value 0.9) between experienced radiologists in acute diverticulitis and unselected patients with abdominal pain. Our results indicate that reports of acute diverticulitis given by residents are comparable to those given by consultants.

6.6 Risk factors for CAD

In Study III, elevated CRP and WBC levels, fever, vomiting, older age and any pre-existing comorbidity were independently associated with a higher risk of CAD. In a systematic review and meta-analysis by Bolkenstein et al. (2017), CRP, WBC, vomiting, constipation and generalised abdominal pain were associated with the risk of CAD, and steroid use, comorbidities and the number of previous episodes were found to be possible risk factors of CAD. However, the evidence is weak, and individually, these factors have little value in estimating the risk of CAD (Bolkenstein et al., 2017). In our study, a history of acute diverticulitis and location of the pain were not found to be risk factors of CAD.

Although elevated CRP levels were previously associated with an increased risk of CAD, the optimal threshold is unclear. Käser et al. (2010) showed that the risk of diverticular perforation increases when CRP exceeds 200 mg/L, and perforation seems unlikely with a CRP level of < 50 mg/L. In a study by Mäkelä et al. (2015), a CRP level of ≥ 149.5 mg/L effectively distinguished between UAD and CAD. However, in their study, low CRP values did not reliably predict UAD. In a study by van de Wall et al. (2013), the probability of CAD increased with an increasing CRP level, and the optimal threshold to discriminate UAD from CAD was 175 mg/L. Elevated WBC has also been proposed as a risk factor for CAD, with a cutoff value of 11×10^9/L (Longstreth et al., 2012). WBC was significantly higher in patients with CAD, but it had no value in discriminating disease severity in a study by van de Wall et al. (2013). In our study, WBC and CRP levels were higher in CAD patients and were associated with CAD. The score attempts to stratify the risk according to different WBC and CRP levels.

Even though mean body temperatures were similar in UAD and CAD patients in our study, a body temperature over 37.0 °C was significantly associated with CAD. Similar findings have been shown in previous studies. For example, Tursi et al. (2008) and Longstreth et al. (2012) found that patients with a body temperature > 37.0 °C and > 37.5 °C, respectively, have a higher risk of having CAD. However, contrary findings have been reported. Bolkenstein et al. (2018) found no significant difference between patients with UAD and CAD in body temperature, with the mean body temperature at 37.5 °C in both groups. van de Wall et al. (2013) also found that body temperature showed no significant difference between patients with UAD or CAD.

Although the absence of vomiting has been suggested to be associated with acute diverticulitis, vomiting has been shown to occur more frequently in patients with CAD (Laméris et al., 2010; Andeweg et al., 2011; van de Wall et al., 2013; Bolkenstein et al., 2018). Notably, vomiting emerged as a significant risk factor for CAD in our study. Previous studies have shown that patients with CAD have significantly more frequent vomiting than patients with UAD (van de Wall et al., 2013).

In previous studies, older age, immunosuppressive or corticosteroid medication and major comorbidities have been shown to be associated with the risk of CAD (Lorimer & Doumit, 2007; Tursi et al., 2008; Nizri et al., 2014; Mäkelä et al., 2015). Patients with CAD tend to be older than patients with UAD, and an age > 70 years has been found to significantly affect the risk of CAD (van de Wall et al., 2013; Mäkelä et al., 2015). Immunocompromised patients and patients with comorbidities have been shown to have an increased risk of severe outcomes (Carmona Agúndez et al., 2024).

6.7 Potentials and limitations of the scoring system

As patients with UAD (and even some cases with CAD) can be treated without antibiotics in outpatient settings, the observational strategy for patients with a low risk of CAD without CT imaging could be safe and feasible (Mali et al., 2016; Daniels et al., 2017; Joliat et al., 2017; Isacson et al., 2019). In our study, the Acute Diverticulitis Severity Score detected patients with CAD with high accuracy. The benefit of clinical scoring is that it could reduce emergency department referrals as well as the need for imaging if a patient is referred to secondary care, leading to healthcare cost savings.

