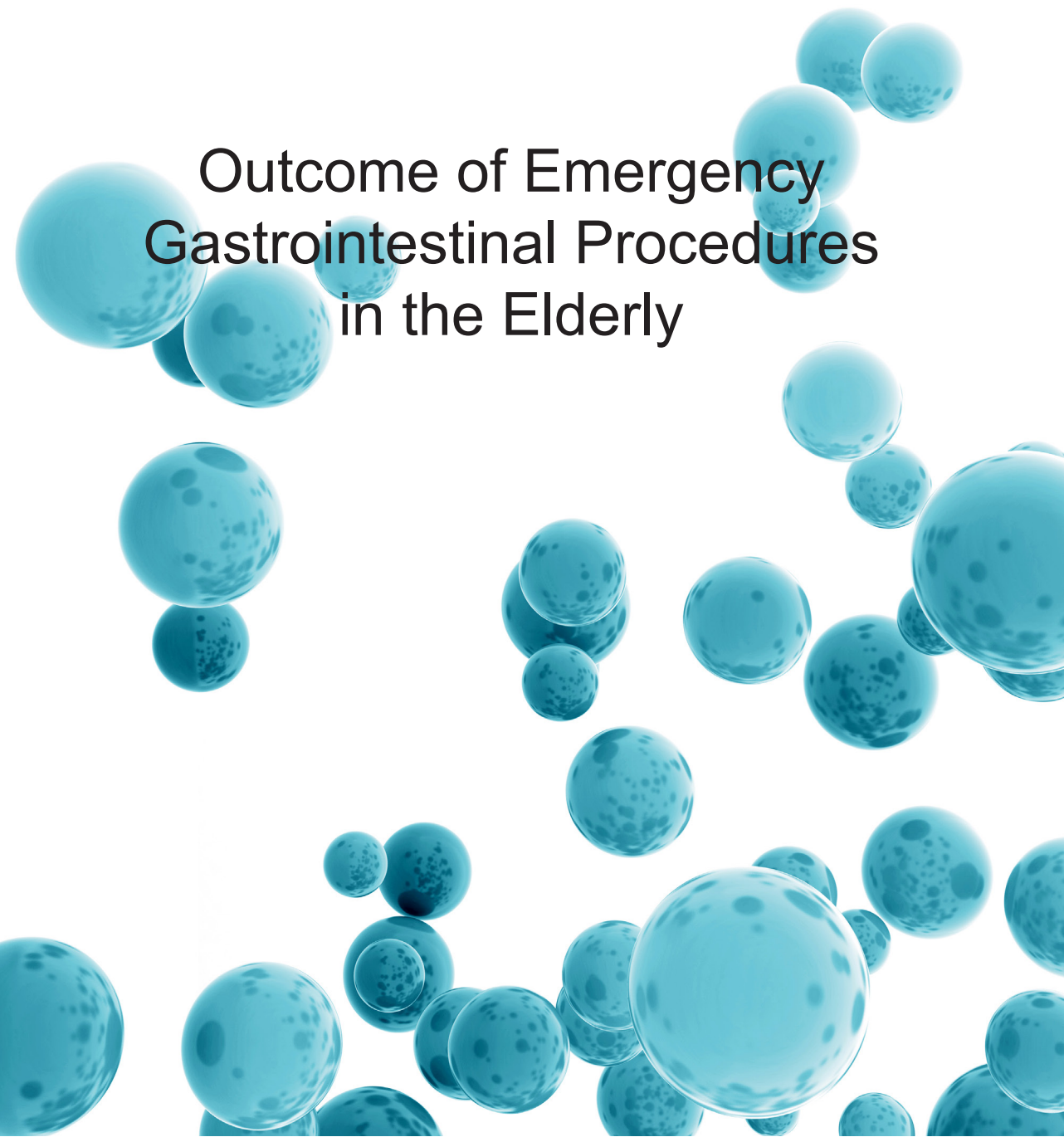
Acta Universitatis Tamperensis 2250

MIKA UKKONEN

Outcome of Emergency Gastrointestinal Procedures in the Elderly



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Outcome of Emergency Gastrointestinal Procedures in the Elderly

ACADEMIC DISSERTATION
To be presented, with the permission of
the Board of the School of Medicine of the University of Tampere,
for public discussion in the small auditorium of building M,
Pirkanmaa Hospital District, Teiskontie 35, Tampere,
on 3 February 2017, at 12 o'clock.

UNIVERSITY OF TAMPERE

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Acta Universitatis Tamperensis 2250
Tampere University Press
Tampere 2017

UNIVERSITY
OF TAMPERE

ACADEMIC DISSERTATION
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Acta Universitatis Tamperensis 2250
ISBN 978-952-03-0326-6 (print)
ISSN-L 1455-1616
ISSN 1455-1616

Acta Electronica Universitatis Tamperensis 1751
ISBN 978-952-03-0327-3 (pdf)
ISSN 1456-954X
http://tampub.uta.fi

Suomen Yliopistopaino Oy – Juvenes Print
Tampere 2017

441 729
Painotuote

"The more sand that has escaped from the hourglass of our life, the clearer we should see through it"

Richter

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ABSTRACT

The elderly are more likely than younger adults to experience gastrointestinal emergencies. As the normal aging-related physiological changes and comorbidities reduce older people's tolerance of acute illness and associated treatments, they are more susceptible to postoperative adverse events. In this thesis the focus is on gastrointestinal emergencies and associated outcomes in elderly patients.

First we investigated indications and safety of emergency alimentary tract related surgery in the elderly. The most common reason for surgery was acute cholecystitis. Emergency gastrointestinal operations were still associated with significant morbidity and mortality. Regardless of novel diagnostic and therapeutic techniques, the outcome has not improved at a similar pace. Older age, concomitant conditions and low body-mass index were among the risk factors for poor outcomes. Infections, including postoperative pneumonia and sepsis, accounted for the majority of postoperative deaths.

Sepsis in gastrointestinal surgery in the elderly was also examined. Acute cholecystitis was the most common reason for the surgery in this patient population. While sepsis was a rare event in surgical patients, it was found to be associated with excessive mortality. The mortality remained high through one-year follow up after successful treatment of the infection. The intensive care unit used scoring systems predicted higher mortality.

Because elderly patients are more prone to gallstone disease and its complications, we also focused on emergency endoscopic retrograde cholangiopancreatography (ERCP) in the elderly. Biliary obstruction caused by bile duct stones was the most common indication for the procedure. There were no procedure-related deaths, and complications occurred less often than has been previously reported in adult population in general. Chronic obstructive pulmonary disease and difficult cannulation were independently associated with increased risk of complications.

Finally we studied surgical outcomes in elderly patients undergoing surgery for acute cholecystitis. The occurrence of postoperative complications or death after surgery was more often reflecting the severity of pre-existing diseases than surgical technique, older

age or hospital type. However, there was a trend towards lower morbidity and mortality in patients undergoing laparoscopic surgery.

