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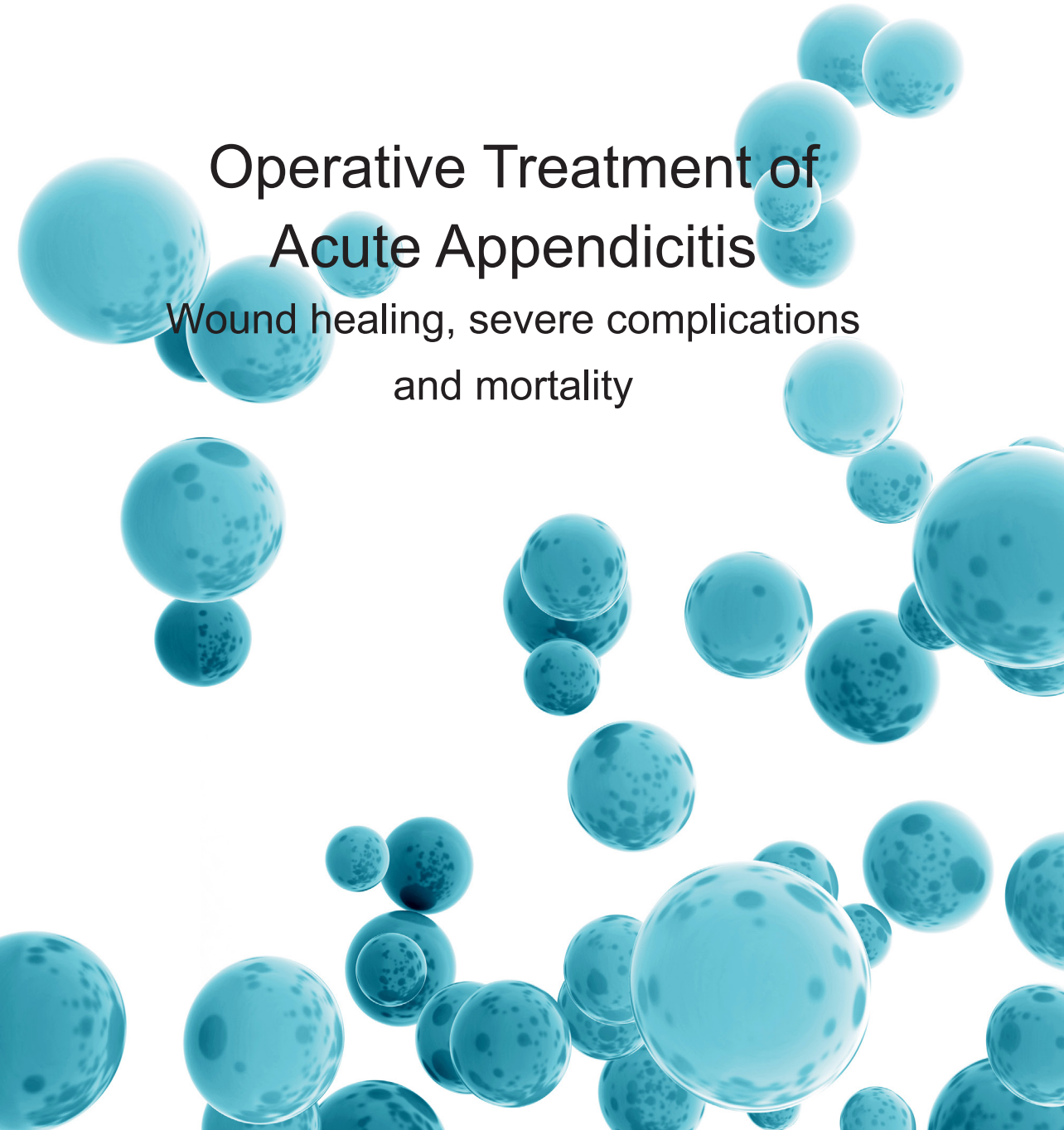
SANNAMARI KOTALUOTO

Operative Treatment of Acute Appendicitis

Wound healing, severe complications and mortality



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Operative Treatment of Acute Appendicitis

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ACADEMIC DISSERTATION
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ABSTRACT

The diagnostics of appendicitis are everyday routine for surgeons at emergency units. In many cases, the diagnosis of appendicitis is straightforward and the decision regarding surgery simple. However, the diagnosis can be challenging, and despite advanced diagnostic imaging, the rate of removal of healthy appendices in suspected cases of appendicitis (negative appendectomies) remains high. Earlier studies have shown a connection between negative appendectomies and increased complications and mortality. Appendectomy-related mortality in Finland is not well defined. Severe complications related to appendectomy have not been studied in Finland previously, and few studies have been published worldwide.

Appendectomy is the most frequently performed emergency operation in the field of alimentary tract surgery worldwide. The open technique of appendectomy was developed over a hundred years ago and has remained more or less unchanged over the years. During the last two decades, laparoscopic appendectomy has increased in popularity and is presently the method of choice in many centres. Worldwide, open appendectomy is still a valid technique, as laparoscopy requires a higher level of skill as well as complex instrumentation and more resources.

Open appendectomy wounds have traditionally been closed with a few interrupted, non-absorbable sutures in the fear of wound infection, which is the most common complication of appendectomy. This wound closure method results in a suboptimal cosmetic outcome, with the inconvenience of stich removal to the patient and a burden to the health care system. Absorbable intradermal suturing has become a common wound closure method. In children, intradermal absorbable suturing is already accepted as a routine method for appendectomy wound closure.

This thesis consists of four independent articles. The aim of the first two was to investigate the feasibility of intradermal absorbable suturing in appendectomy wound closure in adults. In the first study (I), we randomized 200 appendectomy patients into two wound closure groups: traditional non-absorbable interrupted sutures and absorbable intradermal continuous suturing. The result was that the methods were equal in regard to the frequency of wound infection; however, mild wound complications (dehiscence) were significantly more frequent in the non-absorbable suture group.

In the second study (II), we examined the cosmetic outcome of the two wound closure methods. The patients included in the first study were evaluated by means of both subjective and objective scar assessment, which showed a statistically significant benefit for absorbable intradermal wound closure in terms of cosmetic outcome.

In the third study (III), the aim was to define severe complications related to appendectomies based on the Patient Insurance Centre's register data. We found that patient complains related to appendectomy are rare (0.2%). The complaints were more frequently related to laparoscopic operations than to open surgery. This difference equalised towards the end of the study period as the percentage of laparoscopic operations increased. Severe complications were more often related to laparoscopic surgery, a complicated infection, negative appendectomy and aging. We concluded that, with better diagnostics, some of the severe complications may be avoided. The increased complication rate related to laparoscopic appendectomies during the study period correlated with the adoption of a new technique.

In the fourth (IV) study, we investigated the mortality related to appendectomies in Finland based on the register data of the National Institute of Health and Welfare and Statistics Finland. Over the study period of two decades, the appendectomy-related mortality in Finland was 2.1/1,000 operations. The mortality decreased to less than half of the baseline level over the study period. At the same time, the rate of negative appendectomies decreased and the percentage of laparoscopic surgery increased. Mortality was related to male sex, aging, complicated infection, negative appendectomy and open appendectomy. We concluded that better diagnostics may have decreased the appendectomy-related mortality in Finland.

Appendectomy wounds have been traditionally closed in an old-fashioned way in the fear of wound infection. In this thesis, we were able to prove that a more modern wound closure method with absorbable intradermal suturing is safe in terms of wound infection and yields a better cosmetic outcome in appendectomy wounds. Another tradition has been to accept a relatively high rate of negative appendectomies. In our studies on complications and mortality, we were able to conclude that an attempt at better diagnostics may decrease both severe complications and mortality. The importance of knowing the present figures is that they act as a valid reference value when examining the benefits of conservative treatment of acute appendicitis. Our results encourage the use of laparoscopic procedures and a proper diagnostic workup in the operative treatment of appendicitis.

TIIVISTELMÄ

Akuutin umpilisäkkeen tulehduksen diagnostiikka on osa jokaisen päivystävän lääkärin arkipäivää. Diagnostiikka on selkeissä tapauksissa suoraviivaista, ja leikkauspäätös voidaan tehdä ilman monimutkaisia tutkimuksia. Aina näin ei ole, ja terveiden umpilisäkkeiden poistojen (negatiivinen appendikektomia) määrä onkin säilynyt korkeana diagnostiikan kehittymisestä huolimatta. Kuolleisuuden ja komplikaatioiden määrän on todettu olevan yhteydessä negatiivisiin appendikektomioihin. Suomessa kuolleisuutta appendikektomioihin on selvitetty vain 60-luvulla ja mainintana appendisiitin insidenssiin keskittyvässä tutkimuksessa. Appendikektomioihin liittyviä vakavia komplikaatioita ei ole Suomessa aiemmin tutkittu ja maailmallakin vain muutamissa tutkimuksissa.

Umpilisäkkeen poistoleikkaus eli appendikektomia on yleisin vatsakirurginen päivystysleikkaus meillä ja maailmalla. Avoleikkauksen tekniikka on kehitetty jo yli sata vuotta sitten. Pääsääntöisesti toimenpide on säilynyt alkuperäisen tekniikan mukaisena. Vaikka tähystysleikkaukset ovat lisääntyneet viime vuosikymmeninä, perinteinen avoleikkaus on silti monissa päivystyspisteissä yleinen toimenpide. Maailmanlaajuisesti avoleikkaus on edelleen yleisempi kuin tähystysleikkaus, jonka vaatimukset osaamisen, välineiden ja resurssien suhteen ovat korkeammat.

Appendikektomiahaavat on perinteisesti suljettu muutamalla poistettavalla ompeleella lisääntyneen haavainfektioriskin pelossa. Tällaisen haavansulun kosmeettinen tulos on vaatimaton, ja muutaman ompeleen poiston vuoksi potilaan hoitoon joudutaan käyttämään terveydenhoidon resursseja. Sulavien ihonsisäisten eli intradermaalisten ompeleiden käyttö on leikkaushaavojen sulussa yleistynyt, ja niiden kosmeettinen tulos on osoitettu hyväksi. Lasten appendikektomioissa sulavan ihonsisäisen ompeleen käyttö on vakiintunut menetelmä.

Väitöskirjatyö koostuu neljästä itsenäisestä osasta. Kahden ensimmäisen osatyön tavoitteena oli selvittää sulavan ihonsisäisen ompeleen käytön soveltuvuus aikuispotilaiden appendikektomiahaavoissa haavan paranemisen ja kosmeettisen tuloksen kannalta. Kahdessa seuraavassa työssä tavoitteenamme oli selvittää appendikektomiaan liittyviä vakavia komplikaatioita ja kuolleisuutta Suomessa. Väitöskirjan ensimmäisessä osatyössä (I) selvitimme sulavan ihonsisäisen ompeleen käytön turvallisuutta aikuispotilailla. Tutkimusasetelmassamme 200 potilasta, joille suunniteltiin umpilisäkkeen poistoa, satunnaistettiin haavan sulun osalta kahteen ryhmään: perinteiseen poistettavien ompeleiden ja sulavan ihonsisäisen haavansulun ryhmään. Tuloksena oli, että sulavan ompeleen käyttöön ei liittynyt merkittävästi enempää haavainfektioita kuin perinteiseen haavan sulkuun. Lie-

vempien haavakomplikaatioiden suhteen (haavan raottuminen ja pitkittynyt eritys) sulava ommel osoittautui merkittävästi paremmaksi kuin perinteinen haavan sulkumenetelmä.

Toisessa osatyössä (II) selvitimme ensimmäiseen tutkimukseen osallistuneiden potilaiden leikkaushaavojen kosmeettista tulosta. Saimme sekä subjektiivisilla että objektiivisilla mittareilla tilastollisesti merkitsevän tuloksen: kosmeettinen tulos on parempi, kun käytetään sulavaa ihonsisäistä ommelta haavan sulkuun.

Kolmannessa osatyössä (III) tavoitteena oli selvittää umpilisäkkeen poistoleikkaukseen liittyviä vakavia komplikaatioita Potilasvakuutuskeskukseen tehtyjen vahinkoilmoitusten avulla. Totesimme appendikektomioihin liittyvien potilasvahinkojen määrän olevan vähäinen. Tähystysleikkauksiin liittyvät komplikaatiot olivat vakavampia kuin avoleikkauksiin liittyvät, lisäksi tähystysleikkauksiin liittyen oli tehty suhteellisesti enemmän potilasvahinkoilmoituksia. Tutkimusjakson aikana ero kuitenkin tasoittui tähystysleikkauksien määrän lisääntyessä. Leikkauskomplikaatiot olivat yhteydessä komplisoituneisiin tulehduksiin, negatiivisiin appendikektomioihin, ikääntymiseen ja lisääntyneisiin perussairauksiin. Tutkimuksemme perusteella totesimme, että paremmalla diagnostiikalla osa komplikaatioista saattaa olla vältettävissä. Uuden tekniikan aloittamiseen liittyen tutkimusjakson aikana on ollut suhteellisesti enemmän potilasvahinkoja tähystysleikkausten yhteydessä.

Neljännessä osatyössä (IV) selvitimme THL:n ja Tilastokeskuksen rekisterien avulla umpilisäkkeen poistoon liittyvää kuolleisuutta Suomessa. Appendikektomioihin liittyvä kuolleisuus Suomessa on 2,1/1 000 leikkausta. Totesimme kuolleisuuden laskeneen alle puoleen lähtötasostaan tutkimusjakson aikana. Samana ajanjaksona tähystysleikkausten määrä lisääntyi ja negatiivisten appendikektomioiden määrä väheni merkittävästi. Kuolleisuus oli yhteydessä ikääntymiseen, negatiiviseen appendikektomiaan, komplisoituneeseen tulehdukseen, miessukupuoleen ja avoleikkaukseen. Monimuuttuja-analyysi tuki näitä löydöksiä. Johtopäätöksenä totesimme parantuneen diagnostiikan todennäköisesti vähentäneen kuolleisuutta appendikektomioihin liittyen.

Umpilisäkkeen poistoleikkauksen perinteenä on ollut haavakomplikaatioiden pelossa sulkea haavat vanhanaikaisella menetelmällä. Tutkimuksessamme pystyimme osoittamaan uuden ihonsisäisen sulavan ompeleen olevan turvallinen ja parempaan kosmeettiseen tulokseen johtava menetelmä. Niin ikään traditiona on ollut hyväksyä kohtalaisen suuri negatiivisten appendikektomioiden määrä. Komplikaatio- ja kuolleisuustutkimuksiemme perusteella totesimme, että pyrkimys hyvään diagnostiikkaan voi vähentää sekä vakavia komplikaatioita että kuolleisuutta. Täsmällinen diagnostiikka on erityisen tärkeää ikääntyvien ja perussairaiden potilaiden kohdalla. Operatiivisen hoidon komplikaatiot ja kuolleisuus ovat tärkeä vertailukohta, kun lähdetään kehittämään akuutin appendisiitin konservatiivista hoitoa. Tuloksemme kannustavat laparoskooppisen tekniikan käyttöön sekä tarkempaan diagnostiikkaan appendisiitin operatiivisessa hoidossa.

LIST OF ORIGINAL COMMUNICATIONS

The present thesis is based on the following original publications, referred to in the text by the Roman numerals I–IV:

I Kotaluoto S, Pauniaho SL, Helminen M, Kuokkanen H, Rantanen T. Wound healing after open appendectomies in adult patients: a prospective randomized trial comparing two methods of wound closure. World J Surg 2012 36:2305-2310

II Koskela A*, Kotaluoto S*, Kaartinen I, Pauniaho S-L, Rantanen T, Kuokkanen H. Continuous absorbable intradermal sutures yield better cosmetic results than non-absorbable interrupted sutures in open appendectomy wounds: a prospective randomized trial. World J Surg 2014 38:1044-1050
*equal contribution

III Kotaluoto S, Pauniaho S-L, Helminen M, Sand J, Rantanen T. Severe Complications of laparoscopic and conventional appendectomy reported to the Finnish Patient Insurance Centre. World J Surg 2016 40:277-283

IV Kotaluoto S, Ukkonen M, Pauniaho S-L, Helminen M, Sand J, Rantanen T. Appendectomy-related mortality: a population based analysis during two decades in Finland. Submitted.

ABBREVIATIONS

A	absorbable intradermal continuous suturing
AA	acute appendicitis
AAS	adult appendicitis score
AIR	appendicitis inflammatory response
ASA	American Society of Anesthesiologists' grades 1–5 for assessing fitness for anaesthesia and surgery
ASGS	Accordion severity grading system
CA	complicated appendicitis
CFR	case fatality rate
CT	computed tomography
ECC	estimated concentration change
GIST	gastro-intestinal stromal tumour
HIPEC	heated intra-peritoneal chemotherapy
HMN	high-grade mucinous neoplasm
LA	laparoscopic appendectomy
LDCT	low-dose computer tomography
LMN	low-grade mucinous neoplasm
LRQ	lower right quadrant
MRI	magnetic resonance imaging
NA	nonabsorbable suturing
NET	neuroendocrine tumour
NOTES	natural orifice transluminal endoscopic surgery
OA	open appendectomy
PIC	Patient Insurance Centre
POSAS	patient and observer scar assessment scale
SD	standard deviation
SDCT	standard dose computer tomography
SMR	standardized mortality ratio
SSI	surgical site infection

UCA	uncomplicated acute appendicitis
US	ultrasonography
VAS	visual analogue scale
VSS	Vancouver scar scale
WBC	white blood cell count

CONTENTS

1 INTRODUCTION

Appendectomy is the most common gastrointestinal operation and appendicitis the second most common diagnosis after unspecific abdominal pain in acute abdomen patients at emergency departments worldwide. The incidence of acute appendicitis is 90–100/100,000 annually, and in Finland approximately 6,000 appendectomies are performed every year. Acute appendicitis is found in individuals of all ages, but the incidence is the highest in childhood and adolescence (Lin et al. 2015; Ilves et al. 2011). The gold standard of treatment is surgery. The commonly used open surgical technique was described over a hundred years ago (McBurney 1894). At first, appendectomy wounds were left open. Subsequently, delayed closure was favoured up until the 1980's when the use of prophylactic antibiotics remarkably lessened the incidence of the most common complication of appendicitis – wound infection (Grosfeld et al. 1968). After antibiotic prophylaxis became routine, primary closure was adopted, but with interrupted sutures to avoid infections (Pettigrew 1981). This tradition remained in the surgical technique even after absorbable suturing became a routine wound closure method in other types of surgery. Paediatric surgeons first started to use absorbable sutures in appendectomy wounds and proved their safety in the aspect of wound healing (Pauniaho et al. 2010; Serour et al. 1996).

Wound infection is the most common complication of appendicitis and strongly related to perforated appendicitis. Severe complications and mortality following appendectomy are considered rare. To avoid perforation, a relatively high incidence of negative appendectomies has been considered acceptable. The lesson passed on to young surgeons has been that, if a number of healthy appendices are not removed, too many appendicitis patients are missed or operated on too late. The acceptable percentage of negative appendectomies has been suggested to be as high as 20% to 30% in order to avoid perforation.

The discussion on the treatment of uncomplicated appendicitis with antibiotics only has emerged in the last decade (Di Saverio et al. 2014; Salminen et al. 2015). Surgery as the first and only line of treatment has been challenged, and its safety needs to be re-evaluated. Antibiotic treatment requires diagnostic accuracy, which may be achievable by computed tomography imaging (Atema et al. 2015; Kim et al. 2015). In addition, the ability of ultrasonography, diagnostic scoring and magnetic resonance imaging to decrease the number of misdiagnosed or negative appendectomies has been studied (Atema, Gans et al.