A concern with CT imaging is repeated exposure to ionising radiation due to recurrent episodes of acute diverticulitis. The incidence of acute diverticulitis is increasing, especially in younger patients (Bharucha et al., 2015). As the risk of recurrence increases over time, younger patients may be repeatedly exposed to

radiation. In cases of recurrent acute diverticulitis, the symptoms and signs of acute diverticulitis are usually familiar for patients, and physicians might be likelier to suspect acute diverticulitis. Additionally, recurrent acute diverticulitis is not associated with an increased risk of complications (Ambrosetti et al., 2002; Chapman et al., 2006; Bharucha et al., 2015; Sallinen et al., 2015b; El-Sayed et al., 2018). In our study, a previous history of acute diverticulitis was not found to be associated with the risk of CAD. Therefore, a clinical scoring system could benefit patients with recurrent diseases, especially in younger age groups.

CT is recommended to confirm the diagnosis and distinguish CAD from UAD in older patients. Older patients have more frequent comorbidities and are more prone to complications due to underlying illnesses; thus, they generally benefit from more frequent CT imaging than younger patients (Gardner et al., 2015; Lehtimäki et al., 2017; Fugazzola et al., 2022). The significance of age was considered in our score.

Morbidity and mortality increase with the increasing stage of acute diverticulitis and sepsis (Carmona Agúndez et al., 2024). All patients with peritonitis in our study had CAD. Therefore, a finding of clinical peritonitis or sepsis in patients was added to the score and given maximum points, indicating the need for a more precise diagnosis. Similarly, for patients receiving antibiotics with ongoing symptoms and not recovering uneventfully, CT imaging is warranted. Previously, the diagnosis of acute diverticulitis was made based on clinical evaluation, and the presence of diverticulosis was confirmed later with further investigations of the colon. This was mainly because CRC might mimic acute diverticulitis. Currently, diverticulitis is increasingly diagnosed with CT imaging. The risks of not using CT in the diagnosis of suspected acute diverticulitis (or in patients with abdominal pain in general) relate to possible delays in diagnosis and treatment (Lehtimäki et al., 2017). Although the scoring system can be accurate and beneficial, it must be emphasised that patients with ongoing symptoms or a deteriorating general condition deserve further evaluation.

One important factor in utilising scoring systems is that they should be easy to use in clinical practice. Our scoring system consists of variables that are easily assessed at emergency departments and primary care appointments. The usability of the scoring system could be further improved with web-based form where the information could be supplemented and the points would be automatically calculated, as in Adult appendicitis score (Sammalkorpi et al. 2014).

6.8 Comparison to previous scoring systems

Few clinical scoring systems have been proposed for predicting acute diverticulitis severity without CT imaging (Bolkenstein et al., 2018; Covino et al., 2021). In

clinical practice, such scoring systems are not widely known or used in the diagnosis of acute diverticulitis.

Bolkenstein et al. (2018) formulated a prediction model with logistic regression analyses combined with ROC analysis using the retrospective data of 942 patients. (Bolkenstein et al., 2018) Abdominal guarding, CRP and WBC were selected for their final predictive model (Bolkenstein et al., 2018). Levels of CRP and WBC were categorised to indicate different risks of CAD. The points for CRP ranged from zero to seven, and for WBC, they ranged from zero to two. Signs of abdominal guarding were given four points. Aggregated points between zero and thirteen estimated a different risk of CAD. As in our study, vomiting and age were first selected based on univariate analysis in their model, but in their later analyses, they did not remain significant (Bolkenstein et al., 2018). In our study, abdominal guarding could not be assessed. Their study found one patient with CAD with normal inflammatory parameters at admission due to a rapid presentation of abdominal pain. Since CRP levels may be misleadingly low at first, we adjusted the CRP levels that were incorporated into the risk score, differentiating patients with symptoms occurring less than and more than 24 hours before clinical evaluation. Comorbidities and body temperature were not associated with CAD in their study, contrary to ours.

Covino et al. (2021) developed a PACO-D score to predict CAD in a retrospective cohort of 1,089 patients and a validation cohort of 282 patients (Covino et al., 2021). In their study, six variables were associated with CAD: male sex, haemoglobin level < 11.9 g/L, constipation, CRP > 80 mg/L, severe obesity and no proton pump inhibitor treatment. Their predictive model comprises these variables, and each is given one point. Score values of 0–1 indicate low risk, 2–3 moderate risk and ≥ 4 high risk of CAD. Fever, comorbidities and vomiting were not associated with CAD in their study. The major difference in their study compared to ours is that they included patients with diverticular bleeding who were considered to have CAD (Covino et al., 2021).