We conclude that 1) acute cholecystitis is the most common indication for emergency gastrointestinal surgery in the elderly and emergency surgery is still associated with significant morbidity and mortality, 2) both short and long-term outcomes are very poor in older patients with severe sepsis related to alimentary tract surgery, 3) biliary obstruction caused by bile duct stones is the most common indication for acutely performed ERCP in the elderly, and the procedure can be performed safely and efficaciously on older patients and 4) older age, hospital type and surgical technique were not independently associated with poorer outcomes after emergency cholecystectomy, whereas severity of concomitant conditions and acute condition itself predicted morbidity and mortality.

TIIVISTELMÄ

Väestön ikääntymisen johdosta vanhusten osuus väestössä kasvaa ja samalla päivystysresurssien tarve lisääntyy. Vatsaelinkirurgisiin päivystystilanteisiin liittyy merkittävä kuolleisuus- ja komplikaatioriski sekä kustannukset, jotka ovat suurempia iäkkäillä potilailla. Tutkimusnäyttö uusien hoitomenetelmien soveltuvuudesta tälle potilasryhmälle on osin puutteellista. Selvitimme tässä väitöskirjatutkimuksessa vatsaelinkirurgisten päivystysleikkausten yleisyyttä ja tuloksia, tehohoitoa vaatineen vaikean sepsiksen ennustetta, endoskoopppisen retrograadisen kolangiopankreatografian (ERCP) tuloksia sekä sappileikkausten jälkeistä toipumista vanhusväestössä.

Osoitimme, että akuutti sappirakon tulehdus on yleisin syy päivystysleikkauksiin yli 65-vuotiailla potilailla. Huolimatta viime vuosien teknisestä kehityksestä (mm. akuutin hoidon resursointi, laadukkaammat ja paremmin saatavissa olevat kuvantamispalvelut sekä entistä parempi tehohoidon laatu) olivat kirurgisen hoidon tulokset vastaavanlaiset kuin on raportoitu 1980–1990-luvuilla. Vanhusten leikkaushoitoon liittyy siis edelleen merkittävä komplikaatioriski ja kuolleisuus, jota lisää ikääntymisen lisäksi vielä merkittävämmin potilaan vaikeat perussairaudet ja aliravitsemus. Infektiot olivat yleisin syy leikkauksien jälkeisiin kuolemiin.

Seuraavana tutkimme tehohoitoa vaatineita vaikeita leikkauksen jälkeisiä systeemisiä infektioita vanhuspotilailla. Osoitimme vatsaelinkirurgiaan liittyvän sepsiksen olevan yhteydessä merkittävään kuolleisuuteen, joka oli korkea paitsi sairaalahoitoajan, niin se myös pysyi toipuneilla ja kotiutuneilla potilailla korkeana koko vuoden seuranta-ajan. Akuutti sappirakon tulehdus oli yleisin syy leikkaukseen myös tässä aineistossa. Korkea ikä ja aiemmat perussairaudet lisäsivät kuolleisuutta. Tehohoidossa käytettävät riskipisteytykset korreloivat iäkkäiden potilaiden ennusteeseen.

Koska komplisoitunut sappikivitauti oli yleinen syy päivystystoimenpiteisiin iäkkäillä, halusimme tutkia myös sen endoskooppisia hoitoja. Selvitimme päivystyksellisesti tehdyn ERCP:n tuloksia iäkkäillä. Sappikivitaudin aiheuttama sappitietukos oli yleisin syy toimenpiteeseen. ERCP osoittautui tehokkaaksi sappitietukoksen sekä myös leikkausten jälkeisten sappitievaurioiden hoidossa. Toimenpide oli vähintäänkin yhtä

turvallinen vanhuksilla kuin mitä aiemmin on raportoitu aikuisilla potilailla. Komplikaatioriskiä lisäsivät vaikea kanulaatio ja keuhkoahtaumatauti.

Viimeisenä kartoitimme akuutin sappirakon tulehduksen leikkaushoidon tuloksia iäkkäillä potilailla. Yllättäen korkealla iällä tai valitulla leikkaustekniikalla ei ollut tilastollisesti merkittävää vaikutusta tuloksiin. Vaikkei eroa saavutettu, oli erityisesti entuudestaan huonokuntoisimpien tähystysleikkauksen läpikäyneiden potilaiden ennuste parempi kuin avoleikkauksella hoidettujen potilaiden. Potilaan aiemmat vaikeat perussairaudet tai hankala tulehdustilanne olivat ennusteellisia sekä korkeammalle komplikaatioriskille että kuolleisuudelle.

Yhteenvetona voidaan todeta, että komplisoitunut sappikivitauti on yleisin syy päivystysleikkauksiin iäkkäillä potilailla. Leikkauksiin liittyy merkittävä komplikaatioriski ja kuolleisuus, joka ei ole huomattavasti laskenut viime vuosina. Postoperatiivinen sepsis on varsin harvinainen tila, johon liittyy erittäin huono sekä lyhyen että pitkän aikavälin ennuste. Sappitiekivitauti on yleisin syy vanhusten päivystykselliseen ERCP:n ja se on tehokas ja turvallinen toimenpide myös iäkkäille potilaille. Potilaan aiemmat vaikeat perussairaudet tai vaikea akuutti sairaustilanne vaikuttivat ennusteeseen akuutin sappirakon tulehduksen jälkeisessä toipumisessa. Vaikka leikkaustekniikan valinnalla ei saavutettu tilastollisesti merkittävää eroa, oli erityisesti tähystysleikkauksen läpikäyneillä entuudestaan vaikeasti sairailla potilailla ennuste parempi.

LIST OF ORIGINAL PUBLICATIONS

I Emergency Abdominal Operations in the Elderly: A Multivariate Regression Analysis of 430 Consecutive Patients with Acute Abdomen. Ukkonen M, Kivivuori A, Rantanen T, Paajanen H. 2015. World J Surg. 2015; 39:2854-2861.

II Severe Sepsis in Elderly Patients Undergoing Gastrointestinal Surgery – a Prospective Multicenter Follow-up Study of Finnish Intensive Care Units. Ukkonen M, Karlsson S, Laukkarinen J, Rantanen T, Paajanen H; Finnsepsis Study Group. J Gastrointest Surg. 2016; 20:1028-33.

III Safety and Efficacy of Acute Endoscopic Retrograde Cholangiopancreatography in the Elderly. Ukkonen M, Siiki A, Antila A, Tyrväinen T, Sand J, Laukkarinen. J. Dig Dis Sci. 2016;61(11):3302-3308.