2015; Saucier et al. 2014; Blitman et al. 2015; Toorenvliet et al. 2010). The current tendency is towards more accurate diagnostics and fewer negative appendectomies. Few studies have been conducted on appendectomy-related mortality and morbidity. Some of them suggest that morbidity and mortality are higher after negative appendectomies compared to correctly diagnosed patients (M. N. Andersson et al. 2011; Blomqvist et al. 2001). As the treatment of appendicitis is changing with the use of better diagnostics, with a significant shift from open to laparoscopic surgery and towards treatment with antibiotics, it is time to re-evaluate the outcome of surgery.

2 REVIEW OF THE LITERATURE

2.1 Epidemiology of appendicitis

The appendix vermiformis is an approximately 4–10 centimetres long, hollow, blind-ended bowel extremity located in the bottom of caecum. Its position varies from intra-peritoneal and freely hanging to retroperitoneal and retro-caecal (picture 1). The appendix has been identified since ancient history, but its true purpose is yet to be discovered. Appendectomy is associated with a reduced risk of ulcerative colitis and an increased risk of Clostridium difficile colitis, and hence its role has been suggested to be related to the immune balance of the bowel (Yong et al. 2015; Frisch 2006; Frisch 2009). The probable function in this role would be to act as a container for normal bacteria of the bowel or as a lymphoid organ.

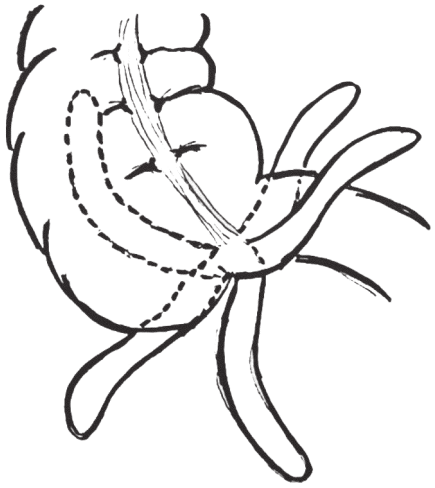

Figure 1. Varying anatomy of the appendix in relation to the caecum

The incidence of appendicitis is 80–100/100,000 persons, according to various studies. The incidence is highest among children aged 10–14 years. A declining incidence has been reported over the last decade (Lin et al. 2015; Ilves et al. 2011). The studies show some differences in the incidence between various ethnic groups. In the U.S., the incidence of appendicitis is higher in the Caucasian and Hispanic and less common in the African-American and Asian population (Anderson et al. 2012). On the other hand, geographical

differences show a higher incidence in Asia than in the U.S. and the lowest incidence in Africa (Lee et al. 2010; Lin et al. 2015; Ohene-Yeboah et al. 2009; Richardsen et al. 2015). Seasonal variation has also been noted, with the peak incidence of appendicitis occurring during the summer months. In addition, men have slightly higher incidence rates than women. (I. Ilves et al. 2014; J. H. Lee et al. 2010; Lin et al. 2015; Ohene-Yeboah et al. 2009; Richardsen et al. 2015; Salo et al. 2015.) The environmental and genetic factors related to appendicitis are under investigation (Sadr Azodi et al. 2009). The variations in the incidence according to ethnic background, geographic origin or seasonal presentation suggest that these factors may play a role in the aetiology of appendicitis. A three-fold risk of appendicitis has been shown in patients with a family history of appendicitis, which also suggests the presence of genetic factors (Ergul 2007).

2.2 The aetiology of appendicitis

The aetiology of appendicitis is not fully understood. The commonly suggested aetiology for acute appendicitis is the theory of luminal obstruction. Obstruction can be caused by an appendicolith (a fecalith, stoned faeces in the lumen of the appendix), other intra-intestinal material, a tumour or parasites (Adehossi et al. 2004; Clerveus et al. 2014; Hegazi et al. 2013). Lymphoid hyperplasia has been suggested to be the underlying cause of purulent appendicitis if a fecalith (or other obstructing process) is not present, the cause of the hyperplasia being unknown (Swischuk et al. 2015).

2.2.1 Obstructive causes

The most common obstructive cause of appendicitis is an appendicolith, in other words hardened faeces inside the appendix. It is found in approximately 13%–30% of acute appendicitis specimens (Ramdass et al. 2015; Alaedeen et al. 2008). The presence of an appendicolith is found to be more frequent in perforated appendicitis, thus predicting the development of complicated appendicitis (Alaedeen et al. 2008).

The incidence of appendicular tumours has been 0.7%–1.7% in the specimens retrieved from appendectomies. These tumours are commonly small in size and asymptomatic, thus being difficult to diagnose unless they are presented by acute appendicitis. (Bucher et al. 2004; Akbulut et al. 2011; Connor et al. 1998.) Misdraji and Young classified appendicular tumours comprehensively in 2004. A simplified classification is presented in Table 1 (Misdraji & Young 2004).

Table 1. Classification of appendicular neoplasms. Modified from the original classification of Misdraji and Young 2004.

Primary epithelial
Benign: hyperplastic polyp, serrated adenoma, colonic-type adenomas Malignant: low-grade mucinous neoplasms (LMN), high-grade mucinous neoplasms (HMN)/ adenocarcinoma
Primary non-epithelial
Neuroendocrine tumours (carcinoid tumours): classical carcinoid, Goblet cell carcinoids/adenocarcinoids Mesenchyme tumours: Gastrointestinal stromal tumours (GIST), neuroma, lymphoma Secondary tumours (metastatic): ovarian, colonic, other rare

The most common tumours of the appendix are neuroendocrine tumours (NET), formerly referred to as carcinoid tumours in the literature. They are found in 0.3%–0.9% of all appendectomy specimens (Connor et al. 1998; Carr et al. 2004; Goede et al. 2003). A goblet cell carcinoid is a variant of appendicular NETs with mixed characteristics of a NET, adenocarcinoma and mucinous tumour (Rossi et al. 2015).

Low-grade mucinous neoplasms (LMN) of the appendix are borderline tumours with malignant potential for developing pseudomyxoma peritonei syndrome (Fujiwara et al. 1996). If a perforation of an LMN occurs, as the consequence of luminal swelling or acute appendicitis, the mucinous cells spread into the abdominal cavity, producing mucinous ascites. The prognosis of an LMN is solely dependent on whether there is a perforation; if so, the pseudomyxoma peritonei inevitably follows. The condition is rare and the treatment is radical, with complex and high post-operative morbidity (Sugarbaker 2001).

In the elderly (patients 65 or older), caecal cancer is a rare obstructive cause of acute appendicitis found in 0.8%–1.8% of all appendectomies (Bizer 1993; Lai 2006).

Occasionally, a foreign body or other ingested material causes appendicitis. These cases are presented as case reports in the literature, and no knowledge of the exact incidence exists.

2.2.2 Infectious causes

Several infectious agents have been associated with appendicitis (Table 2). The most common aerobic bacteria found in an inflamed appendix are Escherichia coli, followed by Streptococci. The most frequently found anaerobic bacteria are Bacteroides species. The bacterial flora of an inflamed appendix thus reflects the normal flora of the bowel, with an increased expression of the bacteria mentioned (Roberts 1988). The most common viral agents cultured in acute appendicitis specimens are adenovirus and rotavirus. The path of the inflammation has been found to be related with the pathogen involved; in perforated cases, E. coli, Streptococci and Pseudomonas aeruginosa were found more often than viral agents (Richardsen et al. 2015). Cytomegalovirus (CMV) involvement in the appendicitis

of immune-defected patients should be kept in mind while treating these patients (Dzabic et al. 2008).

Parasites are a rare cause of appendicitis in developed countries but constitute a considerable risk in developing countries and among those travelling in high-risk countries. The incidence of parasite-induced appendicitis in a Turkish study was 1.4% for adult patients and 0.49% for children (Yabanoglu et al. 2014; Yildiz et al. 2015). An Omani study found parasites in 5.5% of all appendicitis patients, with Enterobiasis (51.1%), followed by Aschariasis (26.1%) and Schiostosomiases (9.1%) (Zakaria et al. 2013), as the most common parasites found. Parasite-induced appendicitis may more often lead to complications and morbidity than other types of appendicitis. In addition, the parasite infection needs to be recognized and treated properly. This can be achieved only by examining the resected appendices routinely (Yabanoglu et al. 2014).

Table 2. The infectious agents found in appendicitis specimens

Viral	Bacterial	Parasites
Adenovirus	E. coli	Ascaris sp
CMV	Bacteroides species (sp)	Schistosomes
Epstein-Barr virus	Streptococci (Str. Milleri)	Enterobius vermicularis
Measles	Enterococci	Echinococcus
	Pseudomonas aerunginosa	Cryptosporidium
	Yersinia	Entamoeba histolytica
	Cambylo bacter sp	ToxoplasmaBalantidum coli
	Shigella sp	Trichiris sp
	Salmonella sp	

(Roberts 1988; Lamps 2010)

2.3 Classification of appendicitis

Not all appendicitis cases lead to necrosis and perforation. On the contrary, there is evidence of spontaneous recovery from acute appendicitis. These facts support the theory of at least two courses of the inflammatory process – the acute perforating severe pathway and self-limiting mild inflammation with spontaneous recovery or response to antibiotic treatment alone (Livingston 2007; Andersson 2007).

Appendicitis is commonly classified as uncomplicated acute appendicitis or complicated acute appendicitis. The latter is, in most studies, considered to include appendicitis with perforation, necrosis of the appendicular wall, appendicular abscess, and appendicitis with an appendicolith. Uncomplicated appendicitis involves none of the previous and represents the early phase of the disease or the milder inflammation type. Some studies categorize the mere existence of an appendicolith as a sign of complicated appendicitis,

but in this thesis, the involvement of an appendicolith is not categorized as complicated appendicitis unless otherwise stated. Classification into perforated appendicitis and non-perforated appendicitis is used in several studies, but, for clinical use, this division may be too concise (Farzal et al. 2015). Classification according to the severity of inflammation has also been presented. The disease severity score for appendicitis is a five-step grading; 1=inflamed, 2=gangrenous, 3=perforated with free fluid, 4=perforated with an abscess, and 5=perforated with generalized peritonitis (Garst et al. 2013). The classification has great importance in the treatment of appendicitis. Furthermore, an early diagnosis of complicated appendicitis is one of the major challenges in the decision of treatment. The problem with all classifications is the differences in the interpretation of clinical, histopathological and radiological findings between specialists (Kim et al. 2015).

2.4 Diagnostics of acute appendicitis

Acute appendicitis (AA) is the most common diagnosis of acute abdomen leading to surgery in emergency units, and yet the diagnostics are not easy. The negative appendectomy rate is 19%–30% of all appendectomies if the decision to operate is based on a clinical examination alone. The diagnostic accuracy has increased over the last decades due to the widespread use of CT in the diagnostics of acute abdomen patients (Laurell et al. 2013). The number of misdiagnoses is significantly higher in women of fertile age due to the difficulty of differentiating lower abdominal pain related to gynaecological problems from acute appendicitis (M. Lee et al. 2014).

In children, the diagnostics can be challenging. The younger the patient, the more difficult the diagnostics is. Young patients' history is received from accompanying adults and is often observational; small children do not have the ability to describe their symptoms comprehensively. Another challenging group of patients are pregnant women. Changing physiology and anatomy alter the clinical findings. The incidence of abdominal emergencies is one out of 500–700 pregnancies, and surgery is needed in 0.2%–2% of the cases. Appendicitis is the most common cause for surgery (Bouyou et al. 2015).

In the elderly, the differential diagnostics become more of a challenge. The elderly have comorbidities, malignancies and other underlying causes expressing as the symptoms of acute abdomen. At the same time, appendicitis becomes more infrequent. Consequently, the outcome of appendectomy in the elderly is significantly worse than in younger patients, with a higher incidence of complicated appendicitis and postoperative morbidity. (Segev et al. 2015.)

Regardless of the wide use of diagnostic imaging and convincing results in individual studies on the sensitivity and specificity of diagnostic scores combined with imaging, the population-based reviews show no decrease in the rate of negative appendectomies, and the question of how to differentiate complicated appendicitis from uncomplicated appendicitis persists (Raja et al. 2010; Flum et al. 2001; Markar et al. 2011; Suh et al. 2011).

The negative appendectomy and perforated appendicitis rates are both important quality measures of the treatment of acute appendicitis. There is an inverse relationship between these two measures (Velanovich et al. 1992; Tan et al. 2015).

2.4.1 Clinical diagnosis – signs/symptoms and laboratory tests

The clinical history of appendicitis typically includes abdominal pain migrating from the upper or mid-area to the lower right quadrant (LRQ) of the abdomen. Most patients report nausea and mild fever. The duration of symptoms is short, 1–2 days. Local tenderness in the right iliac fossa, rebound tenderness (direct or palpated from contralateral side), right-sided anal tenderness and local guarding are the most commonly described clinical manifestations (Laurell et al. 2013). The historically named clinical tests include the following: increased pain in the LRQ when coughing (Dunphy's sign), increased pain with flexion and internal rotation of the right hip (the Obturator sign), increased pain with passive extension of the of the right hip (the Psoas sign), and increased LRQ pain upon palpation of the contralateral side (Rowsing). (Wray et al. 2013.) The value of each of these individual tests is minor, but when combined to patient history, a thorough physical examination and laboratory tests, they provide reliability to the clinical decision-making.

The laboratory tests of AA patients show raised levels of CRP, neutrophil count and white blood cell count (WBC). The average leucocyte count for appendicitis found in studies is 14.3–15.0 x 109 l-1 (SD 0.4) and for a healthy appendix 10.2–10.9 x 109 l-1 (SD 0.2–0.4), with a sensitivity of 85%–88% and specificity of 31%–53%. The sensitivity and specificity for CRP are 48%–76% and 26%–57%, respectively, with a range of 24–31 mg/l in uncomplicated appendicitis (Grönroos et al. 1999; Grönroos 2001; Yang et al. 2006). CRP and WBC have proven to be more valuable in the diagnostics of appendicitis when used together than separately (Grönroos et al. 1999; Yang et al. 2006). If the neutrophil percentage is added (over 74%), an even higher sensitivity of 99% can be achieved (Yang et al. 2006). WBC is a better indicator of appendicitis in general, whereas a high CRP value (>96–99 mg/l) refers to complicated appendicitis with a high specificity of up to 90%. If both values are normal, appendicitis is highly unlikely in adult patients (Grönroos et al. 1999; Gröönroos 2001; Sammalkorpi et al. 2015). However, this does not apply to children. In a study of two hundred child patients, seven out of a hundred children were found to have normal CRP and leucocyte count with an inflamed appendix (Gröönroos 2001).

High bilirubin (>17–20) and procalcitocin (>1.5 ng/dl) levels predict complicated appendicitis according to studies. However, the clinical value of these tests is limited as the decision to perform surgery in perforated cases is most often made on the basis of a clinical examination. Even if the predictive value of laboratory tests alone is limited, they provide additional support for the clinical decision-making (Al-Abed et al. 2015; Burcharth et al. 2013; Wu et al. 2012).

2.4.2 Imaging

The perfect imaging method for appendicitis would be safe with no or minor radiation, in addition to being fast, economical, achievable and accurate. Ultrasonography has been favoured especially among paediatric patients to avoid radiation. The sensitivity of US has varied from 44% to 100% and the specificity from 47% to 99% (Pinto et al. 2013). The wide range reflects the variation in skill of the examining physician as well as patient-dependent variables such as obesity, bowel movement and anatomical variations. Albeit US is not a perfect diagnostic tool for acute appendicitis patients, it is useful in selected patients, with children in particular, and is suggested as the first-line imaging in many studies. (Toorenvliet et al. 2011; Toorenvliet et al. 2010; Nielsen et al. 2015; Bachur et al. 2015.) In children, an as low as a 3%–5% negative appendectomy rate can be reached by the use of ultrasound as the first-line imaging and the selective use of CT (Saucier et al. 2014; Blitman et al. 2015; Toorenvliet et al. 2010).

Magnetic resonance imaging (MRI) is more accurate than US, with a sensitivity of 90%–97% and specificity of 90%–95%, which is comparable to CT results (Leeuwenburgh et al. 2013; Aspelund et al. 2014). The disadvantages of MRI are that it is not universally available, it is costly, the imaging takes time, and the radiologist must be specially trained to interpret the images. Most studies conclude that the use of MRI is efficient with pregnant patients and as the second-line imaging after US in children and adolescents who especially benefit from nonradioactive imaging (Aspelund et al. 2014; Burke et al. 2015). The sensitivity and specificity of MRI are as high as 96.8% and 99%, respectively, in the diagnostics of appendicitis in pregnant women (Burke et al. 2015). Both negative appendectomy and perforated appendicitis are considerable risks for the mother and the foetus, and imaging is thus recommended to support the challenging clinical diagnoses (Aggenbach et al. 2015).

The current recommendation for imaging in AA patients favours low-dose CT (LDCT) compared to traditional standard-dose CT (SDCT). The sensitivity and specificity for LDCT and SDCT are equal, with an average of 95% and 90%, respectively. The latter exposes patients to higher radiation levels, and the use of LDCT may thus reduce the risk of cancer, although the benefit is considered debatable. (Kim et al. 2012; Pickuth et al. 2001.)

In some countries, the majority of AA patients undergo preoperative CT. The diagnostic accuracy with CT can reduce the number of negative appendectomies to 1%–7% (Raja et al. 2010). Furthermore, according to some studies, the overall cost analysis also supports routine CT imaging (Raja et al. 2010; Rao et al. 1998). On the other hand, the time loss before treatment is increased with systematic imaging, and some of the patients are exposed to unnecessary radiation. In conclusion, most studies still favour the critical use of CT imaging in AA patients' diagnostics. (Atema, Gans et al. 2015; Gaitini 2011.) A comparison of the sensitivity and specificity of US, MRI and CT is presented in Table 3.

Table 3. Sensitivities and specificities of US (ultrasonography), MRI (magnetic resonance imaging) and CT (computed tomography) in the diagnostics of appendicitis

Imaging	Sensitivity	Specificity	Reference (number of patients in the study)
US	87%	74%	Pickuth D. et al. (n=120)
	77%	94%	Leeuwenburgh M. et al. (n=230)
MRI	98%	93%	Leeuwenburgh, M. et al. (n=230)
	97%	99%	Burke L. et al. (709)
CT	95%	89%	Pickuth D. et al. (n=120)
	97%	91%	Leeuwenburgh M. et al. (n=230)

(Pickuth et al. 2000; Leeuwenburgh et al. 2013; Burke et al. 2015)

Despite the high accuracy of CT in AA diagnostics, the sensitivity of CT for differentiating perforated appendicitis from non-complicated appendicitis has been somewhat disappointing, with numbers varying from 30% to 60% (M. S. Kim et al. 2014; Bixby et al. 2006; Leeuwenburgh et al. 2014). Appendicular diameter, intra-peritoneal collection of fluid and appendicular fat infiltration have been proven to be specific signs of complicated appendicitis (T. H. Kim et al. 2015). The conservative treatment of AA with antibiotics requires an accurate diagnosis of non-complicated AA for patient selection. In addition, some surgeons still prefer open appendectomy instead of laparoscopy in perforated cases. Attempts have been made to improve the accuracy of predicting perforation by combining the CT or US findings with laboratory tests and clinical signs. Two studies represented a new scoring system to distinguish complicated from uncomplicated appendicitis, with a sensitivity of 89% and specificity of 94%–95% (Atema et al. 2015; Kim et al. 2015). Further studies are still needed to resolve this issue.

2.4.3 Scoring systems as diagnostic tools

Several scoring systems have been developed to reduce the need for systematic imaging of acute appendicitis patients without increasing the rate of negative appendectomies (Tan et al. 2015). The scoring systems take into consideration various clinical signs, symptoms and laboratory results, transforming them into numerical values. The points are summed and certain cut-off values used to predict the probability of acute appendicitis. The negative appendectomy rates vary from 12% to 25% according to different scoring systems (Erdem et al. 2013).