6.9 Limitations of the studies

All the studies in this thesis were retrospective cohort analyses; therefore, some parameters could not be identified and analysed. In Study I, the proportion of CT-verified AD was relatively small, although nearly 1,700 patients had an ICD-10 diagnosis code for diverticular disease during the study period. At that time, CT imaging was not as easily and widely available as it is currently. The number of patients with CT-verified AD increased annually during the study period. However, by using data from 2003 to 2012, we were able to obtain long-term follow-up data on the patients. In addition, some further colonic investigations were made elsewhere and with CE, which is no longer used in clinical practise. Due to the retrospective

nature of the data in Study II, numerous individual radiologists analysed the CT scans. Therefore, we assessed interobserver agreement only between all residents and consultants. Additionally, it was not certain that all the patients had acute diverticulitis in Study II, even after reassessment, although no alternative diagnosis was found in the patients' records. The limitation of Study III was the lack of validation of the score. Before utilising the score, further validation in a prospective patient cohort is needed to improve the score's reliability. Due to the retrospective nature of the data, some previously suggested risk factors were not implied in the analysis.

6.10 Future prospects

The rising incidence of acute diverticulitis presents a significant burden on healthcare systems. To alleviate the economic and individual impacts of acute diverticulitis, further investigation into its etiology and risk factors is essential for developing effective prevention strategies.

Although studies on non-antibiotic and outpatient management of UAD have shown to be safe and shown a reduction in healthcare costs, the widespread acceptance of new treatment methods in clinical practice often requires time (Isacson et al. 2018; Mora-López et al. 2021). Encouraging results have also been observed in the outpatient treatment of CAD, yet further research is needed to identify optimal management approaches for CAD as well (Joliat et al. 2017).

While CT imaging is likely to remain the gold standard for diagnosing acute diverticulitis in emergency settings, concerns regarding radiation exposure, particularly for patients with recurrent disease, are increasingly prominent. Recent studies have shown promising outcomes using point-of-care US for the diagnosis of acute diverticulitis (Cohen et al. 2020). As the field of emergency medicine evolves in Finland, point-of-care US, when operated by emergency medicine specialists, may provide a viable alternative that reduces both costs and ionizing radiation associated with CT imaging. Further research in this area is warranted. Additionally, the scoring system we have developed may prove beneficial in decreasing the reliance on CT imaging for the diagnosis of acute diverticulitis. Prior to its implementation in clinical practice, validation through a prospective multicenter study will be essential.

Future research on the surgical management of diverticular disease is also necessary. The optimal approach for operating on patients with perforated acute diverticulitis remains unclear. We await the results of the RCT examining the management of severe acute diverticulitis, and prospective multicenter studies may provide further insights (Kirkpatrick et al. 2018). As decisions regarding elective surgery are made by individually weighing potential benefits against risks, future investigations should focus on identifying risk factors associated with recurrence and

complicated acute diverticulitis. Our ongoing research aims to explore whether sarcopenia is a risk factor for CAD or recurrence, as well as whether sarcopenic patients experience higher rates of complications following surgery for diverticular disease.

7 Conclusions

The conclusions of the studies are as follows:

I The risk of CRC after CT-verified acute diverticulitis was low in UAD compared to CAD. No additional CRC associated with acute diverticulitis was found in the long-term follow-up. Colonic evaluation is not mandatory after a CT-verified, conservatively treated UAD.

II The reassessment of CT imaging reports in emergency settings was found feasible, since 5 % of the reports changed after the reassessment. The experience of the radiologist was not significant in emergency settings.

III Increased levels of CRP and WBC, older age, body temperature over 37.0 °C, the presence of vomiting and comorbidities were found to be associated with the risk of CAD. The Acute Diverticulitis Severity Score, which was created based on these risk factors, reliably separated patients with a potentially severe disease from those without.

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