IV The impact of hospital type, surgical technique, ASA score and patient's age on surgical outcomes in elderly patients undergoing emergency cholecystectomy. Kivivuori A, Ukkonen M, Suuronen S, Rantanen T, Paajanen H. Submitted

ABBREVIATIONS

APACHE	Acute Physiology and Chronic Health Evaluation score
ARDS	Acute respiratory distress syndrome
ASA	American Society of Anesthesiologists
BMI	Body-mass-index
COPD	Chronic obstructive pulmonary disease
ERCP	Endoscopic retrograde cholangiopancreatography
ICU	Intensive care unit
MODS	Multiple Organ Dysfunction Score
POSSUM	Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity.
qSOFA	Quick Sequential (Sepsis-related) Organ Failure Assessment
SAPS	Simplified Acute Physiological Score
SIRS	Systemic Inflammatory Response Syndrome
SOFA	Sequential Organ Failure Assessment

1 INTRODUCTION

Abdominal emergencies cause an indisputable burden on the health care services, and the elderly are at highest risk of these conditions (Scott et al. 2016; Gale et al. 2014). Consequently, as the world population is ageing, even greater numbers of older patients are likely to be admitted to emergency departments. As the elderly are at higher risk for associated morbidity and mortality, and a major cause of overall healthcare costs, the pressure is increasing to improve the quality of these patients' care (Bruns et al. 2015; Havens et al. 2015; Ogola et al. 2015).

Older age should not be a contraindication for surgery. Concomitant diseases, ongoing medications, surgical technique and the acute condition itself all contribute to poor outcomes. The prevalence of comorbidities increases with age, as does the number of drugs used to treat these conditions. However, as there is a vast heterogeneity in the older population, chronological age may seem somewhat inappropriate for defining the elderly. Yet, no other widely accepted definition is available, and therefore the age at which a person becomes eligible for retirement has been used as a definition in many studies. Subsequently the chronological age of 65 years or more is the most widely adopted for research (WHO 2012).

Postoperative complications are a strong predictor of poor outcomes in geriatric patients. In addition to known comorbidities, the elderly often have unknown conditions that render their care more complex. While these previously undiagnosed conditions may be difficult to recognize in the acute phase prior to emergency surgery, current risk assessment scores offer practical and replicable means for predicting the outcome in older patients undergoing surgery according to known conditions (Oliver et al. 2015; Rix and Bates 2007). If the decision-making is not standardized, it involves individualized preconceptions and subsequently lacks both objectivity and consistency. Despite this, none of the tools developed have been widely adopted into routine practice. Some certain limitations do exist, which have decreased the applicability of existing systems.

Improving outcomes in emergency surgery is particularly challenging in the elderly, and the growing geriatric population will pose a worldwide challenge. The need to better understand acute presentations and outcomes will be paramount to ensure optimal care. For these reasons this PhD thesis is concerned with emergency gastrointestinal operations in the elderly. The purpose was to evaluate the prevalence of gastrointestinal emergencies and septic postoperative complications in elderly patients. A further aim was to examine general outcomes of emergency alimentary tract surgery as well as modern treatments of complicated gallstone disease.

2 REVIEW OF THE LITERATURE

2.1 Gastrointestinal emergencies in the elderly

Gastrointestinal emergencies are a major cause of all emergency admissions and an important cause of all healthcare costs (Scott et al. 2016; Ogola et al. 2015; Gale et al. 2014; Stewart et al. 2014). These admissions increase annually, and in the USA, for example, the costs already exceed those of treating diabetes, myocardial infarctions and new cancer diagnoses (Paul 2016; Ogola et al. 2015). Consequently, together with the expected upsurge in the older population there will be mounting pressure on health care systems and emergency services in particular.

2.1.1 Emergency surgery and endoscopy in the elderly

According to earlier studies, the typical indications for emergency alimentary tract surgery in the elderly have included acute cholecystitis, acute appendicitis, intestinal obstruction and incarcerated hernias (Lees et al. 2015; Kärkkäinen et al. 2015; Ingraham et al. 2011; Miettinen et al. 1996; Kettunen et al. 1995; Telfer et al. 1988). Moreover, the vast majority of cancers are diagnosed in older patients (López-Otín et al. 2013), and are a common reason for emergency operations. Acute mesenteric ischemia is more prevalent among geriatric patients, while it is almost non-existent in younger adults (Kärkkäinen et al. 2015). Whereas alimentary tract emergencies are more frequent as age increases, the incidence of appendicitis is considered to be lower in older patients (Anderson et al. 2012; Ilves et al. 2011). The distribution of emergency conditions and surgical care is age dependent, as illustrated in Table 1. Overall, these typical emergency operations in older patients account for a significant proportion of all gastrointestinal operations (Scott et al. 2016).

Table 1. Distribution (%) of emergency gastrointestinal operations in the elderly (65 years or more) and in younger patients (According to Ingraham et al. 2011)

Procedure	Aged ≥ 65 years n=17,806	Aged < 65 years n=50,197
Partial or total colectomy	28.8%	9.7%
Appendectomy	13.7%	56.7%
Small bowel resection	11.8%	4.1%
Cholecystectomy	9.2%	8.5%
Hernia repair	8.7%	5.1%
Explorative laparotomy	8.3%	3.9%

A similar increasing trend with older age can be observed in endoscopic procedures (Jafri et al. 2010), where typical indications for emergency endoscopy have included upper and lower gastrointestinal bleeding, bowel and biliary obstruction. The elderly are more likely to suffer from all these conditions than are younger adults (Hreinsson et al. 2013; Ahmed and Stanley 2012; Enochsson et al. 2010; Festi et al. 2008; Yachimski and Friendman 2008; Siegel and Kasmin 1997; Rockall et al. 1996). For example, in octogenarians the risk of upper gastrointestinal bleeding is almost 20-fold compared to that among patients aged less than 30 years (Hreinsson et al. 2013). Likewise, the mean age of patients undergoing ERCP in a Swedish nationwide registry study was 68 years (Enochsson et al. 2010). Typical indications for this procedure (i.e. biliary obstruction caused by malignancies or gallstones) are more common among the elderly (Festi et al. 2008; Siegel and Kasmin 1997).

2.2 The role of ageing in the healing process

Ageing is an inevitable progressive process that causes structural and functional changes in all organ systems. Consequently it has a significant impact on the normal healing process. In addition to age, each individual's genetic background, lifestyle and environment play a role in the ability to recover.

2.2.1 Circulation, perfusion and hypoxemia

Ageing causes changes in both the cardiovascular and pulmonary system. Due to changes in the cardiovascular system, older patients are at increased risk of chronic cardiac diseases (e.g. heart failure and cardiac arrhythmias), the physiological capacity to deal with cardiac stress is decreased and the effectiveness of repair processes from ischaemic damage are reduced (Epstein et al. 2012; North and Sinclair 2012; Strait and

Lakatta 2012; Kovacic et al. 2011). In the pulmonary system, gas exchange is impaired and both chest wall compliance and respiratory muscle strength are reduced, which in turn leads to an increase in the work of breathing (Sharma and Goodwin 2006). Consequently, an increased metabolic demand may more often lead to respiratory fatigue or even to respiratory failure. Alterations in the swallowing response and in protective cough make the elderly more prone to aspiration and pneumonia (Ebihara et al. 2012). In addition, higher sensitivity to respiratory depressants makes the elderly more prone to unwanted events related to anaesthesia (Sprung et al. 2006).