The most referred scoring system in literature is the Alvarado score. It was presented by A. Alvarado in 1986 and lists eight known predictive factors that are useful in the diagnostics of AA: signs of localized tenderness in the right lower quadrant, leucocytosis, migration of pain, shift to the left of the WBC, temperature elevation, nausea and vomiting, anorexia-acetone, and rebound pain. Each factor equals one point, except for leucocytosis and tenderness in the right iliac fossa, which count for two points each (Alvarado 1986).

The cut-off value is 7 points for a high probability for appendicitis in most studies and yields high sensitivity in men and children (88%–100%) but lower sensitivity in women (68%–78%) (Kalan et al. 1994). The appendicitis inflammatory response (AIR) score takes into account eight variables of clinical signs and laboratory values and has been found to be comparable to the Alvadore score or slightly outperform it (Andersson 2008). The Finnish contribution to the scoring systems is the Adult Appendicitis Score (AAS), which takes into account patient's sex and the onset of symptoms. Promising results concluded that the new scoring system was superior to a clinical examination alone and to the two earlier scoring systems, and it reached the specificity of CT. The authors also succeeded to halve the need for imaging by using the new scoring system (Sammalkorpi et al. 2014).

The Erdem group compared four known scoring systems in their study in 2013. They found in their prospective data that the respective sensitivity and specificity levels of the scoring systems were 82% and 75% for the Alvarado, 100% and 28% for the RIPASA, 96% and 42% for the Ohmann, and 100% and 44% for the Eskelinen score. They also assessed the negative appendectomy rates of the Alvarado, RIPASA, Ohmann and Eskelinen scoring systems; these were found to be 12%, 25%, 22% and 21%, respectively. (Erdem et al. 2013.) The scoring systems are costless, easy and fast to adapt. Again, they can be used to identify the high- and low-probability patients for direct surgery and observation without the need for unnecessary imaging or other further examinations. Scoring systems have also been developed to distinguish perforated appendicitis from uncomplicated cases. These systems included the use of CT or US imaging. They might bring some solutions in the future to the problem of identifying uncomplicated appendicitis for conservative treatment (Atema et al. 2015; Kim et al. 2015).

2.5 Conservative treatment of appendicitis

2.5.1 Non-operative treatment of acute appendicitis

The theory of two different pathways of appendicitis has raised discussion over the antibiotic treatment of acute appendicitis. The theory suggests that the inflammation does not necessarily lead to necrosis and perforation. The course of disease can be self-limiting and thus prone to resolve with antibiotics or even without treatment. (Livingston 2007.) The investigators supporting antibiotic treatment refer to diverticulitis, which is treated by antibiotics and drainage if needed, unless generalized peritonitis is involved (Livingston et al. 2011). The antibiotic treatment of appendicitis is not a new idea. It has been suggested over the last decades but has not received wide acceptance. The latest studies report promising results. The observational NOTA (Non-Operative Treatment for acute Appendicitis) study used amoxicillin-clavulanate for non-specific lower right quadrant abdominal pain with a failure rate of 14%. The diagnosis of appendicitis was made using the Alverado and AIR (Appendicitis Inflammatory Response) scores, thus including a reasonable amount

of misdiagnoses (Di Saverio et al. 2014). The largest multicentre APPAC study used ertapenem 1g/day for three days, followed by oral levofloxacin (500mg/d) combined with metronidazole (500mg x 3/day) for seven days. The patients with suspected appendicitis were randomized into open appendectomy or non-operative treatment with antibiotics as described. Patients with complicated appendicitis observed in CT (perforation, abscess, appenicolith) were excluded. The success rate of conservative treatment was 69% in the APPAC study (Salminen et al. 2015). The result was comparable to other randomized studies on conservative treatment (Rocha et al. 2015; Vons et al. 2011).

The main problem with the conservative treatment is the reliable recognition of the patients with uncomplicated appendicitis. The APPAC study used low-dose CT to confirm the diagnoses. In earlier studies, the sensitivity of CT in recognizing uncomplicated appendicitis has been only 30%–60% (Bixby et al. 2006; M. S. Kim et al. 2014). One of the reasons for the failures of antibiotic treatment may have been the difficulty to recognize the right patients. Another problem with the conservative treatment is the consequential increase in the use of broad-spectrum antibiotics, with possible long-term effects considering the already growing antibiotic resistance problem. Thirdly, the risk of leaving appendicle tumours behind in the adult population is considerable. The incidence of tumours in removed appendices has been reported to be 1%, but the incidence is considerably higher in the elderly (Emre et al. 2013; Jones et al. 2007). There is no guaranteed way to exclude the tumour possibility by imaging or another non-operative means. Routine colonoscopy and/or imaging after conservative treatment of an appendicular abscess are suggested for excluding tumours (Lai, Loong, Chiu et al. 2006).

There are only two non-randomized studies in children regarding conservative treatment for acute appendicitis. The first of these was based on selecting patients with mild symptoms (Hartwich et al. 2015) and the second on patient selection by the preference of the patients and parents (Steiner et al. 2015) for non-operative treatment. The success rate was 81% in the first and 71% in the latter study. In the absence of randomized controlled trials, treatment with antibiotics is not yet accepted in the treatment of appendicitis in children.

With these concerns still unresolved, a recent review on the treatment of appendicitis suggests that non-operative treatment should be performed in adult patients included in randomized controlled trials only, or the patients should at least be informed of the 25%–30% failure rate during the first year as well as of the disadvantages and the benefits of both operative and non-operative treatment. The present understanding is that antibiotic treatment can be used on a subgroup of patients with accurate diagnoses (including CT imaging) and mild symptoms who are otherwise suitable for conservative treatment. The appropriate criteria are yet to be identified in future trials. (Bhangu et al. 2015.)

2.5.2 Treatment of appendicular abscess

Prolonged or atypical symptoms such as high fever, abdominal tenderness over three days, diarrhoea, and a palpable low right quadrant mass refer to an intra-abdominal abscess. The diagnosis is, in most cases, retrieved by CT or, in children, with US, both indicating a collection of fluid with a capsule in the lower right quadrant of the abdomen and an inflammatory process around the area. Immediate surgery of an appendicular abscess has been considered demanding, often leading to bowel resections and an increased complication rate. According to a recent trial, laparoscopic appendectomy is safe and feasible even in the abscess stage when performed by experienced surgeons. The length of hospital stay has been found equal in the laparoscopic and conservative treatment groups, but there were fewer additional interventions in the operatively treated patients (Mentula et al. 2015). The common clinical practice for an appendicular abscess is conservative treatment, with or without interval appendectomy, i.e. removing the appendix after a period of time when the acute infection has been successfully treated. Conservative treatment includes the application of a drain, typically by a radiologist, the extraction of a bacterial sample to identify the infectious agents, and the administration of intravenous antibiotics.

An area of considerable debate is the necessity of interval appendectomy. Similar risks of recurrent appendicitis and of missed pathological findings apply to the conservative treatment of abscess as acute appendicitis. If an appendicolith is involved, the risk of residual appendicitis is considerably high – a retrospective cohort study reported a 2.8 relative risk (Tannoury et al. 2013; Ein et al. 2005). In specimens of an interval appendectomy after an appendicular abscess, the number of unexpected findings has been as high as 12%–28%, and 16% in the elderly (Carpenter et al. 2012; Wright et al. 2015). The evidence supporting interval appendectomy is controversial. Some studies recommend performing interval appendectomy in all patients (Tannoury et al. 2013; Deelder et al. 2014), whereas others suggest abandoning interval appendectomy and recommend close follow-up, colonoscopy and imaging to rule out underlying tumours (Meshikhe 2008).

2.6 Operative treatment of appendicitis

The timing of surgery has been a controversial issue in the operative treatment of appendicitis. Delaying the operation has been thought to yield the risk of perforation, thus leading to complications. This assumption is based on the theory that an inflammation of the appendix inevitably results in necrosis and perforation. In many cases, however, appendicitis resolves without an operation, and the necrotic disease may represent a different pathway of appendicitis rather than the end result of inflammation (Livigston et al. 2007). Current literature on this issue is controversial. Some studies show no difference in surgical site infection or complication rates if surgery is delayed 12–24 h after admission to the emergency department, nor do they report there a difference in the perforation rate

(Boomer et al. 2015; Chen et al. 2015; Drake et al. 2014). Delaying surgery by more than 48 hours has been shown to increase the complication rate (Fair et al. 2015). A prospective study of 266 patients showed increased morbidity if appendectomy was delayed more than 12 hours after the onset of abdominal pain (Saar et al. 2016). However, the earlier studies measured the time from the admission to surgery. The patients' pre-hospital delay is unpredictable, and a probable conclusion is therefore that an in-hospital delay of up to 12–24 hours is acceptable when the diagnosis is unclear.

2.6.1 Open appendectomy

2.6.1.1 Technique

The operative treatment of appendicitis was first performed over a hundred years ago (McBurney 1894). The general technique of open appendectomy has changed only in minor details over the years. The incision is usually made in the lower right quadrant (LRQ) of the abdomen, overlying McBurney's point, two thirds of distance from the umbilicus towards the anterior iliac spine. Some surgeons prefer to mark the point of maximum pain to optimize the placement of the incision relative to appendix origin. Para-umbilical and lower midline incisions have been used especially if the diagnosis has been uncertain. The appendix is mobilized and lifted out of the wound. Sometimes the mobilization of the caecum is needed. The mesentery of the appendix with the appendicular artery, rising from the ileocaecal artery, is ligated. The appendix is then ligated and excised close to its origin in the caecum. The traditional surgical technique includes the crushing of the appendicular lumen to avoid any intra-luminal material in between the ligation of the appendix. After excision, the stump is either buried with a purse-string suture into the bottom of the caecum, or left unburied. Sometimes additional sutures are used to complete the burying in the case of inflamed tissue in the stump. The routine burying of the appendicular stump decreased with the introduction of the laparoscopic technique and has been found to be unnecessary (Qian et al. 2015).

2.6.1.2 Wound closure

The appendectomy wound closure technique has followed the general trends in abdominal surgery. Earlier, the peritoneum was closed but is presently left unclosed. The muscle layer is closed by a few interrupted sutures, and the fascia is sutured with continuous slowly absorbing suturing material. A delayed closure of the skin was favoured in the early years. Later, together with the use of prophylactic antibiotics, closure with a few interrupted non-absorbable sutures became routine. Absorbable sutures are presently favoured especially in paediatric surgery as the discomfort of suture removal is a considerable burden on children.

Skin closure with absorbable sutures has been shown to be as safe as other skin closure methods in regard to wound complications. In paediatric patients, the safety of intradermal suturing after appendectomy has been demonstrated even in complicated appendicitis cases (Pauniaho et al. 2010; Serour et al. 1996). Currently, open appendectomy wounds in children are routinely closed with intradermal absorbable suturing. Furthermore, studies support better cosmetic result after intradermal absorbable suturing (Xu et al. 2015).

2.6.2 Laparoscopic appendectomy

The first laparoscopic appendectomy was performed by a gynaecologist in the 1980's (Semm 1983). Technological development and the wide-spread adoption of laparoscopic technology was fast during the 1990's. Laparoscopic appendectomy was primarily recommended for female patients as the technique allows the diagnosis gynaecological conditions often mimicking appendicitis (Tzovaras et al. 2007). The benefit was next noted in the context of obese patients for whom an open operation is often challenging and demands extended incisions. Obese patients are also at risk for wound complications (wound rupture, infection, incisional hernia) (Sauerland et al. 2010; Tan-Tam et al. 2012; Woodham et al. 2012). Laparoscopy offers the option of leaving a normal appendix in place; the macroscopic appearance is not, however, necessarily reliable. A study demonstrated that the surgeon's ability to identify inflammation without perforation and neoplasms is poor. Some 33% of the inflamed appendixes were deemed normal, and only 3 out of 16 neoplasms were macroscopically noted. They concluded that all appendices should be removed in the case of explorative laparoscopy for suspected appendicitis (Roberts et al. 2008).

It took two decades for laparoscopic appendectomy to convince the surgeons. As the laparoscopic technique has increased its popularity in surgery in general and the instruments and technique have developed, many prefer laparoscopic appendectomy to the open technique today (Jaschinski et al. 2015; Guller et al. 2004). There has been some concern about a possible increase in intra-abdominal abscess development after a laparoscopic operation for perforated appendicitis, but the results are controversial. Some studies suggest that the laparoscopic approach offers better possibilities for the lavation of the abdominal cavity of pus than open appendectomy (Markides et al. 2010; Nataraja et al. 2013; Wilson et al. 2013). Laparoscopic appendectomy has also been considered expensive and time-consuming compared to the open technique. The benefits of laparoscopy are smaller wounds, shorter hospital stay and shorter sick leaves (Hansen et al. 1996). The overall expenses with the fewer hospital days and shorter leave from work equalise the difference in immediate expenses. However, laparoscopic appendectomy requires a learning curve, whereas the open technique is straightforward and easily adapted. The current trend based on a meta-analysis of randomized trials is favouring laparoscopic appendectomy as the first-line operative treatment for appendicitis (Sauerland et al. 2010).

Laparoscopic appendectomy is favoured for paediatric patients in the treatment of appendicitis even if the outcome in children is found to be the same with both open and laparoscopic appendectomy (Svensson et al. 2015). A population-based study recommends open surgery for young children less than 6 years of age and in complicated appendicitis cases. The recommendation is based on to the higher rates of intra-abdominal abscesses after laparoscopy in complex appendicitis and a high number of such cases in the young age group (van den Boom et al. 2015).

In most studies, a laparoscopic procedure is reported to be safe during pregnancy (Cheng et al. 2015; Chung et al. 2013). The evidence is slightly controversial, though, as some studies have shown a mild increase in foetal loss after laparoscopic appendectomy compared to open appendectomy (Cox et al. 2015). Most studies support laparoscopic appendectomy at least during the first and second trimester of pregnancy and open appendectomy in the third trimester (Cheng et al. 2015; Chung et al. 2013; Eom et al. 2012; Walker et al. 2014).

2.6.2.1 Technique

For appendectomy, the laparoscopy ports are placed for convenient approach towards the caecum, the operator positioned on the left side of the patient. The camera port is placed in the umbilical region or on the left upper quadrant of the abdominal wall. Two additional ports are commonly used. Coagulating instruments or clips are used to ligate the vessels of the appendix. For the ligation of appendix clips, ligation loop strings or a stapler are used. A large retrospective study supports the routine use of endo-loops and selective use of a stapler, which is a more expensive device but feasible in complicated circumstances (Sahm et al. 2011). Clips, metal or polymeric material, have also been found safe, feasible and economical if the width is sufficient for the ligation of the appendix (Partecke et al. 2011; Gomes et al. 2013; Sohn et al. 2014; Strzalka et al. 2016). The stump is not buried. The appendix is extracted from the abdomen through a port wound in a retrieval bag or inside a port to avoid introducing bacteria to the wound. Variations in the surgical technique depend on the surgeon's laparoscopy skills and the circumstances of the operation.

2.6.3 Novel Techniques

A single-port laparoscopic technique has been introduced in most laparoscopic operations to reduce the number of ports needed, targeting surgery without scars and decreasing the risk of wound complications. The technique is based on a gel port, which is commonly placed through the umbilicus. Multiple instruments can be placed through the gel port and used in the same way as is done in conventional laparoscopy. The curved arms allow working through a single port. Variations of the single port technique have been developed especially for appendectomy, such as using laparoscopy only to visualize and capture the

appendix and then pulling the appendix trough the same incision to make the actual excision (Suh 1998). The single-port technique also seems to be a feasible option for children (Zhao et al. 2015; Sesia et al. 2015). However, the technique has little advantage over conventional laparoscopy and is hence likely to be practised only in units specialized in this kind of surgery (Carter et al. 2014; Clerveus et al. 2014).

Natural orifice trans-luminal endoscopic surgery (NOTES) takes advantage of the natural luminal organs to approach the target of surgery. A flexible endoscope is used to operate either through the alimentary tract or vagina. A hybrid technique has been introduced with a single laparoscopy port assisting the flexible endoscope (Knuth et al. 2014). The advantage of this technique is completely scarless surgery. On the other hand, it requires penetration through an organ, which is a considerable risk, with completely new complications (Wood et al. 2014). Due to the complexity of this surgery, it is unlikely that the technique will be widely adopted in the treatment of acute appendicitis (Yagci et al. 2014).

2.7 Complications of appendectomy

There are only a few population-based studies on the complications of appendectomy. According to them, open and laparoscopic appendectomies have equal complication rates, varying from 8% to 31%, but the types of complication vary according to the technique used. The classification of complications is heterogeneous through the studies, making it difficult to compare the outcomes (R. E. Andersson 2014; Brugger et al. 2011; Margenthaler et al. 2003).

2.7.1 Wound infection

Surgical site infection (SSI) is the most common complication after open appendectomy. The commonly used classification for SSI is superficial/incisional and deep/organ/space infection according to the layer of the abdomen that is affected. The major risk factor for post-appendectomy surgical site infection is complicated appendicitis. The overall wound infection rate after appendicitis is approximately 3%–5% compared to the 10% after complicated disease. Other risk factors for infection are obesity, co-morbidity such as diabetes, pre-operative SIRS (severe inflammatory respiration syndrome) and smoking (Sadr Azodi et al. 2008). In addition, open appendectomy seems to be an independent risk factor for incisional SSI compared to laparoscopy. However, the finding may be influenced by selection bias because many surgeons still prefer open appendectomy in perforated appendicitis (R. E. Andersson 2014; Xiao et al. 2015).

Delayed wound closure was the method of choice in contaminated wounds until the 1970's (Grosfeld et al. 1968). As the delayed closure leads to morbidity, discomfort and

prolonged hospital stay, it has later been abandoned by most surgeons (Pettigrew 1981). The routine use of prophylactic antibiotics has decreased the SSI rate and the primary closure has proved to be safe (Siribumrungwong et al. 2014).

The most common method currently is to perform primary closure with prophylactic intra-venous antibiotics administered in the induction of anaesthesia in open appendectomy. The antibiotics are continued after the operation in the case of perforated appendicitis (Daskalakis et al. 2014; Hurst et al. 2015). The commonly administered antibiotics are intravenous cefalosporins, ciprofloxacin or gentamycin combined with metronidazole or broad-spectrum antibiotics such as ertapenem or piperacillin, which have shown equal effectiveness in both complicated and uncomplicated appendicitis (Daskalakis et al. 2014; Hurst et al. 2015). The duration of antibiotic treatment is not well defined. In perforated cases, the treatment is clearly indicated, whereas in other kinds of complicated cases (necrosis, appendicolith), there has been no difference in SSI weather the treatment course lasts three days or longer (van Rossem et al. 2015). Drainage is used in selected patients, usually with an abscess or considerable amount of pus at the time of the operation. By this widely adopted pathway of care, the overall wound infection rate has dropped from 20% to 5% (Ein et al. 2013).

2.7.2 Intra-abdominal abscess

In the early years of laparoscopic appendectomies, open appendectomy was considered better in perforated cases to avoid intra-abdominal abscess formation. Many studies have found significantly higher rates of abscesses after laparoscopic appendectomies (R. E. Andersson 2014; Swank et al. 2011; Xiao et al. 2015). The results are controversial, however. A Swedish study with a population of 160,000 patients found a 0.3% abscess rate after open and 0.5% after laparoscopic appendectomy; the difference was statistically significant, but has questionable clinical significance. Other studies have shown that the intra-abdominal abscess rate may not be especially related to laparoscopic appendectomy. Perforation of the appendix has been proven to be a significant factor in abscess formation, but the role of laparoscopy is controversial, as many studies show no difference in abscess formation between laparoscopic and open appendectomy. (Asarias et al. 2011; Markides et al. 2010; Nataraja et al. 2013; Partecke et al. 2014.) These results support the trend to perform laparoscopy in perforated appendicitis.

2.7.3 Other complications after appendectomy

Two major studies on the short- and long-term outcome of appendectomy are presented in Table 4. Bowel obstruction, bowel lesion or perforation, and wound rupture are the next common complications reported after appendectomy. In a population-based Swedish study

on post-appendectomy morbidity, wound rupture and postoperative bowel obstruction were related to open appendectomy (OA) more frequently than to laparoscopic appendectomy (LA). A bowel lesion was reported to be more common after LA. Overall surgical complications were more frequent after open appendectomy. (R. E. Andersson 2014.) Due to a large study population, statistical significance was shown, but the clinical significance can be questioned for these results. Another comprehensive single-institute study found a significant difference in the rate of readmissions in favour of open appendectomy. The long-term results were equal for both surgical techniques. (Swank et al. 2011.)

A rare entity of appendectomy complication is stump appendicitis, which refers to the infection of the residual of a previously removed appendix. It can occur days or even decades after the primary operation. The diagnosis is challenging and requires adequate imaging. The treatment of choice is the resection of the remnant appendix. (Hendahewa et al. 2015.)

Table 4. Short-term outcome of laparoscopic (LA) and open appendectomies (OA) in terms of post-operative complications

	Wound infection	Wound rupture	Bowel obstruction/ ileus	Intra-abdominal abscess/deep infection	Readmission	Bowel lesion/ perforation
Swank et al. 2011						
OA (%) n=545	2.6	nr	2.4	1.5	2.2	nr
LA (%) n=201	1.4	nr	3.4	6.2	6.7	nr
p-value	ns	nr	ns	0.001	0.004	nr
Andersson 2014						
OA (%) n=136,754	0.1	0.1	5.28	0.3	5.8	0.2
LA (%) n=3,3142	0.1	0.0	4.15	0.5	6.9	0.2
OR*	0.54	0.44	0.81	1.58	1.10	1.32
p-value	0.03	0.002	0.033	<0.001	<0.001	0.042

ns=not significant, nr=not reported, * Odds ratios indicate the risk of complication after laparoscopic compared with open appendectomy

2.7.4 Mortality after appendectomy

Mortality related to appendectomy is not well investigated. Few studies report mortality rates on a population basis, the results varying from 0.09% to 0.24% in developed countries, and from 1% to 4% in low-income countries (Ali et al. 2012; Bliss et al. 2015; Faiz et al. 2008; Ohene-Yeboah et al. 2006). A Scandinavian population-based study showed increased mortality related to negative appendectomy (M. N. Andersson et al. 2011; Blomqvist et

al. 2001). Furthermore, a study from England found a relation of increased mortality to male sex, age, co-morbidity and open surgery (Faiz et al. 2008). Another earlier study reported 1.8% mortality among veteran patients. The authors found mortality to be related to complications, current pneumonia, completely dependent functional status, bleeding disorder and steroid use. An increased number of deaths among these patients was probably related to the high mean age of the patients (50 years) (Margenthaler et al. 2003).

3 AIMS OF THE STUDY

The aims of this study were to evaluate the operative treatment of appendicitis in regard to the aspect of complications and mortality, and to bring new aspects and knowledge to clinical practice, in terms of wound closure, for the benefit of appendicitis patients. The specific aims were:

1. To study the safety and feasibility of the modern wound closure technique with continuous absorbable intradermal suturing in open appendectomy patients. The research question was whether it is safe, from the point of view of wound infection, to close appendectomy wounds with intradermal absorbable suturing (I).
2. To compare the cosmetic result of absorbable intradermal suturing to that of traditional interrupted non-absorbable suturing. The research question was whether the new technique provided a better cosmetic result (II).
3. To define the severe complications related to appendectomy, the factors related to these complications as well as the incidence of patient insurance claims related to appendectomy, and to compare the outcomes of laparoscopic and open appendectomy based on the insurance claims (III).
4. To determine the mortality related to appendectomy in Finland, in addition to the related risk factors. We also aimed to define the trends of the mortality over the 21-year study period in comparison to the trend of the negative appendectomy rate and increased laparoscopic appendectomies (IV).

4 MATERIALS AND METHODS

4.1 Wound healing after open appendectomy (I)

Two hundred patients with suspected appendicitis scheduled for open appendectomy were recruited for the wound closure study. Patients eighteen years of age or older were included in the study. All patients received oral and written information, and a signed consent was obtained. Computer-produced numbers were used to randomize patients into two groups of wound closure. The first group underwent traditional wound closure with interrupted non-absorbable (NA) sutures and the second group with absorbable (A) continuous intradermal sutures (Figure 2).

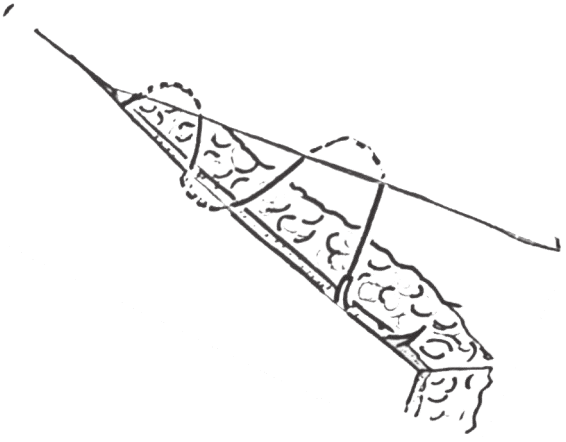

Figure 2. The technique of intradermal suturing

Demographic data were collected of the study groups as well as information on the procedure. The operation technique was standardized to be similar for both groups, with the exception of the skin closure technique. Follow-up included wound inspection on the first postoperative day by a surgeon other than the one who performed the surgery, or an experienced nurse at the ward. A nurse's appointment and evaluation of the wound were carried out after one week at the time of the removal of the NA sutures. The patients were interviewed over the phone by the investigators at a median of 21 days post-surgery. Standard questionnaires were used for all steps of the evaluation. The questionnaire included an

evaluation of tenderness, redness, swelling and exudate of the wound by severity from 1 to 4. At the last control, the patients were additionally asked of any treatment received for a possible wound infection.

4.2 Cosmetic result of appendectomy wounds (II)

Patients who were randomized in the first part of the wound closure study were invited to an outpatient clinic one year post-appendectomy. Photographs were taken of the scars, and the patients filled in the subjective scar evaluation assessment form. Two independent plastic surgeons evaluated the scars from the photographs, blinded from the closure method. For subjective assessments, the Vancouver Scar Scale (VSS), the Patient and Observer Scar Assessment Scale (POSAS) and the Visual Analogue Scale (VAS) were used. The Vancouver Scar Scale grades four variables (vascularity, pigmentation, pliability and height) with points from 0 (normal) to 2–5 maximum (worst outcome). The Patient and Observer Scar Assessment Scale grades five variables (vascularity, pigmentation, pliability, thickness and relief) as assessed by the observer with 1–10 points each, with a maximum total of 50 points. The scale also takes into account the patient's own perception of the scar with six questions worth one to ten points each, with a maximum total of 60 for the worst outcome. The Visual Analogue Scale gives points from 0 (normal) to ten (worst possible scar). Spectrocutometry was used for objective assessment to measure the estimated concentration change (ECC) of melatonin and haemoglobin in the scar (Kaartinen et al. 2011). Spectrocutometry is a technique combining standardized digital imaging and spectral modelling for scar assessment, and it is a new, completely objective method of scar evaluation (Kaartinen et al. 2011). Additionally, the scar's mean width and surface area were measured for objective evaluation.

4.3 Severe complications of laparoscopic and conventional appendectomy (III)

The Finnish Patient Insurance Centre (PIC) provides compensation for patients suffering an injury or harm related to (medical) treatment. Patients are advised to make a claim after complications, especially severe ones. There is no need for proof of malpractice or guilt, and health care personnel do not feel uncomfortable advising patients to make the claim. Patient insurance is mandatory for physicians in Finland. PIC therefore provides a reliable national register of severe complications and has previously been used to study complications; the register is not, however, absolutely comprehensive (Rantanen et al. 2008). The PIC register was searched for appendectomy patients operated on between 1990 and 2010. The PIC was established in 1987, and the first three years were left out of the study to avoid any problems that may have occurred in the first years. There is a three-year period during

which claims can be made after the injury; all claims were thus available at the time of data collection in February 2013. The register was searched for ICD-9 and ICD-10 codes for open and laparoscopic appendectomy (6541, JEA00, JEA01 and JEA10). The register is in paper format and includes the patient records providing detailed information, which were collected for analysis.

Complications were classified into 6 grades using the Accordion Severity Grading System (ASGS), which has been developed for the evaluation of postoperative complications (Table 5) (Strasberg et al. 2009). Severe complications (ASGS 4–6) were analysed in more detail. LA and OA were compared in terms of the variety of complications, compensated claims and total claims. Complications related to laparoscopic appendectomy were also analysed for specific chronological phases as laparoscopic operations were introduced during the study period.

Table 5. Accordion Severity Grading System (ASGS) classification

ASGS grade	Description
1	Treatment of complication requires only a minor invasive procedure (intravenous line, nasogastric tube, drainage of wounds)
2	Complication requires medical treatment
3	No general anaesthesia required, treatment with endoscopy, reoperation without general anaesthesia
4	General anaesthesia required for reoperation or single organ failure has developed
5	General anaesthesia is required and single organ failure has developed or multiorgan failure has developed
6	Postoperative death as a consequence of complication

(Strasberg et al. 2009)

4.4 Appendectomy-related mortality (IV)

Public hospitals in Finland are obligated to report patients to the National Institute for Health and Welfare's Hospital Discharge Register. Emergency surgery is performed only in public hospitals, and the register thus covers all appendectomies in Finland. The Hospital Discharge Register was searched for the appendectomy codes (6541, JEA00, JEA01 and JEA10), and this information was combined with Statistics Finland's archive of death certificates. The patients who had died within 30 days of the operation were identified, and copies of these patients' death certificates were obtained from Statistics Finland. The data on overall mortality were provided by Statistics Finland for the comparison of the risk of death. Patients' demographics, causes of death and time of death were collected and analysed. The study period of 21 years was divided in to three-year sequences to evaluate the trend of mortality. The negative appendectomy rate and the rate of laparoscopic appendectomies were defined for the same time sequences for comparison.

5 STATISTICAL ANALYSIS

The power analysis for the wound closure study was calculated with the assumption of an equal wound infection rate of 10%–20% with a 10% margin accepted. The sample size was set to 100 patients in each group to prove this result. Differences between the groups for the first two studies were analysed using the appropriate tests (the Mann-Whitney test, student T-test or χ-square test), depending on the whether the variables were categorical or continuous, or normally distributed or skewed. A p value of <0.05 was considered statistically significant.

For the complication study (III), the difference between OA and LA was analysed with Fisher's exact test in terms of ASGS grades. Two severity groups were defined as ASGS 1–3 and 4–6. Compensation yes/no as dependent variable logistic regression was used with independent variables: age, operation technique (OA/LA), hospital (district/central or university), appendicitis (CA/UCA), surgeon (consult/resident), operating time (day/night). The change in the rate of LA was tested in R (software for statistical computing and graphics, version 2.13.0, the R Foundation for Statistical Computing) with the "Mann-Kendall" function.

The results in the mortality study were presented in absolute values and percentages, or means with standard deviations (SD) or min/max values. One-way analysis of variance (ANOVA) or the χ-square test were used for analysis, depending on whether the variable was continuous or categorical, respectively. Statistical significance was considered if $p<0.05$. Mortality was calculated for age groups in ten-year intervals. A standardized mortality ratio (SMR) of the observed number of deaths to the expected number of deaths was used to illustrate the primary outcome. Binary logistic regression analysis was used to calculate odds ratios and 95% confidence intervals (CI) for risk factors associated with increased 30-day mortality. Statistical analyses were performed using SPSS Statistics version 22 for Windows (IBM Corp., Armonk, NY, USA).

6 ETHICAL CONSIDERATIONS

The studies in this thesis were conducted according to the Declaration of Helsinki. Patients recruited for the study signed an informed consent. Each independent study (I–IV) was approved by the Ethics Committee of Pirkanmaa Hospital District.

7 RESULTS

7.1 Wound healing after open appendectomy (I)

A total of 206 patients were recruited and randomized into two wound closure groups. Of them, 185 had adequate follow-up data and were included. The non-absorbable (NA) wound closure group included 95 and the absorbable (A) group 90 patients. Follow-up percentages are presented in Table 6. The lowest adherence to follow-up was in the absorbable sutures group at one week. These patients did not need stich removal and were therefore probably were poorly motivated for early control. If both second and third follow-up points were missed, the results were excluded from analysis.

Table 6. Follow-up data from two wound closure groups

Follow-up	NA wound closure group	A wound closure group
1st postoperative day	100%	100%
One week	87.5%	81.1%
Median 3 weeks	89.5%	95.6%

NA= non-absorbable sutures, A=absorbable sutures

Both groups were similar in terms of patient demographics and surgical details. The only statistical difference was in blood loss between the two groups, which was a mean of 15.8 ml higher in NA group. The total blood loss was low in both groups (range 0–200ml), and this difference was therefore considered clinically insignificant. The primary outcome, wound infection, was defined as wound excretion, redness, tenderness and swelling leading to the need for treatment by lavage, drainage and/or antibiotics. The rates of wound infection were 7.4% and 3.3% in NA and A groups, respectively. The difference was statistically insignificant, and the primary assumption was thus confirmed and absorbable suturing found equal to traditional wound closure. Dehiscence of the wound, defined as a locally treated, mild wound complication, was found statistically significantly more frequently with interrupted non-absorbable suturing than absorbable intradermal suturing. In multivariate analysis, absorbable suturing was found to be the only significant factor for the decreased wound complication rate regarding both wound infections and mild wound complication/dehiscence. The results are presented in Table 7.

Table 7. Characteristics of the non-absorbable and absorbable sutures groups. Primary and secondary outcomes of the two appendectomy wound closure groups, presented as number of patients and percentage.

	NA group n=95	A group n=90	P value
Blood loss (ml)	40.9	25.1	0.043
Negative appendectomy rate	12.6%	8.9%	ns
Complicated appendicitis	34.7%	37.8%	ns
Perforation rate	18.9%	18.9%	ns
Wound infection	7 (7.4%)	3 (3.3%)	ns
Dehiscence	11 (11.6%)	0	0.002

NA= non-absorbable sutures, A=absorbable sutures, ns=not significant

7.2 The cosmetic result of appendectomy wounds (II)

All patients with adequate data were invited to the outpatient clinic (n=193) in at average of 14 months postoperatively. Of these patients, 138 arrived: one was excluded for protocol violation, and the final analysis thus included 137 patients. Two of the subjective scar assessments (POSAS, both patient and observer, and VAS) showed a statistically significant benefit of absorbable sutures. The Vancouver Scar Scale (VSS) did not reach statistical significance, with a p value of 0.069, but could be interpreted to support the result of the other assessments. For the objective assessments, scar surface and width were significantly larger in the NA group. In addition, ECC values for melanin were significantly lower for the A group, yielding a better cosmetic outcome. The difference in ECC values for haemoglobin did not reach statistical significance. The results are presented in Table 8.

Table 8. Mean values of objective and subjective scar assessments in the non-absorbable (NA) and absorbable (A) wound closure groups

Scar assessment	NA (n=68)	A (n=69)	p-value
POSAS (patient) (6–60)	14.9	12.0	0.032
POSAS (observer) (5–50)	11.8	9.9	0.001
VAS (1–10)	4.0	3.1	0.002
Scar width (mm)	5.6	3.6	0.003
Scar area (mm)	597	338	0.002
ECC melanin (%)	0.011	0.038	0.034
ECC haemoglobin (%)	0.28	0.26	ns
VSS (0–13)	2.8	2.3	ns
Scar length (mm)	98.1	89.0	ns

ns=not significant

7.3 Severe complications related to conventional and laparoscopic appendectomy (III)

During the study period of 21 years, some 341 claims concerning appendectomies were reported to the Patient Insurance Centre (PIC), 14% of which concerned laparoscopic and the rest open appendectomy. The total number of appendectomies as the main operation during the same period of time was 161,414 – therefore, 0.2% of all appendectomies led to an insurance claim. The number of laparoscopic appendectomies increased during the study period, from 3% in 1996 (the first year the diagnostic codes for laparoscopic appendectomy were available) to 23% over the last year of the study, 2010. The mean LA rate was 7% during the study period. Laparoscopic appendectomies led to a claim more often than open appendectomies – 0.4% and 0.2%, respectively ($p<0.001$) – but there was a declining trend in the claims concerning LA as the popularity of the laparoscopic technique increased ($p=0.013$). There were 114 (34%) severe complications (ASGS 4–6). Only two deaths were reported to the PIC during the study period.

Of the 114 (34%) severe complications, 104 (92%) patients' medical records were available for detailed analysis. The mean age of these patients was 39 years and the mean ASA (American Society of Anesthesiologists grades 1–5 for assessing fitness for anaesthesia and surgery) score was 1.5. The negative appendectomy rate was 39% of the claims concerning severe complications, and a diagnostic CT scan had been performed only in 4% of the cases. The complications leading to an insurance claim were more often severe (ASGS 4–6) and more often related to laparoscopic than open appendectomy ($p=0.03$). The negative appendectomy rate within the compensated claims was 43%. The complications are presented in Table 9.

Table 9. The most common complications after appendectomies and their severity reported to the Finnish Patient Insurance Centre over the study period of 1990–2010, reported in number of patients and percentages

Complication/severity	All claims n=341	OA n=293 (86%)	LA n=48 (14%)
Wound infection	75 (22%)	71 (24%)	4 (8%)
Intra-abdominal abscess/deep infection	46 (14%)	36 (12%)	10 (21%)
Bleeding	58 (17%)	44 (15%)	14 (29%)
Bowel perforation	33 (10%)	27 (9%)	6 (13%)
ASGS 1–3	192 (56%)	167 (57%)	25 (52%)
ASGS 4–6	114 (34%)	91 (31%)	23 (48%)
Misdiagnose/delay in surgery	34 (10%)	34 (12%)	

OA=open appendectomy, LA=laparoscopic appendectomy, ASGS=Accordion Severity Grading System

7.4 Appendectomy-related mortality (IV)

The number of appendectomies as the main operation during the study period was 164,579 and the number of deaths 347, constituting a case fatality rate (CFR) of 2.1/1,000 operations (0.21%). The mean standardized mortality rate (SMR) of appendectomy patients was 4.0, gradually increasing after 60 years of age. The negative appendectomy rate (NAR) started to rise after 40 years of age (Figures 3 and 4).

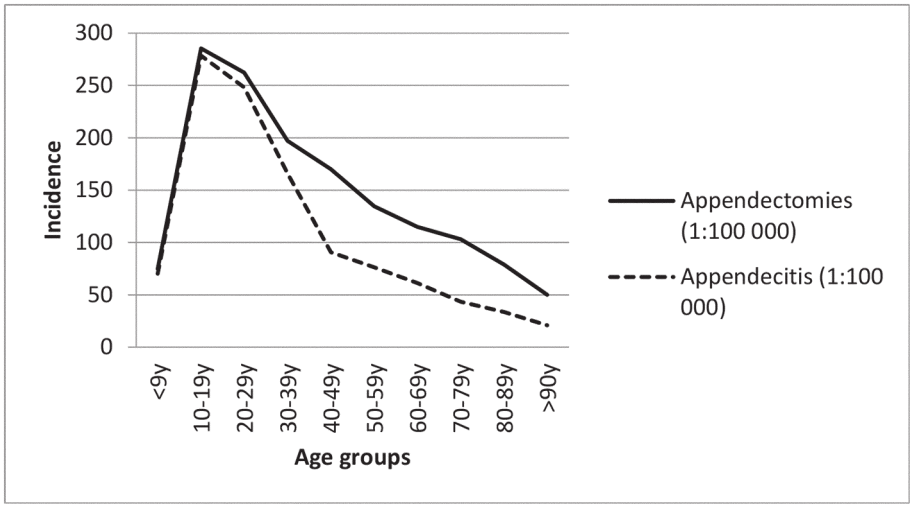

Figure 3. Rate of appendectomies and verified appendicitis in age groups. Finland 1990–2010.