2.2.2 Inflammation and infection

Ageing is accompanied by substantial changes in the immune system (Rymkiewicz et al. 2012). While many elements degenerate, some are preserved or even enhanced; these inappropriate elevations, decreases and dysregulation of immune response cause increased risk of infections and lead to more severe presentations (Montgomery and Shaw 2015). Altered endocrine function, comorbidities (e.g. diabetes and peripheral vascular disease) and physiological states (e.g. malnutrition) have additional negative influence on the immune function (Giefing-Kröll et al. 2015; Montgomery and Shaw 2015; Pellegrina et al. 2015). Chronic, low-grade systemic inflammation is often present, and may play a role in failure to resolve immune response (Pawelec et al. 2014; Chung et al. 2009). This may subsequently lead to collateral tissue damage (Pawelec et al. 2014). In addition, diagnosing infections may be difficult, as the elderly often present with signs and symptoms different from those encountered in younger adults (Duin 2012).

2.2.3 Wound healing

Normal wound healing is an innate immune response to tissue injury intended to restore tissue integrity (Shaw and Martin 2009). It starts immediately after the injury with haemostasis, followed by three overlapping phases, i.e. inflammation, proliferation and maturation. While the elderly go through the same phases, they have a slower healing process affecting all these phases (Bentov and Reed 2014; Sgonc and Gruber 2013). In addition to normal aging related changes, various factors with a negative impact on wound healing manifest more frequently among the elderly. These include some concomitant conditions (e.g. diabetes, peripheral arterial disease and chronic venous insufficiency), some ongoing medications (e.g. corticosteroids and chemotherapy), malnutrition, decline in the production of sex steroid hormones, psychological stress and immobilization (Sgonc and Gruber 2013).

2.3 Role of medication in the healing process

Many medications may inhibit the normal healing process and contribute to the development of postoperative complications. Typical examples include glucocorticoid steroids, non-steroidal anti-inflammatory drugs and chemotherapeutic or immunomodulating drugs (Kotagal et al. 2016; Hakkarainen et al. 2015; Busti et al. 2005). Interruption of ongoing anticoagulation therapy increases the risk of thromboembolic events, while continuing is linked with higher risk of perioperative bleeding (Gallego et al. 2012). Additionally, multiple medications (i.e. sedative hypnotics, antiarythmatics, lithium and scopolamine) have been associated with specific postoperative adverse events, such as the development of delirium (Alagiakrishnan and Wiens 2004). Overall, older patients are particularly susceptible to medication-related problems not only because they take medications more often than younger patients, but also because normal ageing-related changes have a negative impact on pharmacokinetics and drug metabolism (Klotz 2009). Concomitant diseases and polypharmacy increase the risk of drug-related problems even further (Klotz 2009).

2.4 Age-related morbidity and mortality after endoscopic and surgical procedures

The association between emergency surgery and postoperative morbidity and mortality in the elderly has been comprehensively documented in the literature (Shah et al. 2015; Sheetz et al. 2013; Symons et al. 2013; Saunders et al. 2012; Akinbami et al. 2011; Bentrem et al. 2009; Massarweh et al. 2009; Turrentine et al. 2006). Endoscopy, on the contrary, is considered to be relatively safe, with no greater risk than in younger adult patients undergoing similar procedures (Jafri et al. 2010). Earlier studies have reported 44–53% overall morbidity and 12–16% mortality in elderly patients after emergency gastrointestinal surgery (Lees et al. 2015; Rangel et al. 2015; Fukuda et al. 2012; Ingraham et al. 2011), while in endoscopy the morbidity has been around 1.6–7% and the mortality less than 1% (Garcia et al. 2016; Finkelmeier et al. 2015; Day et al. 2014; Day et al. 2011; Clarke et al. 2001). However, risks vary widely between procedures performed, as illustrated in Table 2.

Table 2. Postoperative outcomes after emergency gastrointestinal operations in the elderly (including studies reporting both morbidity and mortality in patients aged 65 years or more)

Procedure	n	Morbidity	Mortality	References
Cholecystectomy	679 (68–395)	10% (4–13%)	1.2% (0–2.0%)	Lee et al. 2015; Yetkin et al. 2009; Bingener et al. 2003; Tagle et al. 1997
Appendectomy	6226 (53–3335)	17% (9–26%)	1.4% (0–1.8%)	Kim et al. 2011; Paranjape et al. 2007; Harrell et al. 2006; Wang et al. 2006
Hernia repair	332 (143–189)	34% (25–43%)	5% (4.9–5.0%)	Alvarez et al. 2003; Kulah et al. 2001
Bowel resection	460 (105–355)	19% (17–25%)	16% (16–17%)	Modini et al. 2012; Pavlidis et al. 2006
ERCP	1796 (41–728)	5% (2–11%)	0.6% (0–3.1%)	Finkelmeier et al. 2015; Grönroos et al. 2010; Lukens et al. 2010; Hu et al. 2009; Fritz et al. 2006; Katsinelos et al. 2006; Köklü et al. 2005

2.4.1 Infectious complications

Postoperative infections may be a continuation of the acute illness itself, or they may be related to the care of this condition. Infections are characteristic in surgical emergencies (McCoy et al. 2015), while after endoscopy clinically relevant infections are rare (Kovaleva et al. 2013). Transient bacteraemia may be present, but it rarely has any significant consequences.

Most surgical infectious complications are local, superficial and wound related, rarely require invasive therapies, and they do not have significant influence on the recovery of the patient. Higher frequency of surgical site infections in elderly adults may be secondary to comorbidities and ageing related immunological changes than older age itself (Anderson et al. 2014). While these infections have been reported to have a negligible impact on mortality (Scarborough et al. 2016; McCoy et al. 2015; Sørensen et al. 2005), they are a significant reason for hospital readmissions, prolonged hospital stay and increased costs of care (Jenks et al. 2013; Shepard et al. 2013).

Systemic infections occur less frequently, but are more often associated with poorer outcomes. The incidence increases in the elderly, and older age is among the well-identified risk factors for higher mortality (Bouza et al. 2016; Vogel et al. 2010; Martin et al. 2006). For example, in a longitudinal observational study of more than 10 million sepsis patients, elderly individuals accounted for only 12% of the population and 65% of all sepsis cases (Martin et al. 2006). While some studies have reported a decreasing

trend in case-fatality rates, mortality is still reported to exceed 40% in older patients (Bouza et al. 2016). Mortality is considered to be even higher if sepsis is accompanied by organ failure (severe sepsis) or septic shock (Angus and Poll 2013). However, according to a recent consensus statement, the old term severe sepsis no longer exists as a concept, there is simply sepsis (Singer et al. 2016). The new diagnostic criteria rely on known or suspected infection with associated organ failure. In addition to high mortality, the costs of sepsis care are considerable throughout the entire care pathway, and its significance in overall healthcare costs is well-recognized (Lagu et al. 2012).