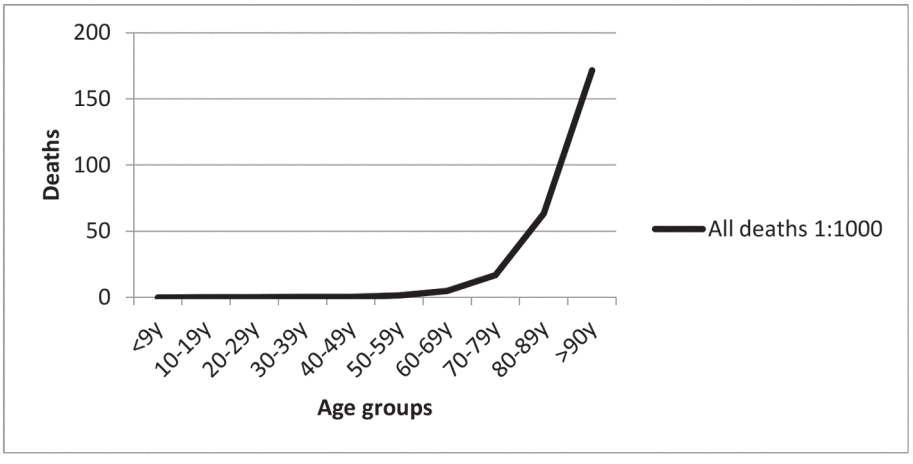

Figure 4. Mortality after appendectomy in age groups defined as deaths per operations (case fatality rate). Finland 1990–2010.

Mortality was related to aging, male sex, complicated appendicitis, negative appendectomy and open appendectomy. The results of multivariate analysis correlated with these findings and are presented in Table 10. According to the multivariate analysis, there was a 39-fold increase in mortality among the elderly patients aged over 65 years, a four-fold increase in connection with negative appendectomies and a six-fold increase in connection with open appendectomies.

Table 10. Results of the multivariate analysis, odds ratios (OR) with 95% confidence interval (CI)

Variable	OR	95% CI	p-value
Elderly patient (age≥65 years)	38.7	29.7–50.4	<0.001
Negative appendectomy	4.2	3.2–5.5	<0.001
Complicated appendicitis*	3.2	2.4–4.3	<0.001
Male sex	1.5	1.2–1.8	<0.001
Open surgery	6.0	1.9–18.8	0.002

*perforated, necrotic, abscess

The negative appendectomy rate declined over the study period from 27.3% during the first to 18.2% during the last three-year period (p<0.001). The rate of laparoscopic appendectomies increased to 21.3% during the last three-year period (p<0.001). At the same time, mortality declined from 2.6/1,000 in the first three-year sequence to 1.0/1,000 operations in the last (p=0.001) (Figures 5–7).

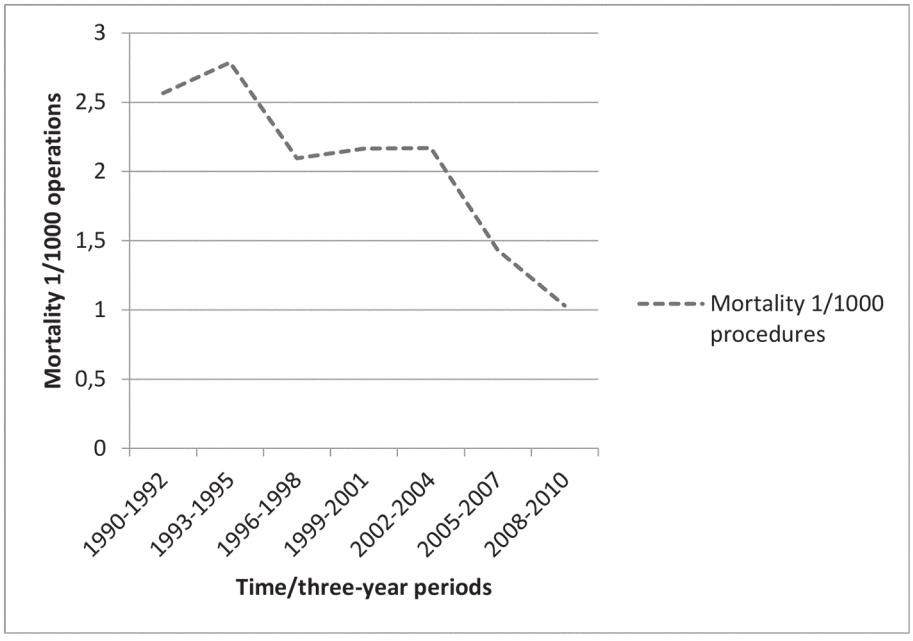

Figure 5. Post-appendectomy mortality. Finland 1990–2010.

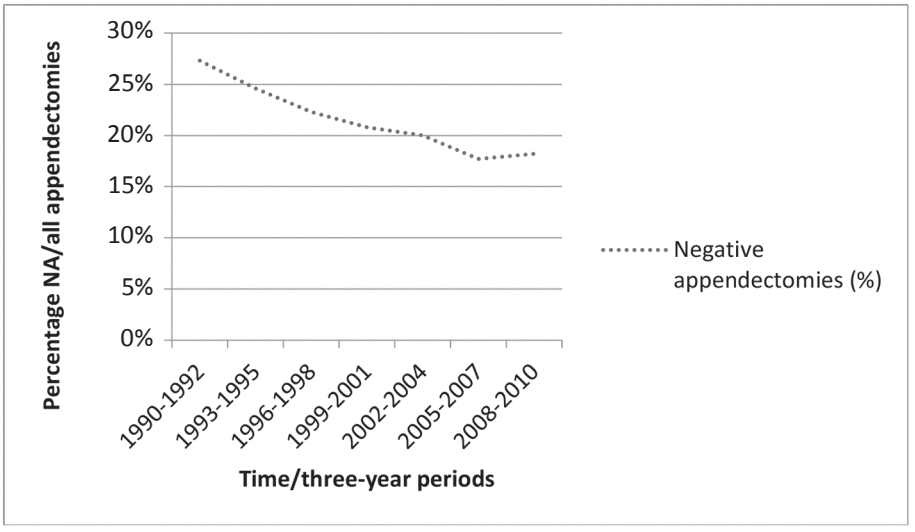

Figure 6. Negative appendectomy (NA) rate. Finland 1990–2010.

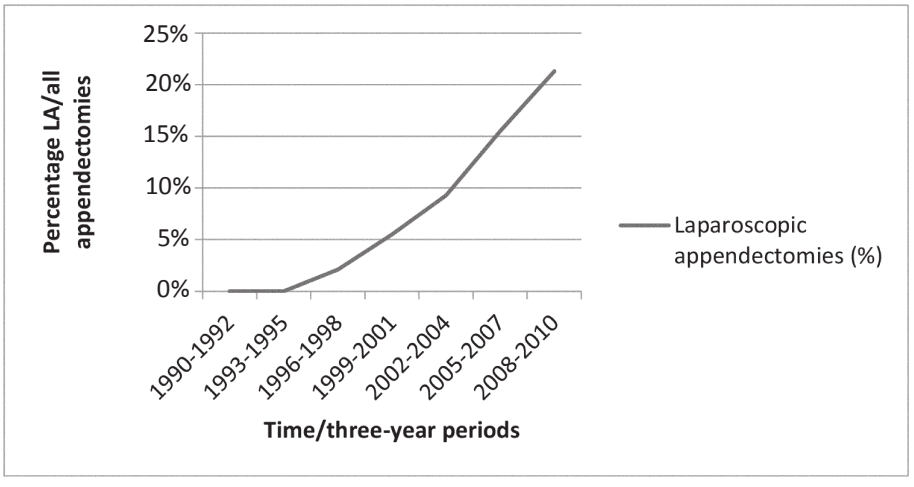

Figure 7. Laparoscopic appendectomies. Finland 1990–2010.

8 DISCUSSION

Wound healing, complications and mortality are important outcome measures of any surgery. The most common complication after appendectomy is wound infection. In order to avoid infection, the standard method of wound closure has been interrupted non-absorbable sutures in open appendectomy wounds. The benefit of absorbable suturing in surgery in general has been shown in many studies (de Waard et al. 2006; van den Ende et al. 2004; Zhang et al. 2011). In addition to diminishing the patient's discomfort, the use of absorbable sutures reduces the burden on the health care system. This is a significant aspect at a time when resources are limited. Wound closure with absorbable intradermal suturing has previously been accepted as a standard wound closure method in children's appendectomy wounds (Serour et al. 1996). In laparoscopic wounds, absorbable suturing is used routinely, and appendectomy is no exception, even in complicated appendicitis cases. Yet superficial surgical site infection has been shown to be even less frequent after laparoscopic appendectomies (Xiao et al. 2015).

Appendectomy-related severe complications are known to be rare, and the same applies to mortality. Still, there are very few population-based comprehensive studies on either topic. The treatment of appendicitis has been evolving through the last two decades. Laparoscopic surgery has become a routine method and the diagnostic accuracy has increased, especially with the wide use of CT scanning. (Jaschinski et al. 2015; Raja et al. 2010.) These developments have raised the question whether the safety of operative treatment has changed over these years. Additionally, conservative treatment of appendicitis with antibiotics alone is an issue of interest at present. The promoters of the antibiotic treatment often emphasize the burden of surgery with complications and mortality related to it (Salminen et al. 2015).

In this thesis, we were able to show the benefit of continuous absorbable sutures in appendectomy wounds of adult patients. The first study showed that absorbable sutures are a safe and feasible wound closure method in terms of wound infection when compared to traditional closure with interrupted non-absorbable sutures in open appendectomy wounds. Open appendectomy is still an procedure of importance, as many surgeons prefer it in complicated appendicitis cases. Additionally, laparoscopy is not yet available in many emergency centres worldwide as it is more demanding in terms of equipment and

skill (Ekwunife et al. 2014). Our study showed that, even in complicated appendicitis, absorbable continuous sutures are a feasible wound closure method in open appendectomy wounds, with no more wound infections compared to traditional wound closure. Similar results were earlier confirmed for paediatric patients in a study from our own institution (Pauniaho et al. 2010). In line with our results, an earlier study including adult patients with a relatively small study group of 100 patients found absorbable sutures to be better in terms of wound healing outcome compared to non-absorbable sutures in uncomplicated appendicitis wounds (Onwuanyi et al. 1990).

In our study, we also found wound dehiscence after non-absorbable sutures but not after absorbable sutures. This result may be an issue of relevance in the matter of cosmetic result. An earlier study, including both adult and paediatric appendectomy patients, found the cosmetic result to be better with absorbable intradermal suturing (Onwuanyi et al. 1990). However, no objective scar assessment was conducted in that study. In our study, we were able to confirm that intradermal absorbable sutures yield a cosmetic result superior to that of non-absorbable stitches in adult open appendectomy patients. Our study included standardized scar scales for both objective and subjective scar assessment. In addition, we used an objective scar measurement method, spectrocutometry, which compares the haemoglobin and melanin levels of the scar to the patients' own skin and measures the scar dimensions by pixel from a digital image. With this comprehensive study protocol, we found significant benefit for intradermal absorbable wound closure in terms of cosmetic result. Appendectomy patients are mainly young, and the cosmetic outcome of a surgical scar has been shown to play an important role in terms of body image and quality of life (Brown et al. 2008).

The strength of the studies concerning wound healing was the concise cohort of randomized patients with structured wound closure methods and comprehensive follow-up. We were not able to blind the wound closure method from the evaluating surgeon/nurse, as we found careful wound evaluation to be impossible with a dressing covering the wound from the evaluator. However, even if full blinding was not possible, the evaluation was always carried out by a person other than the operating surgeon, and the wound infection criteria were clearly bound to the need of treatment. In the study concerning the cosmetic result, the dropout rate can be criticized as being relatively high. The patients were contacted by both letter and telephone and offered additional options for outpatient clinic appointments. Additionally, the patients' travel expenses were covered if necessary. The university hospital catchment area is a geographically large region, and some patients found it time-consuming and complicated to participate in the follow-up. Despite the dropouts, the result was positive and confirmed the study outcome of better cosmetic result with absorbable sutures.

The study of severe complications based on the Patient Insurance Centre's register showed that patient claims regarding appendectomies are rare. The complications resulting in patient claims were more frequently related to laparoscopic appendectomies. This

difference, however, equalised towards the end of the study period. The trend of a diminishing number of claims while the number of laparoscopic appendectomies increased is most likely related to the learning curve of the novel technique. Complications related to laparoscopic appendectomy were more severe than those related to open appendectomy, which can be interpreted to reflect the complexity of the laparoscopic technique in comparison to the open technique. The nature of complications related to laparoscopy, such as bleeding and intra-abdominal abscess, more often lead to additional operations and prolonged hospital stay than the most frequent complication of open surgery, wound infection. An individual surgeon's learning curve is always involved in an advanced technique, and the possibility of severe complications should be taken into consideration when educating surgical residents in laparoscopic appendectomy.

In line with earlier studies, we found the negative appendectomy rate to be related to severe complications. This finding strengthens the understanding of the importance of diagnostic accuracy. As the Patient Insurance Centre's register includes all patients' documents, we were able to investigate the cases in detail. The alarming finding was the infrequent use of diagnostic imaging or any method other than a clinical examination in the decision regarding surgery. As the time frame in the present study was long, 21 years, the attempt to achieve an accurate diagnosis and a lower negative appendectomy rate is most likely more meticulous today. The negative appendectomy rate in the patient claim cases was unacceptably high. However, misdiagnosed patients are probably prone to complain more often than correctly diagnosed ones, which may explain some of the correlation.

The expenses of surgery and the burden for the patient are best resolved by operating on the correctly diagnosed patients. The PIC's register is regarded reliable regard to severe complications, but it does not represent the true incidence of complications. This was most obvious in cases of death; only two were reported to the PIC over 21 years, which is why we were urged to study the mortality of appendectomies in Finland using the National Institute for Health and Welfare's Hospital Discharge Register and Statistics' Finland's Death Certificate Register.

A Finnish group has previously reported the mortality of appendicitis in the 1960's, obviously not reflecting the treatment in the present (Antila et al. 1964). Another study on the incidence of appendicitis and non-specific abdominal pain reported an appendectomy-related mortality of 0.2% in Finland (Ilves et al. 2011). This nationwide study focused on the incidence of appendicitis and non-specific abdominal pain and did not analyse mortality in detail. Interestingly, a large population-based Swedish study had found the relation between negative appendectomy rate and mortality, but this study was carried out before laparoscopy gained popularity (Blomqvist et al. 2001). Our study included the era of laparoscopic appendectomy.

Previous studies on mortality have found an association between increased mortality and the patients' co-morbidities, male sex and aging, as well as the negative appendectomy rate (Drake et al. 2013). These findings were confirmed in our study. The earlier Swedish

study showed a seven-fold mortality rate related to negative appendectomy, while our finding was four-fold mortality (Blomqvist et al. 2001). In the elderly (patients over 65-years of age), we found a 39-fold mortality rate. Non-productive explorative surgery is a considerable risk especially to elderly patients and those with co-morbidities. We were able to identify two cut-off points – after 40 years, the rise in the negative appendectomy rate and, after 60 years, the increasing mortality.

Another interesting finding was the declining trend of mortality. Over 21 years, the deaths after appendectomy were more than halved and, at the same time, the negative appendectomy rate declined and the rate of laparoscopy increased to up to 21% of all appendectomies. This indicates that advances in diagnostic accuracy may have decreased post-appendectomy mortality and that the trend towards avoiding unnecessary surgery is justified. In the multivariate analysis, these findings showed significant correlation.

The role of laparoscopic surgery is likely to remain significant in avoiding explorations by open surgery. Open appendectomy was related to mortality in our study and earlier studies – hence, the inverse relationship between laparoscopy and mortality is convincing. Over two decades, the safety of surgery and anaesthesia as well as perioperative care have developed. These advances are major factors in the decreased mortality rate of any surgery. In conclusion, it can be stated that laparoscopy is safe, or even beneficial, in the aspect of mortality and diagnostic accuracy has true value in the outcome of appendectomy patients.

9 SUMMARY AND CONCLUSIONS

This study constitutes a comprehensive analysis of appendicitis and appendectomies, focusing on the wound healing and severe complications of the operative treatment of appendicitis. The data of this thesis supports the following conclusions:

In our randomized controlled trial on appendectomy wound closure (I), we found the wound infection rate to be equal in the two compared wound closure methods – the traditional method with non-absorbable sutures and the modern method with absorbable intradermal sutures. Wound dehiscence is more frequent with traditional wound closure. Intradermal absorbable suturing is a safe and recommendable wound closure method for adult appendectomy patients.

The study on the cosmetic result of appendectomy wounds in adult patients (II) showed a better cosmetic outcome when using intradermal absorbable suturing compared to conventional wound closure with non-absorbable interrupted sutures, evaluated by both subjective and objective scar assessments.

Severe complications after appendectomy (III) we found to be related to aging, co-morbidities, negative appendectomy, complicated appendicitis and laparoscopic appendectomy. The relation to laparoscopic appendectomy is possibly explained by the learning curve of the novel technique during the study period. The complications related to laparoscopic appendectomies were more severe compared to those involving open appendectomies. Patient insurance claims were infrequent after appendectomy in both the open and the laparoscopic technique.

Finally, mortality related to appendectomies in Finland is 2.1/1,000 operations (IV). Mortality after appendectomy is related to aging, negative appendectomy, open appendectomy, complicated appendicitis and male sex. The mortality declined over the last two decades, which may be related to the increase in diagnostic accuracy and laparoscopic surgery, in addition to advances in perioperative care.

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12 ORIGINAL COMMUNICATIONS

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Wound Healing after Open Appendectomies in Adult Patients: A Prospective, Randomised Trial Comparing Two Methods of Wound Closure

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Abstract
Background The skin is closed in open appendectomy traditionally with few interrupted nonabsorbable sutures. The use of this old method is based on a suggestion that this technique decreases wound infections. In pediatric surgery, skin closure with running intradermal absorbable sutures has been found to be as safe as nonabsorbable sutures, even in complicated cases. Our purpose was to compare the safety of classic interrupted nonabsorbable skin closure to continuous intradermal absorbable sutures in appendectomy wounds in adult patients.
Methods A total of 206 adult patients with clinically suspected appendicitis were allocated to the study and prospectively randomized into two groups of wound closure: the interrupted nonabsorbable (NA) suture and the intradermal continuous absorbable (A) suture group. Primary wound healing was controlled on the first postoperative day, at 1 week clinically and after 2 weeks by means of a telephone interview. Follow-up data were obtained from 185 patients (90 in group NA and 95 in group A).
Results Continuous absorbable intradermal suturing was as safe as nonabsorbable sutures in regard to wound infections.
Conclusion Continuous, absorbable sutures can be used safely even in complicated appendicectomies without increasing the risk of wound infection. Considering the benefits of absorbable suturing, we recommend this method in all open appendectomies.