2.4.2 Pulmonary complications

Ageing-related physiological changes and concomitant conditions make the elderly prone to postoperative pulmonary complications. Consequently these adverse events are among the most common complications in both surgical and endoscopic procedures (Travis et al. 2012; Smetana et al. 2006). The occurrence and severity of these events ranges widely and the aetiology is multifactorial, as illustrated in Table 3. Most of these events are mild (e.g. changes in oxygen saturation during anaesthesia and postoperative atelectasis) and have no relevant impact on recovery. However, even a minor incident may deplete already limited functional reserves in a vulnerable patient and subsequently lead to exacerbation of pre-existing pulmonary disease and to other events (Magnusson and Spahn 2003).

Severe pulmonary complications (e.g. pneumonia, respiratory failure and acute respiratory distress syndrome) occur less often, but have more drastic consequences with the associated mortality in elderly patients exceeding 50% in some conditions (Scarborough et al. 2016; Kim et al. 2015; Stefan et al. 2013; Eachempati et al. 2007; Chastre and Fagon 2002). Postoperative pneumonia is considered to have the greatest overall impact as it is relatively common and exhibits a strong association with postoperative deaths in all surgical patients but especially among the elderly (Scarborough et al. 2016; McCoy et al. 2015). As pneumonia is relatively common and associated with significant costs, its overall healthcare impacts are undeniably significant (Thompson et al. 2006).

Table 3. Postoperative pulmonary complications; definitions and possible aetiologies

Complication	Definition	Aetiology	Reference
Atelectasis	Collapse or closure of a lung, resulting in reduced oxygen exchange	Multifactorial; compression atelectasis, absorption atelectasis, loss-of-surfactant atelectasis	Magnusson and Spahn 2003
Pneumonia	Infection / inflammation of lung tissue	1) Ventilator associated; 2) Aspiration in non-ventilated patients; 3) Oropharyngeal bacterial colonization of the lungs in non-ventilated patients	Kikawada et al. 2005; Marik and Kaplan 2003; Marik 2001
Respiratory failure	Cannot to be extubated within 48h of surgery	1) Chronic heart failure and pulmonary oedema (most commonly in the elderly); 2) Pneumonia; 3) Exacerbation of chronic lung disease	Delerme and Ray 2008; Ray et al. 2006
ARDS	Widespread inflammation of lungs	Many causes, although sepsis and reperfusion syndrome most commonly	Eachempati et al. 2007

2.4.3 Cardiovascular complications

An acute illness, invasive therapies and postoperative complications may result in haemodynamic and cardiac stress, which may further expose an elderly patient to adverse cardiac events (Table 4). These events usually occur in patients with pre-existing systemic cardiovascular diseases (Kristensen et al. 2014). Therefore it is not surprising that the elderly, who more often suffer from these conditions, are at higher risk. However, even in healthy older patients, the normal ageing-related physiological changes decrease the functional capacity to recover from acute homeostatic changes. Consequently, acute stress may lead to exacerbation of pre-existing chronic disease or precipitate a new cardiovascular event. The clinical consequence of cardiac events depends on multiple factors related to the complication, the patient and the disease. However, in general, all have a significant impact on recovery, and are a major cause of increased morbidity, mortality, prolonged hospital stay and increased costs (Devereaux and Sessler 2015; Bhave et al. 2012; Hammill et al. 2008; Brathwaite and Weissman 1998).

Table 4. Common postoperative cardiovascular complications

Complication	Aetiology	Reference
Atrial fibrillation	Multifactorial, may be triggered by perioperative increased sympathetic activity	Walsh et al. 2007; Hollenberg et al. 2000
Heart failure	1) Caused by other cardiac events; 2) Caused by volume overload; 3) Caused by major bleeding and anaemia	Johnson 2014
Acute myocardial infarction	1) Imbalanced oxygen supply and demand; 2) Thrombosis related to a vascular plaque	Landesberg et al. 2009

2.4.4 Postoperative delirium

Many pathways may precipitate delirium in a vulnerable patient, and older age and emergency surgery are both among the well-known risk factors (Scholz et al. 2016; Ansaloni et al. 2010). The occurrence of delirium varies widely, and as many as 17–25% of geriatric patients undergoing major abdominal surgery have been reported to suffer from postoperative delirium (Ansaloni et al. 2010; Brouquet et al. 2010; Morimoto et al. 2009). While the association between surgery and postoperative delirium may be well-recognized, the importance of endoscopy as a triggering mechanism has not been identified. It is likely that post-endoscopic delirium may more importantly reflect the severity of the disease necessitating the procedure than the procedure itself. In addition to being relatively common in older patients, delirium has been found to be associated with poor outcomes, including higher mortality, prolonged hospital stay, higher risk of institutionalization, functional decline and greater treatment costs (Dasgupta and Brymer 2014; Witlox et al. 2010).

2.4.5 Urinary tract related complications

Urinary tract related complications are typical in older patients (Baldini et al. 2009; Kheterpal et al. 2007). These events range from common and typically mild events (e.g. urinary retention and non-systemic urinary tract infection) to rare and serious events (e.g. septic urinary tract infections and acute kidney injury). However, even a minor event (e.g. urinary retention) may lead to severe presentations if not diagnosed in time (e.g. in the case of urinary retention to bladder distention or damage) (Baldini et al. 2009). Severe complications, including septic infections and acute kidney injury are associated with poor outcomes, including high mortality, prolonged hospital stay and increased risk of chronic kidney disease, including end-stage renal disease (Kerr et al. 2014; Bucaloiu et al. 2012; Coca et al. 2011; Tal et al. 2005).

2.4.6 Postoperative ileus and mechanical bowel obstruction

Postoperative bowel dysmotility may be caused by a functional (paralytic) or mechanical (obstructive) process. Functional disruption of the propulsive ability of the bowel (i.e. ileus) is considered normal after any gastrointestinal surgery and the risk is higher after emergency procedures (Chapuis et al. 2013). Ileus is a generally benign condition that resolves without serious sequelae within a few days after surgery (Vather et al. 2013). If paralysis is persistent, it must be differentiated from mechanical obstruction or from other postoperative complications mimicking ileus. Ileus is associated with prolonged hospital stay and increased costs of care (Doorly and Senagore 2012; Asgeirsson et al. 2010). In addition, persistent bowel dysmotility may worsen nutritional status. Therefore, it may play a role in the development of poor outcomes, particularly in older and critically ill patients, and especially if they are already malnourished (Havens et al. 2016; van Stijn et al. 2013).

2.4.7 Bleeding complications

Bleeding may be due to multiple causes, and while it often manifests during the operation, it may become evident postoperatively. Bleeding may be related to anticoagulative conditions including anticoagulant treatments. Given the increased use of these medications and the more common presentation of other risk adjusting conditions in elderly patients, the risk of bleeding complications is often higher (Kearon et al. 2012; Brotman and Jaffer 2008). Furthermore, balancing between adequate prophylactic anticoagulative therapy and the risk of bleeding in this group of patients may be difficult.