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Introduction

Acute appendicitis is the most common cause of acute abdomen leading to surgery. The incidence of appendicitis is 100–120/100,000, and the majority of the patients are young. The highest incidence of appendicitis is in the age group of 10–20 years [1, 2]. Laparoscopic surgery has become increasingly popular, but open appendectomy still has its place as a simple and cost-effective operation [3–5]. Even though the operation is common and the surgical technique was described in the nineteenth century [6], the method of the appendectomy wound closure is not well studied. Interrupted, nonabsorbable sutures remain the most common method of skin closure, because it is suggested to be better in contaminated wounds. Absorbable sutures are used widely in elective surgery to gain a better cosmetic result, to decrease financial costs, and to improve patient satisfaction [7–9]. An early study by Foster et al. [10] published in the *Lancet* in 1977 showed an increased rate of wound infections when absorbable sutures were

applied in appendectomy wounds. However, wound infection rates have been low after the introduction of prophylactic antibiotics [11].

Serour et al. [12] demonstrated in a nonrandomized study that absorbable sutures were safe in pediatric appendectomies when prophylactic antibiotics were used. In 2003–2008, a randomized, prospective trial (166 cases, including cases with perforated appendicitis) was performed at our institution for children younger than age 18 years. That study compared interrupted nonabsorbable and intradermal absorbable skin closure in open appendicectomies. The study clearly demonstrated that absorbable sutures did not increase the wound infection rate [13].

Materials and methods

Patient allocation

For this study, 206 adult appendectomy patients (18 years or older) were recruited at Tampere University Hospital. The cohort size was based on power analyses with the assumption that both wound closure methods would yield equal results. The diagnosis of appendicitis was based on a physical examination and clinical findings. If a clinical diagnosis could not be established, imaging studies, such as abdominal ultrasound or CT, were performed. Patients received written and spoken information about the study, and signed consent was obtained from the patients. The patients were then randomized into two wound closure groups by computer-produced random numbers: the nonabsorbable interrupted suture (NA), and absorbable continuous intradermal suture (A) groups (Fig. 1). All adult patients (age 18 years or older) were included at this point with no other exclusion criteria besides age.

Interventions and follow-up

Information concerning the patient's weight, height, smoking, other diagnoses (diabetes, inflammatory bowel disease, COPD, etc.), medication, sex, and age were recorded. Preoperative laboratory tests—CRP, white cell count, and blood glucose—were taken. Patients received prophylactic antibiotics (cefuroxime 1.5 g and metronidazole 500 mg) at the induction of the anesthesia. In the case of an allergy, 500 mg of levofloxacin was used instead of cefuroxime. The operating surgeons were surgical registrars or consultants, all of whom were experienced in open appendectomies. The operation was performed in a commonly accepted manner, with a lower right abdominal incision, followed by ligation of the mesoappendix and resection of the appendix. Inversion of the appendical stump was optional and left to the surgeon's decision. Wound closure was performed in the following way: the peritoneum was not closed; the muscles were adapted with absorbable sutures. The external fascia was closed with polyfilament 0-0 sutures (continuous or interrupted). The subcutaneous layer was not closed. The randomization result was then revealed to the surgeon and the skin was closed per protocol: group A, intradermal continuous absorbable 4-0 monofilament sutures (Monocryl, Monosyn); and group NA, nonabsorbable 4-0 interrupted sutures (Ethilon, Monosof). All wounds received infiltration anesthesia with levobupivacaine (Chirocaine) 0.5 % 5–10 ml (depending on the length of the wound) at the end of the operation. The wound was covered with a semiocclusive dressing (Mepilex Border), which was removed on the first postoperative day when the wound was evaluated for the first time. Postoperative laboratory tests were taken only when necessary (remarkable blood loss, fever >38 °C, wound complication). In cases of complicated appendicitis (perforated or gangrenous appendix, periappendicular abscess or peritonitis), postoperative intravenous antibiotic treatment was continued according to the clinical response (fever <38 °C, CRP, or white blood cell count lowering). This was followed by oral antibiotics for 7–14 days.

The first evaluation of the wound was performed by a surgeon in charge of the ward or by a nurse if the surgeon had performed the operation. Additionally, the following information about the surgery was recorded: blood loss, operation time, histopathologic diagnosis, and intraoperative diagnosis. The wounds were evaluated and/or sutures removed 7–9 days postoperatively by a district nurse who completed an evaluation form. All patients were interviewed over the telephone at an average of 21 days postoperatively, and the same questions as in the evaluation form were asked. The patients also were asked about other possible postoperative problems. The interview was performed by two surgeons (authors SK and TR).

The primary outcome measure was wound infection with intention to treat (antibiotics, drainage, or both) following the Centers for Disease Control and Prevention (CDC) criteria for surgical site infection (SSI) (www.cdc.com). The secondary outcome measure was wound infection symptoms detected but no need for antibiotics or drainage (dehiscence, only treatment).

This study was performed according to the principles of the declaration of Helsinki. The study was approved by the Research and Ethics Committee at the University of Tampere. The study was registered at www.clinicaltrials.gov (NCT00913445).

Statistical analysis

According to earlier studies, wound infection frequency is 10–20 % after appendectomies. Appropriate sample size

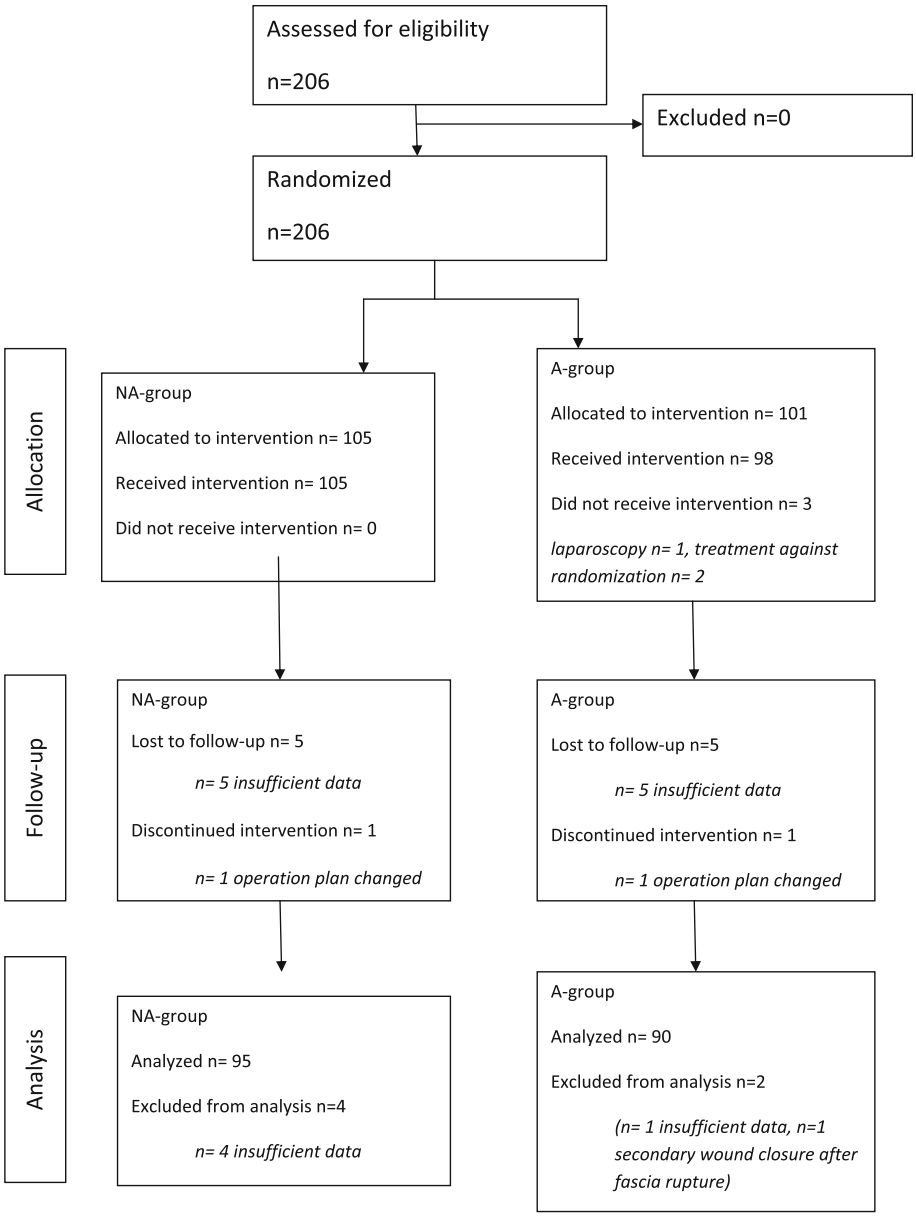

Fig. 1 Consort *diagram*

was calculated based on the assumption that methods yield equal results regard to wound infections; a margin of 10 % was considered acceptable. A sample size of 100 patients in each group was needed to prove this result (α set at 0.05; β set at 0.1; power = 90 %).

Frequency distribution tables are presented separately for the absorbable and nonabsorbable group. Group differences were analyzed with appropriate tests (Mann–Whitney, *t* test, χ^2 test), depending on whether the variables were categorical or continuous, or normally distributed or skewed. Two separate multivariable logistic regression models with binary outcomes (complication or no complication) also were constructed. Group (absorbable or nonabsorbable), sex, BMI, age, smoking status (yes/no), and complicated appendicitis were used as independent variables in both models. $p < 0.05$ was considered statistically significant, and 95 % confidence intervals were calculated. SPSS® version 17.0 (SPSS Inc., Chicago, IL) was used in statistical analyses.

Results

A total of 206 patients were recruited and randomized into two wound closure groups: 105 in the nonabsorbable suture (NA), and 101 in the absorbable suture (A) group (Fig. 1). Follow-up data were obtained from 185 patients: 95 in the NA and 90 in the A group. At 1 week, wound evaluation forms were received from 83 of 95 (87.4 %) patients in NA group and from 73 of 90 (81.1 %) patients in the A group.

Table 1 Demographic data on the appendicitis wound closure groups

Variable	Nonabsorbable group	Absorbable group
Age, years (mean, min–max)	40.5 (18–83)	40.6 (18–88)
Male:female ratio	63.2 %:36.8 %	50 %:50 %
BMI (mean, min–max)	25.8 (16.4–40.7)	26.1 (18.2–35.7)
Smoker:nonsmoker ratio	24.2 %:75.8 %	22.2 %:77.8 %
Comorbidity (*n* patients)	22	19
COPD, asthma	4	5
Diabetes	3	3
Cardiovascular	12	14
Pregnancy		1
Other immunosuppressive	2	1
Other	1	2

Table 2 Final diagnoses of operated appendectomy patients

Variable	Absorbable group	Nonabsorbable group
Appendicitis (%)	91.1	87.4
Complicated appendicitis total (%)	37.8	34.7
Gangrenous (%)	13.7	14.4
Perforated (%)	18.9	18.9
Abscess (%)	4.2	2.2
Other total *n*	8	12
Diverticulitis *n*	1	
Nonspecific abdominal pain *n*	4	10
Ileitis, gastroenteritis *n*	2	2
Urinary tract infection	1	

The follow-up telephone interview reached 86 of 95 (89.5 %) and 86 of 90 (95.6 %) patients in NA and A groups, respectively. If both late follow-up points were missed, the patient in question was excluded from the analysis due to insufficient data.

Patients in both groups were well matched for age, sex, BMI, and smoking (Table 1). Average blood loss was 40.9 (range 0–200) ml in group NA and 25.1 (range 0–200) ml in group A. The difference between the groups was statistically significant ($p = 0.043$), but blood loss was low in both groups and considered to be of no clinical significance. Operating time was comparable in both groups, with a mean of 38 (range 12–120) min in group NA and 41 (range 18–122) min in group A. Twenty percent of the patients had comorbidities in the NA group and 24 % in the A group (Table 2). In addition groups were comparable with comorbidities. Comorbidities were heterogeneous and few and thus not included in multivariate analyse but described separately.

In the NA group, 83 of 95 (87.4 %) patients and in the A group 82 of 90 (91.1 %) patients had appendicitis. Complicated appendicitis (gangrenous, perforated, abscess) occurred in 33 of 95 (34.7 %) patients in group NA and 34 of 90 (37.8 %) patients in group A.

Primary and secondary outcome measures

The wound infection (primary outcome, intention to treat) rates were 7.4 % (7/95) and 3.3 % (3/90) in the NA and A groups, respectively. There was no statistically significant difference between the groups ($p = 0.23$; Table 3). In the NA group, four patients with wound infection required drainage and three were treated with antibiotics only. Additionally, in the NA group, one patient had an intraperitoneal drain left at the operation and removed on the first postoperative day but subsequently required only antibiotic treatment for wound infection. In the A group, two patients required drainage and antibiotics, and one patient was treated with antibiotics only (Table 4).

Table 3 Odds ratio calculated for the risk of wound infection defined with intention to treat (primary outcome)

Variables	Significance	Odds ratio	95 % Confidence interval	
	p Value		Lower	Upper
Complicated appendicitis	0.023	7.229	1.314	39.786
Female	0.584	1.496	0.354	6.319
Smoker:nonsmoker	0.326	2.196	0.458	10.539
Absorbable sutures	**0.206**	**0.387**	**0.089**	**1.686**
BMI	0.071	1.155	0.988	1.35
Age (years)	0.884	1.003	0.959	1.049

Absorbable sutures outcome is in bold

The regression model showed that when all wound complications were included in the analysis (secondary outcome, dehiscence, locally treated infections), the number of complications was higher in the NA group. Absorbable suturing yielded less complications, with an odds ratio of 0.139 ($p = 0.002$; Table 5).

Discussion

The method of appendectomy wound closure is of clinical relevance to thousands of patients throughout the world every year. The benefits of absorbable sutures are obvious: less discomfort and no need for stitch removal, lessening the costs and increasing patient satisfaction. In addition, the cosmetic result is suggested to be better [7–9]. Our prospective, randomized study clearly shows that running intradermal absorbable sutures is as safe for closing appen-

Table 4 Complications in wound closure groups

Complications	Nonabsorbable group ($n = 95$)	Absorbable group ($n = 90$)
Wound complications	18 (18.9 %)	3 (3.3 %)
Antibiotic treatment and/or drainage	**7 (7.4 %)**	**3 (3.3 %)**
Wound dehiscence	11 (11.6 %)	0
Other complications (pneumonia, fasciae rupture)	3 (3.1 %)	3 (3.3 %)

Primary outcome results are in bold

Table 5 Odds ratio calculated for the risk of wound infection and all wound complications included in analysis (secondary outcome)

Variables	Significance	Odds ratio	95 % Confidence interval	
	p Value		Lower	Upper
Complicated appendicitis	0.113	2.336	0.819	6.662
Female	0.661	1.248	0.464	3.358
Smoker	0.847	1.119	0.357	3.508
Absorbable sutures	0.002	0.139	0.039	0.498
BMI	0.607	1.03	0.921	1.151
Age (years)	0.66	0.993	0.962	1.025

dectomy wounds as traditional interrupted, nonabsorbable sutures. In fact, there were fewer complications in group A when all wound complications were included.

Our study compared two common ways of closing appendectomy skin wounds: interrupted nonabsorbable sutures and continuous absorbable intradermal sutures. Previous nonrandomized studies have suggested that intradermal sutures are as good as or better than interrupted nonabsorbable sutures in noninfected wounds [7–9]. In an early study from 1977, absorbable subcuticular sutures were associated with an increased risk of infection in appendectomy wounds [10]. More recent studies, performed with modern prophylactic antibiotics, have shown that subcuticular absorbable sutures can be used in appendectomy skin closure [11, 12]. Only one randomized study (100 patients) of appendectomies closed with absorbable subcuticular sutures, including adult patients, has been published previously. In that study, however, patients with perforated appendicitis were excluded. The results were better in terms of both primary wound healing and cosmetic result in the subcuticular wound closure group [14]. Absorbable intradermal sutures have been proven to be safe in pediatric surgery even in complicated appendicitis [13] and our study confirmed this finding in adult patients.

Appendectomy is the golden standard for treating acute appendicitis. Open appendectomy is a safe operation with few complications, and it remains competitive with the laparoscopic approach. As in all bowel surgery, there is a significant risk of wound infection after appendectomies. Although wound infections are usually relatively easy to treat with antibiotics, there is no excuse to use methods that would increase this risk. Throughout history, many ways of preventing infection have been attempted from all imaginable local methods to various methods of closing or not closing the wound. Prophylactic antibiotics combined with careful clinical practice and surgical methods provide the basis for preventing wound infection. Primary skin closure with adequate prophylactic antibiotics has been proven to be a safe and comfortable method for closing the appendectomy wounds.

In our study, patients were allocated in one hospital and operations were performed by several surgeons. However, all operating surgeons were consultants or senior registrars with adequate experience in surgery. Wound closure was well defined, and dressing and local anesthesia were standardized. Exceptions were excluded from the analysis. The questionnaire was equal in all control items making it easy to compare the results. Although pain, redness, edema, and discharge were scored and enquired about, these values were considered remarkable only if there was intention to treat the infection. The control point at 1 week was missed more often in the absorbable suture group (81.1 vs. 87.4 %), which is understandable as stitch removal was not required. The latter control point was considered even more important, and a high percentage of patients were reached in both groups: 89.5 % (NA) and 95.6 % (A). The time of this second control point varied, with a mean of 21 (range 12–39) days from the surgery. This control was performed as phone interview; clinical control might have been better option in consideration of milder complications. None of the acute wound infections, the primary outcome, occurred this late and those were all clinically defined. Additionally patients were instructed to contact the hospital should they have wound problems later and if there were any problems patients were controlled clinically or by phone until final recovery. Wound infection was defined with intention to treat, following the CDC criteria for surgical site infection (SSI), and the treatment was administered with antibiotics alone or with antibiotics and drainage. Both wound closure methods were found to be equally safe considering the wound infection rate, which was comparable to earlier studies.

Wound infection rate was low (A group 3.3 %, NA group 7.4 %, total 5.4 %) but comparable to children's study (1.8 %) in our institute, which was performed with same

protocol [13]. This could be achievement of systematic and correctly timed antibiotic prophylaxis. Wound infection rate was particularly low considering the high rate of complicated appendicitis (A group 37.8 %, NA group 34.7 %). This same trend was found in the children's study (40.1 % complicated cases) [13]. Complicated appendicitis was defined if abscess, perforation, or gangrenous occurred, diagnosed either clinically or by pathologist. Especially gangrenous appendicitis might have been overdiagnosed.

At the 1-week control point, a significant amount of patients had mild infections reported as wound dehiscence (wound skin opening 5–30 mm, extended discharge other than purulent, need for local treatment) by district nurses. These patients were all in the nonabsorbable group. Although some patients had only minor skin opening and relatively mild discharge, this result was considered clinically important, because these symptoms clearly increase patient discomfort and may affect the cosmetic result. Using interrupted sutures can lead to overlapping of the wound edges, which could be one reason for dehiscence.

Conclusions

Absorbable intradermal suturing is a safe wound closure technique in adult appendectomy patients, even in complicated cases. Patients benefit from absorbable suturing in regards to comfort and satisfaction. Therefore, we suggest the use of absorbable sutures in all appendectomy cases.

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Continuous Absorbable Intradermal Sutures Yield Better Cosmetic Results than Nonabsorbable Interrupted Sutures in Open Appendectomy Wounds: A Prospective, Randomized Trial

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Abstract
Background Acute appendicitis is the most common reason for abdominal surgery in young adults and children. Open appendectomy is still the treatment often chosen because it is simple, safe, and effective. Our aim was to study whether cosmetic results of appendectomy wounds are better after using continuous absorbable intradermal (A) sutures compared with wound closure with interrupted nonabsorbable (NA) sutures.
Methods A total of 206 adult patients with clinically suspected appendicitis were allocated to the study and prospectively randomized into two wound-closure groups: the interrupted NA suture group and the A suture group. Of these, 193 patients with sufficient data were invited to the outpatient clinic for cosmetic analysis. Cosmetic results were evaluated after a median of 14 months. For subjective scar assessment, the Vancouver scar scale, the patient and observer scar assessment scale (POSAS), and a visual analog scale (VAS) were used. Objective evaluation was carried out by measuring surface area, average width, and estimated concentration change (ECC) of hemoglobin and melanin in the scar using spectrocutometry. For statistical analyses we used the Mann–Whitney test and Student's *t* test.
Results Both objective and subjective analyses showed better cosmetic results for absorbable intradermal suturing. The difference between the two groups was statistically significant as regards POSAS in both patient ($p = 0.032$) and observer scales ($p = 0.001$), and VAS ($p = 0.002$). Scar surface area was significantly smaller in group A than in group NA ($p = 0.002$). ECC measurements showed higher values for melanin in group NA than in group A ($p = 0.034$).
Conclusion Continuous intradermal absorbable suturing yields a better cosmetic result than interrupted nonabsorbable suturing in lower abdominal transverse appendectomy.

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Introduction

Wound closure is one of the basic aspects of all surgery. Decisions made when choosing suture material and technique should be based on awareness of primary wound healing and the expected cosmetic result. Most studies on wound-closure methods have been focused on surgical site infection as it is the most frequent complication in all surgery. After primary healing of the wound, a permanent scar remains, the importance of which to the well-being of

patients should not be underestimated [1]. In addition, early wound healing affects scar formation; hence, optimal wound closure yields fewer wound complications and thus a better cosmetic result [2].

The effect of suture material on scar appearance is challenging to study objectively. Most studies on scars have been based on subjective scar scales. The Vancouver scar scale (VSS, Table 1) was first developed for evaluation of burn scars and has since been used for evaluation of linear scars as well [3]. The patient and observer scar assessment scale (POSAS, Table 2) was designed for linear scars and it takes into account the patient's own perception of the scar [4]. The visual analog scale (VAS, Table 3) has also been validated for scar assessment and has been shown to be reliable when several observers have been used [5]. More recently, several objective methods of scar assessment have been introduced. Spectrocutometry is a novel innovation that combines digital imaging and spectral modeling to measure differences between scars and normal skin [6]. Earlier studies have shown that it is a usable tool for objective scar assessment [6, 7].

Appendicitis is the most common reason for abdominal surgery in young patients [8]. Laparoscopic surgery has become increasingly popular, but open appendectomy still has its place as a simple and cost-effective operation. Use of interrupted nonabsorbable sutures remains the most common method of skin closure in open appendectomy as this method has been suggested to be superior for contaminated wounds. In an earlier study by Serour et al. [9], the results indicated that intradermal interrupted suturing does not increase the wound complication rate in pediatric appendectomy patients when prophylactic antibiotics are used. In a more recent study from our institution, the same result was reached as regards continuous intradermal suturing [10]. In the first part of the present study, we found that the same applies to adult patients, as the number of surgical site

Table 1 The Vancouver scar scale

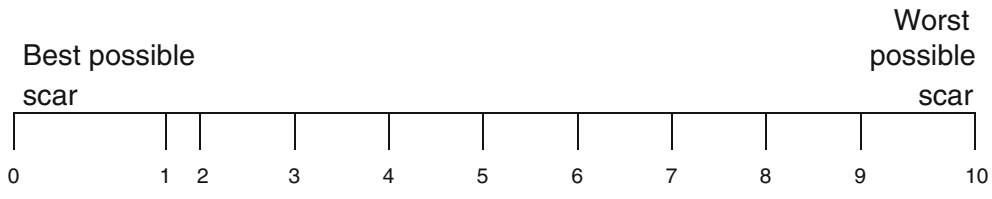
Parameter	Descriptor	Points
Vascularity	Normal	0
	Pink	1
	Red	2
	Purple	3
Pigmentation	Normal	0
	Hypopigmentation	1
	Hyperpigmentation	2
Pliability	Normal	0
	Supple	1
	Yielding	2
	Firm	3
	Banding	4
	Contracture	5
Height	Normal (flat)	0
	>0 and <2 mm	1
	≥2 and <5 mm	2
	>5 mm	3
Total score		/13

Table 2 POSAS observer component

	Normal skin								Worst scar imaginable	
	1	2	3	4	5	6	7	8	9	10
Vascularization	o	o	o	o	o	o	o	o	o	o
Pigmentation	o	o	o	o	o	o	o	o	o	o
Thickness	o	o	o	o	o	o	o	o	o	o
Relief	o	o	o	o	o	o	o	o	o	o
Pliability	o	o	o	o	o	o	o	o	o	o

POSAS patient component										
	No, not at all									Yes, very much
	1	2	3	4	5	6	7	8	9	10
Is the scar painful?	o	o	o	o	o	o	o	o	o	o
Is the scar itching?	o	o	o	o	o	o	o	o	o	o
	No, just like normal skin									Yes, very different
	1	2	3	4	5	6	7	8	9	10
Is the scar color different?	o	o	o	o	o	o	o	o	o	o
Is the stiffness of the scar different?	o	o	o	o	o	o	o	o	o	o
Is the thickness of the scar different?	o	o	o	o	o	o	o	o	o	o
Is the scar irregular?	o	o	o	o	o	o	o	o	o	o

Table 3 The visual analog scale



infections did not increase when using absorbable intradermal suturing [11]. In none of the earlier studies concerning appendectomy wounds have the cosmetic outcomes been reported. In some studies on elective surgery, scar appearance has been suggested to be better when intradermal absorbable sutures have been used [12]. Our aim was to study whether intradermal absorbable sutures yield a better cosmetic result in appendectomy wounds than traditionally used interrupted nonabsorbable sutures.

Patients and methods

Patient allocation

For the first part of our study, a total of 206 appendectomy patients aged 18 or older were recruited at Tampere University Hospital between July 2009 and April 2010 [11]. Age was the only exclusion criterion. The patients received written and spoken information about the study and a signed consent document was obtained in each case. Randomization to one of the two wound-closure groups, the absorbable continuous intradermal suture group (A) ($n = 101$) and the nonabsorbable interrupted suture group (NA) ($n = 105$), was carried out by using computer-generated random numbers. Of these, 193 patients with sufficient data were invited to the outpatient clinic for cosmetic analysis.

Intervention and follow-up

The appendectomy operation was performed with a lower abdominal incision, as described in detail in the first part of our study [11]. The skin was closed according to randomization: group A had intradermal continuous absorbable 4-0 monofilament suture (Monocryl®, Ethicon Inc., Johnson & Johnson, Piscataway, NJ, USA; Monosyn®, B. Braun Melsungen AG, Melsungen, Germany) and group NA had nonabsorbable 4-0 interrupted sutures (Ethilon®, Ethicon Inc.; Monosof®, Covidien, Dublin, Ireland). All wounds were treated by means of infiltration anesthesia with levobupivacaine (Chirocaine®, Baxter Healthcare S.A., Castlebar, Ireland), 0.5 %, 5–10 ml (depending on the length of the wound), at the end of the operation. The wounds were covered with semiocclusive dressing (Mepilex Border®, Gothenburg, Sweden), which was removed on the first postoperative day for wound evaluation.

Information about each patient's age, sex, weight, height, smoking, other diagnoses, and medication was recorded. Early wound healing was monitored according to the study protocol and the results have been published [11].

Subjective assessment

Blind to the closing technique used, the cosmetic result was evaluated at an average of 14 months after the operation

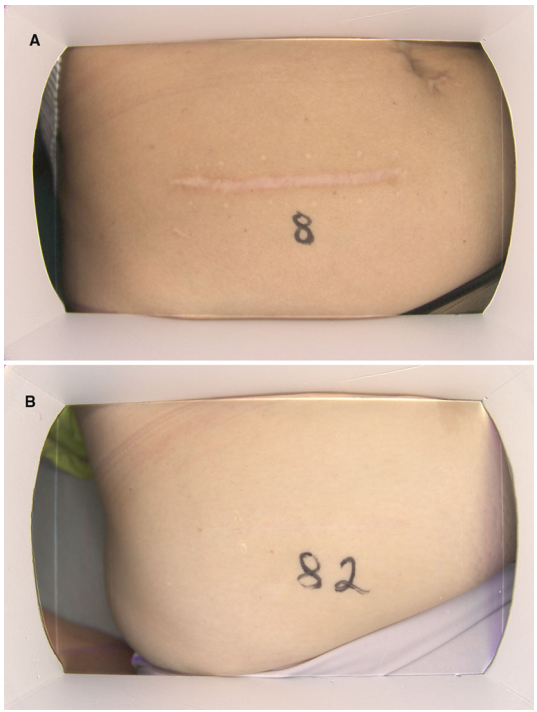


Fig. 1 The cosmetic outcome of fully matured appendectomy scars after use of interrupted nonabsorbable sutures (**a**) and an intradermal absorbable suture (**b**). Running number of the patient marked in *black* below the scar

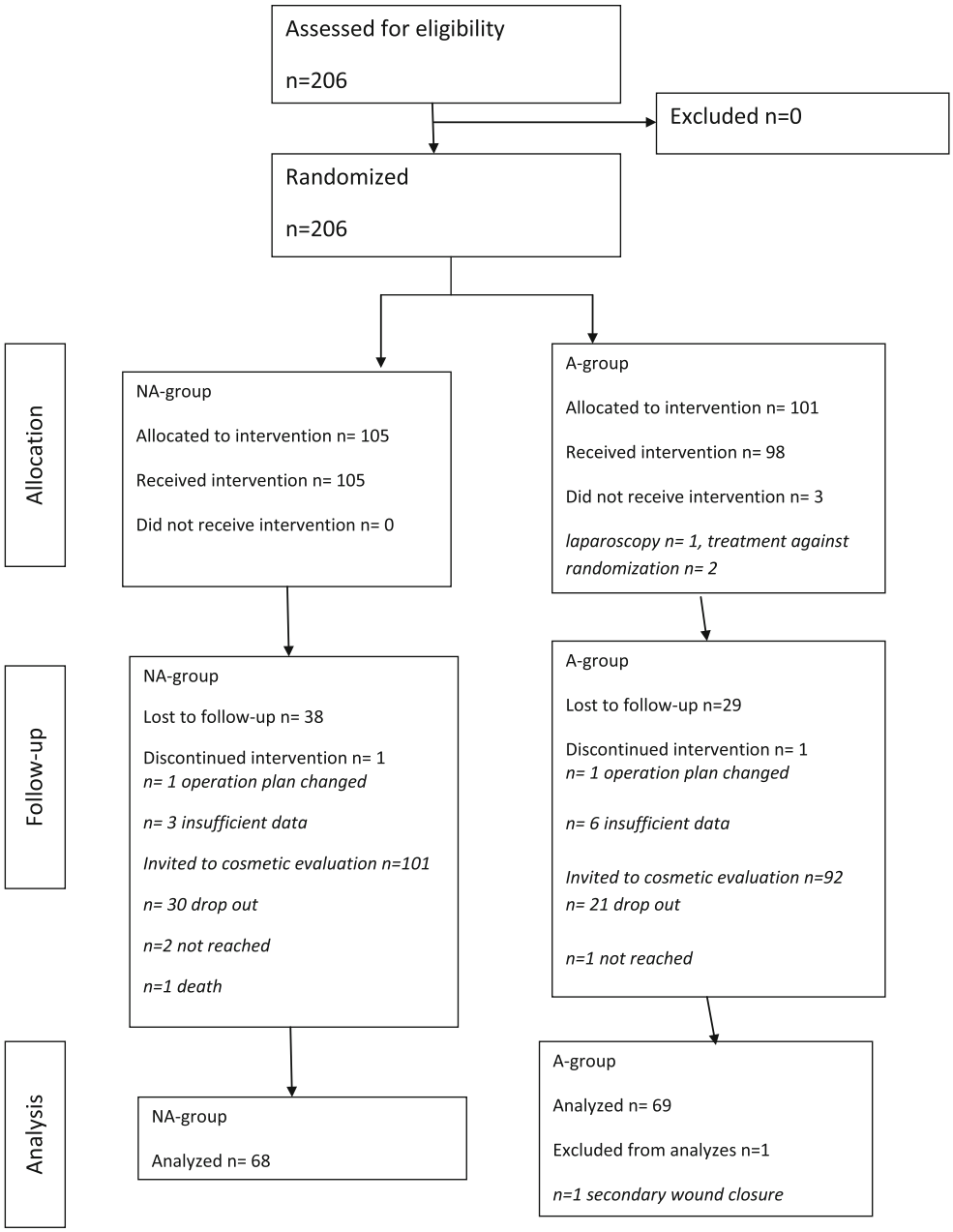


Fig. 2 CONSORT diagram

during a visit to the outpatient clinic (137 in group NA and 68 in group A, 69 [13]). The evaluation was carried out by two of the authors. During the visit the scar was photographed (Fig. 1a, b) and assessed using spectrocutometry, the VSS, and the POSAS. For the patient component a Finnish translation was used. The resulting standardized digital images were evaluated blindly using a VAS by four independent observers, all experienced in scar evaluation. None of those who evaluated the scars had been involved in the patients' care previously.

Objective assessment

Spectrocutometry was used for objective scar assessment. The method has been described in detail previously [6]. The instrument concerned produces standardized, calibrated digital images. The surface area of the scar was calculated from the pictures. The borders of the scars were manually delineated by the first author. All other delineations and calculations were carried out by Dr. Petri Välisuo at the University of Vaasa. The surrounding shadowed

areas, clothes, pen marks, and nevi were excluded. Possible stitch marks resulting from the use of nonabsorbable sutures were not included in the total scar area. A safety margin of 30 pixels around the scars was excluded and the skin baseline representing normal, scarless skin was evaluated. By comparing the scar and the skin baseline, the estimated concentration change (ECC) of hemoglobin was calculated. Higher ECC values of hemoglobin are strongly associated with immature and hypertrophic scars, which are likely to cause symptoms [7]. Higher and lower ECC values for melanin correlate to hyperpigmented and hypopigmented scars, respectively.

This study was performed according to the principles of the Declaration of Helsinki. The study was approved by the Research and Ethics Committee at the University of Tampere (R09060).

Table 4 Demographic data of the two appendectomy wound-closure groups

n	Nonabsorbable 68	Absorbable 69
Male/female	42/26 (62/38 %)	33/36 (48/52 %)
Age (years)	41 (18–88, SD ±17)	42 (18–83, SD ±16)
Follow-up (months)	14.8 (9.6–19.1, SD ±2.3)	14.3 (9.9–19.0, SD ±2.1)
BMI (kg/m^2)	26 (16–37, SD ±5)	26 (18–36, SD ±4)
Smoking	16 (24 %)	12 (17 %)
Diabetes	3 (4 %)	3 (4 %)
Immunosuppression	4 (6 %)	6 (9 %)
Cardiovascular disease	8 (12 %)	13(19 %)
Diagnosis: appendicitis acuta	59 (87 %)	63(91 %)
Complicated appendicitis/ all patients	23 (34 %)	25(36 %)
Wound infection	7 (10 %)	3 (4 %)
Wound dehiscence	9 (13 %)	0

Statistical analyses

Our statistical power calculation was based on the aim of the first part of the study to prove equal wound healing in both wound closure groups with an acceptable margin of 10 %. This calculation set the sample size to 100 in each group (α set at 0.05; β set at 0.1; power = 90 %), assuming the wound infection rate after appendectomy to be 10 % according to earlier studies [11].

Group differences were analyzed by using appropriate tests (the Mann–Whitney test, Student's *t* test), depending on whether the variables were categorical or continuous, or normally distributed or skewed. A value of $p < 0.05$ was considered statistically significant. SPSS version 17.0 (SPSS, Inc., Chicago, IL, USA) was used for statistical analyses. Statistical analyses were carried out by a statistician.

Results

A total of 193 patients (with sufficient data) were invited to the outpatient clinic. Of these, 138 patients (71.5 %) arrived and were evaluated according to our protocol. After excluding one patient (protocol violation), 137 patients were included in the analysis (CONSORT diagram, Fig. 2). Demographic data are presented in Table 4. The results of subjective and objective scar assessment are presented in detail in Table 5.

All three subjective scar scales indicated a better cosmetic outcome in connection with absorbable (A) sutures, with statistical significance in POSAS and VAS evaluation (Table 5). The scar surface areas measured in group NA were larger than in group A and this objective finding was also statistically significant ($p = 0.002$). In addition, the mean scar width was significantly higher in group NA than in group A ($p = 0.003$), while was no statistically significant difference in the mean lengths of the scars. The ECC values for melanin were significantly lower in group A

Table 5 Results of subjective and objective scar assessment in the two appendectomy wound-closure groups

	Nonabsorbable	Absorbable	*p* value
VSS	2.8 (SD ±1.8)	2.3 (SD ±1.5)	ns ($p = 0.069$)
POSAS (patient)	14.9 (SD ±7.7)	12.0 (SD ±4.3)	0.032
POSAS (observer)	11.8 (SD ±3.8)	9.9 (SD ±2.8)	0.001
VAS	4.0 (SD ±1.7)	3.1 (SD ±1.4)	0.002
Scar width (mm)	5.6 (SD ±3.7)	3.6 (SD ±1.8)	0.003
Scar length (mm)	98.1 (SD ±27.7)	89.0 (SD ±23.5)	ns ($p = 0.065$)
Scar area (mm^2)	597 (SD ±573)	338 (SD ±230)	0.002
ECC melanin (%)	0.011 (SD ±0.4)	0.038 (SD ±0.3)	0.034
ECC hemoglobin (%)	0.28 (SD ±0.74)	0.26 (SD ±0.55)	ns ($p = 0.078$)

($p = 0.034$). The ECC values for hemoglobin were higher in group NA, but the difference was not statistically significant.

Discussion

The results of the present study clearly demonstrate a better cosmetic outcome with intradermal suturing. To our knowledge this study is the first randomized controlled trial in which both subjective and objective methods of scar assessment have been used in cases of lower abdominal incisions. We used three different validated scar scales, including POSAS, which takes into account the patient's view. In addition, we used four independent observers, blind to the background, to evaluate the scars by VAS, which has been shown to increase the reliability of subjective scar assessment [5].

Transdermal interrupted nonabsorbable suturing has been a standard method for open appendectomy wound closure for decades. Recognizing the benefits of absorbable sutures, it is now standard for pediatric surgeons to use them for appendectomy wound closure [5, 9, 10]. Intradermal suturing has been shown to be comparable to or even better than other wound-closure methods, with good cosmetic satisfaction as regards tissue adhesions and skin grafts [14–16]. In addition, intradermal suturing has not been found to increase surgical site infection in children [9, 10] or in adults [11], which further supports the use of absorbable sutures in open appendectomies. Treatment of the inflamed appendix is the surgeon's primary concern, but as the patient is left with a permanent scar after appendectomy, the best possible scar appearance should also be recognized as an important objective. Scar appearance can influence a patient's quality of life, playing an important role in body image, well-being, and social life [1]. Most appendectomy patients are young, which leads to even greater concern regarding the cosmetic outcome of the scar.

Scar area and width were significantly greater in the NA group. This could arguably be related to more precise epidermal alignment associated with intradermal suturing. On the other hand, the gradually absorbing intradermal suture might give longer-lasting support to the wound edges. There were more cases of wound infection (10 vs. 4 %) and dehiscence (12 vs. 0 %) in the NA group even though the rate of appendicitis complications was the same in both groups. Delayed primary healing is often associated with unsatisfactory cosmetic results, including wider and larger scars. However, the difference in scar appearance between the two groups cannot be explained solely by these events, since most wounds in both groups healed primarily.

The ECC values of hemoglobin and melanin favored intradermal suturing, although the difference was not statistically significant as regards hemoglobin, indicating that the scars were fully mature in both groups.