According to earlier studies 2-10% of older patients undergoing emergency alimentary tract surgery suffer from bleeding-related complications (Lees et al. 2015; Fukuda et al. 2012; Kettunen et al. 1995). In endoscopic procedures these complications are less common, and reportedly occur after less than 1% of procedures (Day et al. 2014; Day et al. 2012). Bleeding has been found to be among the complications with the greatest overall impact on surgical outcomes, as associated blood loss and anaemia are known to increase mortality (Scarborough et al. 2016; Spolverato et al. 2015; McCoy et al. 2015; Wu et al. 2007). Elderly patients often have limited reserves to cope with any acute condition, and therefore they are more prone to bleeding and anaemia associated mortality.

2.4.8 Thromboembolic complications

Postoperative thromboembolic complications may be arterial (e.g. stroke) or venous (e.g. deep vein thrombosis or its sequel pulmonary embolism) in origin. Both occur more often after emergency surgery, and the risk is also higher in older patients (Pannucci et al. 2014; Anderson et al. 2007; Inderbitzin et al. 2007; Caprini et al. 1991). Reported occurrence of venous thromboembolism after emergency surgery in the elderly is 2%, while 1% of these patients suffer from arterial events (Lees et al. 2015; Kettunen et al. 1995). Endoscopy, on the contrary, has not been identified as an independent risk factor for these events. Despite their relatively rare occurrence, thromboembolic events and especially arterial thromboembolism and pulmonary embolism have a significant socio-economic impact, and are among the complications exhibiting the strongest association with postoperative mortality (McCoy et al. 2015; Saltman et al. 2015; Kazaure et al. 2012; Ruppert et al. 2011).

2.4.9 Other surgical complications

Among the most serious postoperative complications is anastomotic leak. The risk is increased in patients undergoing emergency procedures (Bakker et al. 2014). While age itself may not be related to more frequent occurrence, comorbidities are often more common among the elderly and are accompanied by anastomotic healing problems (Bakker et al. 2014; Hermans et al. 2010). Furthermore, the elderly, and especially the elderly with multiple comorbidities, are at a higher risk of dying after anastomotic leak (Bakker et al. 2014).

2.4.10 ERCP-related complications

Like any invasive procedure, endoscopy carries a risk of post-operative complications. Although the risk is in general considered low, in ERCP complications occur more often than in any other routinely performed endoscopic procedure (Travis et al. 2012). Pancreatitis, bleeding, perforation and infection are typical adverse events of ERCP and a widely applied classification is used to define and grade these events (Table 5; Cotton et al. 1991). While the majority of these events have no serious impact on the outcomes, severe adverse events and deaths do occur (Testoni et al. 2010; Wang et al. 2006; Christensen et al. 2004; Vandervoort et al. 2002; Freeman et al. 2001).

Table 5. Definition and classification of post-ERCP complications (according to Cotton et al. 1991)

Complication	Mild	Moderate	Severe
Pancreatitis	Typical pain and serum amylase ≥ 3x normal 24 h after the procedure	4–10 day hospitalization	> 10 day hospitalization or invasive treatment
Bleeding	Clinical evidence of bleeding, anaemia, no transfusion	Transfusion ≤ 4 units	Transfusion > 5 units or invasive treatment
Perforation	Possible, or only slight leakage of fluid or contrast, treatable conservatively	4–10 day hospitalization	> 10 day hospitalization or invasive treatment
Infection	Clinical signs of cholangitis	≥ 3 day hospitalization or percutaneous intervention	Septic shock or surgery

Two reviews have so far published rates of post-ERCP complications in adult population (Silviera et al. 2009; Andriulli et al. 2007) and one in elderly patients (Day et al. 2014). According to these studies, pancreatitis is the most common complication after ERCP. Interestingly, it seems to occur less often in older than in younger patients. The occurrence ranges 3–7% in all adults (Silviera et al. 2009; Andriulli et al. 2007), and it is reported to be around 1.1–1.5% in the elderly (Day et al. 2014). Other ERCP-related complications are less common; for example the risks of post-ERCP infections, bleeding and perforation are estimated to be 1.6%, 0.8% and 0.4% respectively (Day et al. 2014). While the risk of post-ERCP pancreatitis is associated with younger age, no similar association with older age has been observed with other complications.

In addition to younger age, the rate of complications and the difficulty of the procedure are connected. When the endoscopy is difficult (i.e. cannulation takes longer time and multiple attempts are required) the complication rate is higher (Halttunen et al. 2014; Freeman et al. 2001; Freeman et al. 1996).

2.5 Assessing the severity of postoperative complications

The growing demand for operative treatment, rising costs of treatment, and variations in clinical practice increase the need to measure, improve and standardize the quality of care. Tools such as the Clavien-Dindo classification have been developed for estimating the severity of postoperative complications (Table 6; Dindo et al. 2004; Clavien et al. 1992). This classification is based on the therapy used to resolve a specific complication. Complications are graded from one to five; one being only a minor deviation from normal postoperative course and five the death of the patient.

Table 6. The Clavien-Dindo classification of surgical complications (According to Dindo et al. 2004)

Grade	Definition
I	Any deviation from the normal postoperative course without need for pharmacological treatment, or surgical, endoscopic and radiological interventions. ## Allowed therapeutic modalities are; use of antiemetics, antipyretics, analgesics, diuretics and electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside.
II	Requires pharmacological treatment with drugs other than those allowed for grade I complications. ## Blood transfusions and parental nutrition also included.
III	Requires surgical, radiological or endoscopic intervention ## IIIa: no need for general anaesthesia ## IIIb: performed under general anaesthesia
IV	Life-threatening complication requiring ICU management ## IVa: Single-organ dysfunction ## IVb: Multi-organ dysfunction
V	Death of the patient

The Clavien-Dindo classification has been found to be applicable for emergency surgery patients (Mentula and Leppäniemi 2014). However it has certain limitations. Most importantly, it takes into account only the most severe complication, thus it may underestimate the impact of multiple and less severe events. Subsequently a new system has been developed. The Comprehensive Care Index (Slankamenac et al. 2013) is calculated as the sum of all complications weighted for their severity and expressed on a continuous scale from 0 to 100 in a single patient. As it summarizes the impact of all adverse events, it has been considered to be more sensitive than the original Clavien-Dindo system for grading complications (Slankamenac et al. 2014). Furthermore, as some patients develop complications more often, it is essential to register postoperative complications but also risk factors prior to surgery (Mentula and Leppäniemi 2014).

2.6 Preoperative risk assessment

Risk assessment tools incorporating clinical variables into a predictive score are a practical means of assessing the risk in patients undergoing surgery. Several tools have been developed, but none have been found to be superior to each other or have been widely adopted into routine practice. Some of these scores require intraoperative information, which makes them less applicable to preoperative assessment. Two systematic reviews have so far identified scoring systems for emergency gastrointestinal surgery. The first was focused on risk scoring systems applicable to older patients undergoing emergency abdominal surgery (Rix and Bates 2007), while the second focused on all adult patients undergoing laparotomy (Oliver et al. 2015). The scores presented in these studies can be classified into those predicting general, organ specific or procedure-specific risks. Commonly used scores for assessing risks in critically ill patients are presented in Table 7.

Table 7. Commonly used tools for assessing critically ill patients (according to Oliver et al. 2015, Shah and Hamilton 2013 and Rix and Bates 2007)

Score	Abbreviations	Predicts/assess	Reference
The American Society of Anesthesiologists physical status classification system	ASA	Morbidity, mortality	Saklad 1941
Acute Physiology and Chronic Health Evaluation score	APACHE	Morbidity, mortality	Knaus et al. 1981
Physiological and Operative Severity Score for the enUmeration of Mortality	POSSUM	Morbidity, mortality	Copeland et al. 1991
Simplified Acute Physiological Score	SAPS	Mortality	Legall et al. 1984
Sequential Organ Failure Assessment	SOFA	Organ failure	Vincent et al. 1996
Multiple Organ Dysfunction Score	MODS	Organ failure	Marshall et al. 1995
Mannheim Peritonitis Index	MPI	Mortality	Wacha et al. 1987

2.6.1 General scores

Typical examples of general risk assessment scores include ASA, POSSUM and APACHE scores. Of these, the ASA score is the oldest and the simplest to use. In this classification ASA I refers to a healthy patient, ASA II to a patient with mild systemic disease and ASA III to a patient with severe systemic disease. ASA IV is used when a patient has a life-threatening severe systemic disease and ASA V when a patient is moribund and is not expected to survive without operation. Sixth category was later added, and is used for brain-dead declared organ donor patients. Despite ASA scores' simplicity, and although it is subjective and does not take procedure-specific risks and patients' age into account, it has been found to correlate with postoperative morbidity and mortality in elderly patients (Koo et al. 2015; Duron et al. 2011).

The APACHE score was originally introduced in 1981, and since then it has undergone several revisions. Of these revisions, the APACHE-II (Knaus et al. 1985) is the most commonly used (Shah and Hamilton 2013). The APACHE II score is calculated from a patients' age and 12 physiological measurements. While it does not assess procedure-specific factors, it has been estimated to be better for predicting the outcome than the ASA score (Goffi et al. 1999).

The POSSUM score was introduced during the 1990s, and it has likewise undergone several revisions. The E-POSSUM score is designed for elderly patients undergoing colorectal surgery (Tran Ba Loc et al. 2010). However, this system is not validated to be used for assessing risks in emergency operations. The POSSUM score requires 12 physiological and 6 operative parameters for its calculation. As it requires intra-operative data to be used accurately, the value in preoperative risk assessment is reduced.

Many other scores have been developed. For example, a recently introduced Geriatric Emergency Surgery score is designed for predicting one-year mortality of operated elderly patients (Olufajo et al. 2016). It takes into account five clinical variables and emphasizes the presence of factors such as acute kidney injury, co-existing diseases and malnutrition.

2.6.2 Sepsis scores

General illness severity scores are widely used for assessing patients undergoing intensive care unit (ICU) care for sepsis. These scores can be broadly divided into tools that predict the outcome and to tools that assess the presence and severity of sepsis-related organ dysfunction. Examples of outcome prediction scores include APACHE and SAPS, while SOFA is an example of systems used for assessing severity of organ failure (Vincent and Moreno 2010). All these scores have been found to correlate with mortality in adult patients (Vincent and Moreno 2010), and the predictive value in critically ill elderly patients has also been identified (Qiao et al. 2012; Bagshaw et al. 2009; Vosylius et al. 2005). A recently introduced clinical score the quick Sequential (Sepsis-related) Organ Failure Assessment (qSOFA) score is a simplified version of the SOFA score that can be used for predicting the likelihood of acute organ failure outside the ICU (Singer et al. 2016; Seymour et al. 2016).

2.6.3 Frailty in risk assessment

The elderly are a heterogeneous group of patients and consequently the chronological age may not always accurately reflect the patient's physiological condition. Frailty is defined as a clinically recognizable increased vulnerability resulting from an ageing-associated accumulation of deficits in multiple physiological systems (Xue 2011). It inhibits recovery or the achievement of the same functional level after the acute condition. Assessment takes into account many factors including the patient's physiological, cognitive, social and psychological deficits. Several scores exist to monitor frailty in the elective setting, but none have been found superior in emergency patients (Desserud et al. 2016). However, some promising results have been presented. For example, in two recent studies modified frailty indices were found to correlate with postoperative morbidity and mortality in geriatric patients undergoing emergency surgery (Jokar et al. 2016; Joseph et al. 2016).

2.6.4 Other scoring systems

Numerous other scoring systems have been developed for assessing specific risks. Examples include the Caprini Score (Caprini et al. 1991) for predicting the risk of postoperative venous thromboembolic events and the Revised Cardiac Risk Index for estimating the risk of postoperative cardiac events (Lee et al. 1999). The Rockall Score is used for predicting adverse outcome after upper gastrointestinal bleeding (Rockall et al. 1996), while the Charlson Comorbidity Index is a commonly used tool for assessing the severity of co-existing diseases (Charlson et al. 1987). Although this score was not originally developed for predicting surgical outcomes, it has been found to correlate with risk of perioperative deaths (Laor et al. 2016; Frenkel et al. 2014)

2.7 Increasing attention to emergency operations on the elderly

As already stated, most surgeons acknowledge that gastrointestinal emergencies in elderly patients differ from those in younger patients in terms of diagnosing acute conditions and selecting the appropriate treatment. The care of these patients causes significant costs. Although the importance of this group of patients is well-recognized, research in this field has been long under-prioritized (Søreide and Wijnhoven 2016). The oldest and most morbid patients are often excluded from clinical trials, thereby reducing the applicability of the results to these frailest patients. However, as the economic burden on the system is constantly increasing, more attention will be paid to caring for this patient group. Consequently the need to better understand acute presentations and outcomes will be paramount to ensure optimal care.

3 AIMS OF THE STUDY

The aim of this study was to analyse the outcome of emergency gastrointestinal surgical and endoscopic procedures in elderly patients. The focus was on the incidence of gastrointestinal emergencies, associated outcomes of the treatments and factors predisposing to poor outcome.

The detailed aims were as follows:

1) To report indications and outcomes of emergency gastrointestinal surgery in elderly patients
2) To study the outcomes of ICU treatment in elderly patients with alimentary tract related surgical sepsis
3) To analyse indications, outcomes and predisposing factors for poor outcomes of acutely performed ERCP in the elderly patients
4) To study factors associated with higher morbidity and mortality in elderly patients operated for acute cholecystitis

4 MATERIALS AND METHODS

4.1 Emergency gastrointestinal surgery in the elderly

The study comprised consecutive elderly patients (aged 65 years or more) who underwent emergency gastrointestinal surgery in the period 2007–2009 at Seinäjoki Central Hospital, Finland. Emergency re-operations after elective surgery and emergency endoscopic procedures were excluded from the analysis. All emergencies from the hospital catchment area (approx. 193,500 inhabitants and 37,000 elderly inhabitants) were referred to this hospital.