Our study has some limitations. Statistical significance might have been reached in a larger trial population as regards hemoglobin values and VSS results. Randomization and power calculation were performed during the first part of the study in terms of its primary end point. All patients for whom we had adequate data were subsequently invited to take part in cosmetic analysis. In case of absence from the first appointment, the invitation was repeated by phone to reach maximum participation. University Hospital regions in Finland are large in area. Hence, patients were offered compensation for travelling expenses if long distance was the reason for nonattendance. The follow-up point was set at 1 year to allow full maturity of the scars. The long interval between the operation and the follow-up may again have reduced the number of available patients and their willingness to participate in the follow-up. These factors may have had an impact on the relatively high dropout rate (28 %). Nevertheless, the dropouts were equally distributed between the groups and the results were statistically significant for the majority of scar assessments.

Conclusions

A better cosmetic result as regards appendectomy scars can be reached through the use of an intradermal absorbable continuous suture compared with transdermal nonabsorbable interrupted sutures. The method is safe as regards wound infections and saves a visit to an outpatient clinic for suture removal. We therefore recommend intradermal absorbable wound closure as a standard method for closing appendectomy wounds.

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ORIGINAL SCIENTIFIC REPORT

Severe Complications of Laparoscopic and Conventional Appendectomy Reported to the Finnish Patient Insurance Centre

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Abstract

Background Appendectomy is considered a safe operation, the related complications being minor. Negative exploration is an accepted procedure to avoid complications of appendicitis. Treatment with antibiotics is under debate as a primary treatment for appendicitis. The aim of this study was to collect and analyze detailed information on complications and morbidity related to appendectomy using the information of the nationwide Patient Insurance Association (PIA) database and to study the incidence of patient claims and compensated injuries related to appendectomy in Finland.

Methods Patients' claims from 1990 to 2010 were collected from the PIA register. Complications were classified using the accordion severity grading system. Severe complications were selected for more detailed analyses. Laparoscopic and open surgeries were compared. Factors related to compensated claims were assessed. For statistical analysis, Fisher's exact test, logistic multivariate regression, and the Mann–Kendall function were used.

Results Appendectomy complications leading to a patient insurance claim in Finland are rare (0.2 %). The rate of patients' claims after laparoscopic surgery was higher than after open surgery ($p < 0.001$), but the rate of compensated claims was equal. During the study period, complications after laparoscopic procedures more often led to additional surgery or organ failure ($p = 0.03$). Of the patients with a compensated injury, only 57 % had appendicitis. Preoperative computed tomography was used in only 6 % of these cases.

Conclusions Patient injuries and claims regarding severe complications after appendectomy are rare. The complications related to laparoscopic appendectomy were more severe than those of open surgery.

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Introduction

Appendectomy is the most common operation on the gastrointestinal tract (worldwide). The incidence of appendicitis is roughly 20/10,000 persons per year and slowly declining [1–3]. Surgery (either open or laparoscopic) is the gold standard for the treatment of acute appendicitis [4–6]. Recent prospective studies challenge surgery as the primary treatment for appendectomy and suggest that antibiotics could be the first-line treatment for most adult patients with uncomplicated appendicitis [7–9].

The burden of surgery in general is recognized. Yet, appendectomy has been considered a safe operation with low complication and mortality rates. Negative appendectomies following clinical misdiagnosis have been considered acceptable to avoid perforations and abscesses due to delayed surgery [10, 11]. As the diagnostic accuracy has improved due to the increasing use of ultrasound (US), computed tomography scans (CT), and magnetic resonance imaging (MRI), explorative surgery has been strongly questioned, especially under special conditions such as pregnancy [12–14].

Most studies concerning the complications and mortality after appendectomy focus on comparing the options of surgical treatment or, more recently, conservative versus operative treatment [4, 8, 15]. There are only a few register studies concerning the details or incidence of mortality and complications after appendectomy. These studies reported that negative appendectomies and comorbidity are associated with higher postoperative mortality and that the incidence of complications after appendectomy is growing. They also suggested that laparoscopy may have higher mortality rates than suggested in earlier studies [16, 17]. Another study reported that litigations after appendectomy have to do with failures in surgery, delays in surgery, and misdiagnosis [18]. These studies were impaired by the lack of national registers.

Hence, our aim was to collect and analyze detailed information on complications and morbidity related to appendectomy by using information from the Patient Insurance Association's (PIA) database. To our knowledge, there are no studies on the patient insurance claims of appendectomy patients.

Methods

Data collection

Patient insurance is mandatory for doctors to be able to practice medicine in Finland. The PIA provides compensation for patients' injuries related to treatment in Finland. The patients make the claims, and the compensation does not require proof of guilt or malpractice, and health professionals thus feel comfortable advising patients to apply for compensation. The compensation is granted if there is a complication or failure of treatment, which leads to injury, or damage that might have been avoided by acting in another manner. The criteria of compensation are that the patient's treatment should meet the level of experienced specialist (main criteria) or in some cases, compensation can be warranted if the patient suffers an unexpectedly difficult injury after a complication that is considered inevitable (criteria of unbearable injury). The cases are evaluated by at least two independent specialists. Based on the recommendations of the specialists, the PIAs board makes the decisions on compensations. Approximately one-third of all applications lead to compensation on a yearly basis. The association's database is regarded as a reliable source of information on complications [19–21].

The PIA provides a database and medical records, which warranted researchers can access. After the necessary permissions had been achieved, the data collection was carried out in collaboration with PIA experts. We collected all applications for compensation regardless of whether the compensation was granted or not in order to include all complications (and morbidity). The search criteria were the diagnostic codes for appendectomy (ICD-9 6421; ICD-10 JEA00, JEA01) for patients operated on between Jan 1, 1990 and Dec 31, 2010. The PIA system requires a 3-year period in which time the claims must be reported. Hence, all information on appendectomy-related claims performed by the end of 2010 was available by the end of 2013. The total numbers of yearly operations was received from the National Institute of Health and Welfare.

A specific diagnostic code for laparoscopic appendectomy (LA) was introduced in 1996, and, consequently, the comparison between the open (OA) and the laparoscopic technique was possible after the year 1996. The rate of claims in the LA group was calculated in 5-year periods (1996–2000, 2001–2005, 2006–2010) to identify any detectable learning curve. The compensated claims were analyzed for each group, and hence, they mostly include failures of treatment and the most difficult injuries and thus describe better the overall result of the surgical treatment.

The complications were classified using the accordion severity grading system (ASGS), which was developed in 2009 and has since been used to compare and report postoperative complications [22–24]. The ASGS grades complications into six classes (introduced in detail in Table 1). The medical records of patients who died or suffered severe complications (ASGS 4–6) were selected for a more detailed analysis. The American Society of Anesthesiologists (ASA) grade 1–5 for assessing fitness for

Table 1 ASGS classification

ASGS grade	Description
1.	Treatment of complication requires only minor invasive procedure that can be done at the bedside, such as insertion of intravenous lines, nasogastric tubes, and drainage of wounds
2.	Complication requires pharmacological treatment with drugs other than allowed for minor complications, e.g. antibiotics
3.	No general anesthesia is required to treat complication, requires management by an endoscopic, interventional procedure, or reoperation without general anesthesia
4.	General anesthesia is required to treat complication. Alternately, single-organ failure has developed
5.	General anesthesia is required to treat complication and single-organ failure has developed. Alternately, multisystem organ failure (two or more) has developed
6.	Postoperative death occurred

anesthesia and surgery was registered to describe the comorbidity of patients.

The study was approved by the Ethics Committee of the University of Tampere (R12033).

Statistical analysis

Descriptive statistics are presented as percentages or mean values. The difference in ASGS severity between the OA and LA groups was analyzed with Fisher's exact test, combining ASGS 1–3 and ASGS 4–6. Logistic multivariable regression was built using compensation (yes/no) as a dependent variable. ASA (binary, 1–3 vs. 4–5), age (continuous), operation technique (binary, OA/LA), operating hospital (factorial, university/central/district), and appendicitis (binary, complicated/uncomplicated) were used as independent variables. Again, further modeling was done with two additional variables, operating time (binary, day 07 a.m.–10 p.m./night 10 p.m.–07 a.m.), and the operating surgeon (binary, resident/consultant with or without resident). This was done because these latter variables contained some missing information. The significance of the change in rate of laparoscopic claims during the study period was tested in R (Software environment for statistical computing and graphics, version 2.13.0, the R Foundation for Statistical Computing) with the "Mann–Kendall" function that tests for monotonic trend in a time series based on the Kendall rank correlation.

Results

During the study period, a total of 184,648 appendectomies were performed in Finland. There were 161,414 appendectomies as the main operation, 150,010 (93 %) of them being open and 11,250 (7 %) laparoscopic. The proportion of laparoscopic appendectomies increased during the study period. During the first whole year with a separate diagnostic code for LA (1997), 217 (3 %) laparoscopic operations were performed, whereas during the year 2010, 1453 (23 %) appendectomies were performed laparoscopically. At the same time, the number of appendectomies declined from over ten thousand to approximately 7000 operations over the last 5 years, including all appendectomies, and to approximately 6000 yearly operations when only appendectomies as a main operation are included. The popularity of laparoscopy is still increasing; the latest numbers from 2012 show that 37 % of all appendectomies in Finland are laparoscopic.

A total of 351 appendectomy-related claims were introduced to the PIA in 1990–2010. Ten claims were excluded from analysis as, upon closer inspection, the claims were related to either surgery other than appendectomy, or to failure in medical treatment, or to other treatment not related to appendectomy. Of the overall 341 appendectomy claims, 16 % concerned laparoscopic operations, while the percentage of laparoscopic operations out of all appendectomies during the study period was 7 %. Of the 341 claims that were included in the analysis, 39 % resulted in compensation (39 % in the OA and 35 % in the LA groups, respectively). Of all appendectomies performed, 0.2 % led to a claim (0.2 % in OA and 0.4 % in LA, $p < 0.001$).

The rate of laparoscopic claims declined during the study period (Table 2). The severity of complications differed between the OA and the LA group—in the LA group, ASGS 4–6 class included 48 % of the claims and, in the OA group, 30 % ($p = 0.03$). Only two deaths were reported, both of them in the OA group. There were 35 (12 %) claims that were based on failure in diagnosis and unnecessary surgery, or a delay in surgery, leading to prolonged recovery. However, these were not regarded as true complications. Of these claims, 56 % resulted in compensation. These cases could not be classified by the ASGS and were thus analyzed separately (Table 3). The detailed variety of complications is presented in Table 4. The most common complications were wound infection (27 %) in the OA group and bleeding (29 %) in the LA

Table 2 The percentage of claims after laparoscopic appendectomy (LA) in 5-year periods and *p* value calculated for declining trend

	Non-compensated claims	Compensated claims	All claims	Number of LAs
1996–2000	1.0 %	0.5 %	1.4 %	837
2001–2005	0.3 %	0.2 %	0.5 %	3438
2006–2010	0.2 %	0.1 %	0.3 %	6241
p value for declining trend	$p = 0.0085$	$p = 0.024$	$p = 0.013$	

Table 3 Claims classified according to ASGS, comparing open appendectomy (OA) and laparoscopic appendectomy (LA); number of patients and percentage for each group

Complication class	All *n* (%)	OA *n* (%)	LA *n* (%)
All claims	341	293 (86 %)	48 (14 %)
ASGS 1–3	192 (56 %)	167 (57 %)	25 (52 %)
ASGS 4–5	112 (33 %)	89 (30 %)	23 (48 %)
ASGS 6	2 (0.6 %)	2 (0.7 %)	–
Claims regarding misdiagnosis/delay in surgery	34 (10 %)	34 (12 %)	–

Table 4 Complications reported in all claims, comparing open appendectomies (OA) and laparoscopic appendectomies (LA); number of patients and percentage for each group

Complication	All ($n = 341$)	OA ($n = 293$)	LA ($n = 48$)
Wound infection	75 (22 %)	71 (27 %)	4 (8 %)
Intra-abdominal infection/abscess	46 (14 %)	36 (12 %)	10 (21 %)
Bowel perforation	33 (10 %)	27 (9 %)	6 (13 %)
Leakage of appendicle stump	11 (3 %)	9 (3 %)	2 (4 %)
Wound rupture/early hernia	10 (3 %)	10 (3 %)	–
Bowel obstruction	16 (5 %)	15 (5 %)	1 (2 %)
Bleeding	58 (17 %)	44 (15 %)	14 (29 %)
Pulmonary/venous embolus	4 (1 %)	4 (1 %)	–
Death	2 (<1 %)	2 (<1 %)	–
Other	51 (15 %)	40 (14 %)	11 (23 %)
Misdiagnosis	22 (6 %)	22 (8 %)	–
Delay in surgery	12 (4 %)	12 (4 %)	–

group. Wound infection was considered inevitable complication in most cases and led to compensation only if the patient did not receive the prophylactic antibiotics or the injury was unexpectedly difficult as gas gangrene, usually related to drainage of caecum with catheter, treatment that is no longer used.

There were 113 (33 %) severe complications (ASGS 4–6). Of these, 104 (92 %) patients' medical records were available for detailed analyses. The results are presented in Table 5. Of the severe complications, 54 % were compensated. The decision on surgery was mostly based on a clinical examination, and a preoperative CT scan was performed on only four patients (4 %). Appendicitis was found in 61 % of all patients, 48 % of these being uncomplicated (no perforation necrosis or abscess detected at the time of surgery by the operating surgeon), while 39 % had a perforation or necrosis and 13 % an abscess (complicated appendicitis: perforation, necrosis, or abscess at the time of surgery). Of the patients in the compensated claims group, only 57 % had appendicitis. The mean age of the patients suffering severe complications was 39 years in our study; on the other hand, the highest incidence of appendicitis is between the ages of 15–24 [1–3]. The mean of the ASA scores for the patients with complications was 1.5, indicating higher comorbidity of patients in the severe complication group as compared to a healthy person's ASA score of 1. Multivariate analysis showed no connection between compensated claims and the measured variants presented in Table 5, except for the length of hospital stay which had a positive correlation with compensated claims.

Discussion

In our study, we found that, according to the PIA register, severe complications leading to an insurance claim after an appendectomy are rare (0.2 %). Laparoscopic appendectomies more often led to an insurance claim when compared to open surgery ($p < 0.001$). Additionally, the complications related to laparoscopy were more severe. Only a few of the patients suffering from complications that led to a claim had undergone CT preoperatively, which relates to a high rate of misdiagnosis in this group.

There are only a few studies implicating the complications and mortality after appendectomy. The Swedish study presenting the causes of short-term mortality was large with a detailed analysis. However, the study period did not fully represent the current operative management, since the wide spreading of laparoscopy occurred later [16]. Studies on appendectomy complications are often challenging to design due to a lack of national registries.

The diagnosis of appendicitis is often based on a clinical examination, and typical appendicitis has signs that can be easily recognized. Diagnostic surgery has been accepted in patients with suspected appendicitis. This has been criticized in modern medicine [16]. Recent studies have shown

Table 5 Details of severe (ASGS 4–6) complications in groups of compensated claims (CC) and non-compensated claims (NC); mean values for age, ASA[a] score, and hospital days; number of patients and percentage for other variables

	All	CC	NC
Age mean (min–max)	39 (4.5–87)	41 (6–87)	37 (4.5–85)
ASA[a]	1.5 (1–5)	1.6 (1–5)	1.4 (1–4)
Hospital days mean (min–max)	24 (1–135)	29.6 (2–135)	18.8. (1–64)
Patients (*n*)	104	54	50
Sex (male)	59 (57 %)	28 (52 %)	31 (62 %)
University hospital	29 (29 %)	14 (26 %)	15 (30 %)
Central hospital	40 (38 %)	23 (43 %)	17 (34 %)
District hospital	35 (33 %)	17 (31 %)	18 (36 %)
Open technique	83 (80 %)	44 (81 %)	39 (78 %)
Laparoscopic technique	21 (20 %)	10 (19 %)	11 (22 %)
Appendicitis	63 (61 %)	31 (57 %)	32 (64 %)
Uncomplicated appendicitis	30 (48 %)	14 (45 %)	17 (53 %)
Perforated/necrotic appendicitis	25 (39 %)	15 (48 %)	9 (28 %)
Abscess	8 (13 %)	2 (7 %)	6 (19 %)
Operating time (information available for *n* patients)	70 (67 %)	42 (78 %)	28 (56 %)
Day 7 a.m.–10 p.m.	45 (64 %)	27 (64 %)	18 (64 %)
Night 10 p.m.–7 a.m.	25 (36 %)	15 (36 %)	10 (36 %)
Surgeon (information available for *n* patients)	94 (90 %)	52 (96 %)	42 (84 %)
Resident	44 (47 %)	26 (50 %)	18 (43 %)
Consultant	42 (45 %)	19 (37 %)	23 (55 %)
Resident and consultant	8 (8 %)	7 (13 %)	1 (2 %)

[a] American society of Anesthesiologists grade (1–5) for assessing fitness for anesthesia and surgery; ASGS Accordion Severity Grading system (1–6) to classify complication; no perforation, necrosis or abscess detected at the time of surgery

that CT is a sensitive and specific tool in diagnosing appendicitis [13]. The studies comparing surgical and antibiotic treatment use CT routinely to identify uncomplicated appendicitis, which was an inclusion criterion for the study [8, 9]. In our study, only 61 % of the patients suffering from severe complications (ASGS 4–6) had appendicitis. Therefore, 39 % of these patients had undergone an unnecessary appendectomy. Only 4 % of the patients had undergone CT imaging preoperatively. In the group of compensated claims, the rate of appendicitis was even lower. The experts deciding on the compensation mostly accepted the diagnosis based on a clinical examination, but in a few cases, one of the reasons for compensation was unnecessary surgery. These results may also indicate that severe complications are more often related to unnecessary surgery.

Some complications might have been avoided by better preoperative diagnostics, especially in elderly patients with comorbidities. The study by Bliss and co-workers also found that aging and comorbidities relate to an increasing incidence of complications [17]. On the other hand, in our study, 55 % of the patients who had appendicitis in the compensated claims group had a perforation, necrosis, or abscess, and only 45 % had uncomplicated appendicitis.

The number of severe complications (ASGS 4–6) was higher in claims concerning laparoscopy. In addition, the nature of typical laparoscopic complications in this study (bleeding and intra-abdominal abscess) more often led to a reoperation and/or organ failure than the most common complication of open appendectomy, namely wound infection. Laparoscopy is an advanced surgical technique with a demanding learning curve [25]. When the surgeon starts performing laparoscopic appendectomies, thorough training should be carried out to avoid the complications related to an individual's learning curve. Laparoscopic operations were introduced and increased over the study period, and the severity of complications may reflect the learning curve. The percentage of claims in laparoscopic surgery was higher compared to open surgery during the study period. We looked at the percentage of claims in laparoscopic appendectomies in 5-year periods and found a trend towards decreasing claims during the two decades of the study period. This reflects the overall learning curve of a novel technique. Surgeons' inexperience in evaluating the appearance of the appendix in laparoscopy may explain the high rate of healthy appendixes removed. Had the laparoscopy been used as a diagnostic

tool and innocent appendixes left in place, some of the complications may have been avoided.

The PIA's register in Finland collects patient claims concerning health care and thus provides detailed information on complications. It is considered a reliable source of information on severe complications, but it does not present the incidence of complications and does not include all complications due to a demand of activity on patients' behalf and health care personnel advising patients. Only two deaths were reported to the PIA out of more than 180,000 operated patients. Hence, post-appendectomy mortality cannot be determined using data from the registers of the PIA. This can be considered a limitation of our study. The strength of this study was the long period of 21 years for which we were able to collect detailed information on complications after appendectomies in Finland. The period included the beginning of the era of laparoscopic appendectomies, giving us the opportunity to analyze the complications of a novel technique.

Conclusion

Appendectomy is a safe operation that rarely leads to patient insurance claims, regardless of the technique. Complications after LA lead to organ failure and/or demand reoperations more often than those related to open surgery. Similarly, diagnostic operations may result in severe complications; consequently, better preoperative diagnostics could decrease complications and patient insurance claims.

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Compliance with ethical standards

Conflict of interest None of the authors have any conflicts of interest.

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