The patient and operation-related data was retrieved retrospectively from the hospital's electronic medical records. Post-discharge data from primary care centres or residential care homes, radiological and laboratory examinations were also reviewed. Finnish population data, including mortality data was obtained from Statistics Finland.

The key factors under analysis in this study were the occurrence of major complications or death from any cause within 30 days of the operation. Postoperative adverse events were graded according to the Clavien-Dindo classification presented in Table 6 (Dindo et al. 2004).

4.2 Severe postoperative sepsis in the elderly

Prospectively collected data from 24 multidisciplinary ICUs in 19 participating hospitals and hospital districts in Finland was used to form the study population. During the study period (November 2004 to 28 February 2005) the catchment area of the study hospitals included 90.6% of the Finnish adult population. All consecutive adult admissions were screened for eligibility for this study. Patients were included if they fulfilled previous criteria for severe sepsis or septic shock and had undergone gastrointestinal surgery (Bone et al. 1992). This definition of severe sepsis included suspected or confirmed infection accompanied by systemic inflammatory response (SIRS) and organ failure.

The patient data was collected from the Quality Consortium database (Intensium) and the Finnish population data from Statistics Finland. The SOFA (Vincent et al.

1996), APACHE II (Knaus et al. 1985) and SAPS II (Le Gall et al. 1993) scores were calculated daily for each patient.

The key factor under analysis in this study was death from any cause after surgery. Short (in-hospital) and long-term (one-year) mortality rates were analysed. Age-adjusted mortality of the study group was compared to age-adjusted mortality of general population.

4.3 Acute ERCP in the elderly

A prospectively managed and hospital-based registry containing all ERCP procedures and associated outcomes in Tampere University Hospital, Finland was used to form the study population. All patients aged 65 years or more who had undergone acute ERCP between January 2010 and December 2014 were included. The procedure was considered acute when it was performed during a period of hospitalization beginning with an emergency admission.

Patient related characteristics were extracted from hospital medical records and procedure-related mortality data from the hospital medical records and the Finnish Population Register Centre. The following information was prospectively collected and registered: indication for ERCP, all procedures performed, difficulty of cannulation, outcome of the ERCP, post-ERCP complications and other adverse events. Cannulation was considered difficult if it either took more than five minutes or if there were more than five cannulation attempts on the papilla or if the pancreatic duct was cannulated more than twice (Halttunen et al. 2014).

The primary outcome measures were the occurrence of procedure-related complications or death. For defining and grading adverse events, we used the classification by Cotton et al. (1991) presented in Table 5. The secondary outcome measure was the success of the procedure. Success was defined according to pre-procedural set goals.

4.4 Cholecystectomy in the elderly

The study comprised consecutive elderly patients (aged 65 years or more) operated on for acute cholecystitis in six Finnish hospitals during a four-year study period (2007–2010). The study hospitals included two university hospitals (Kuopio and Tampere), two central hospitals (Mikkeli and Seinäjoki) and two district hospitals (Valkeakoski and Vammala). The annual catchment areas of these hospitals ranged from 40,000 to 260,000 inhabitants. While the smallest hospitals were focused on day unit surgery, some emergency cases were referred to these hospitals.

The data was retrospectively retrieved from patients' medical records. Population based statistics was acquired from Statistics Finland. The ASA score (Saklad 1941) was assessed for each patient. Postoperative adverse events were classified according to the Clavien-Dindo system presented in Table 7 (Dindo et al. 2004).

The primary outcome measures were 30-day mortality and morbidity. Both morbidity and mortality of patients were analysed in accordance with patient and procedure-specific factors, including patient's age, ASA score, surgical technique and hospital type.

5 STATISTICS

Data is presented as absolute values and percentages unless otherwise stated. The relationship between two categorical variables was analysed using either chi-square test or Fisher's exact test, and in the case of non-categorical variables using Mann-Whitney U-test or t-test. Cox regression analysis and logistic regression analysis were used for multiple statistical comparisons. Kaplan-Meier curve was used to describe survival in different age groups in the third study. Statistical significance was set at $p<0.05$. All statistical analyses were performed using SPSS Statistics version 22 for Windows (IBM Corp, Armonk, NY, USA). The first author performed all the analyses and a statistician verified the accuracy of the tests used and results obtained.

6 ETHICAL ASPECTS

All studies were conducted in accordance with the principles of the Declaration of Helsinki and the guidelines for good clinical practice.

Specific ethical aspects in the studies were as follows:

1) The first study (emergency gastrointestinal surgery in the elderly) and the fourth study (cholecystectomy in the elderly) were retrospective and observational. These studies did not evaluate a specific therapeutic or prophylactic intervention and the researchers did not contact the patients. Therefore no ethical approval of the institutional review board was required. Instead, approval was sought and granted by the medical director of the study hospital.
2) In the second study (severe sepsis in the elderly) ethical approval was granted by the respective institutional review boards of each participating study hospital. In addition, all patients or their next of kin provided written informed consent to participate.
3) The third study (ERCP in the elderly) was prospective and observational. This study did not evaluate a specific therapeutic or prophylactic intervention and the researchers did not contact the patients. The protocol for collecting data was approved by the medical director of Tampere University Hospital. No ethical approval was required from the institutional review board.

7 RESULTS

7.1 Emergency gastrointestinal surgery in the elderly

A total of 430 elderly patients underwent emergency gastrointestinal surgery. The mean age of patients was 76 years and 51% were male. Seventy-four percent of patients had pre-existing diseases, with the most common being chronic cardiac disease (67%; hypertension in 51% of patients, coronary artery disease in 23% of patients and atrial fibrillation in 16% of patients). Twenty-six percent had undergone previous abdominal surgery. The clinical characteristics of patients are summarized in Table 8.

Table 8. The baseline characteristics of the study population (n=430)

Variable	
Age, mean (range)	76 years (65–96 years)
Gender, female	49%
BMI, kg/m^2	26 (± 4.7)
Underweight (BMI < 18.50)	2%
Overweight (BMI ≥ 25)	59%
Co-existing disease	74%
None	26%
Cardiac disease	67%
Pulmonary disease	11%
Diabetes	15%
Malignancy	17%
No ongoing medications	11%
Polypharmacy (more than 6 ongoing medications)	44%
Previous abdominal surgery	26%

The most common indication for emergency surgery was acute cholecystitis (32%, annual incidence 125 per 100,000 elderly inhabitants), followed by incarcerated hernia (14%, 54/100,000) and malignancies (12%, 45/100,000). Acute appendicitis was the fourth most common reason for surgery. However, of 59 patients only 46 (78%) were later found to have positive histology for acute appendicitis, while remaining 13 had normal histology (11%, 41/100,000). Of all 112 laparoscopic procedures (26%), 29 (26%) were later converted to open surgery. Figure 1 illustrates distribution of diagnoses.

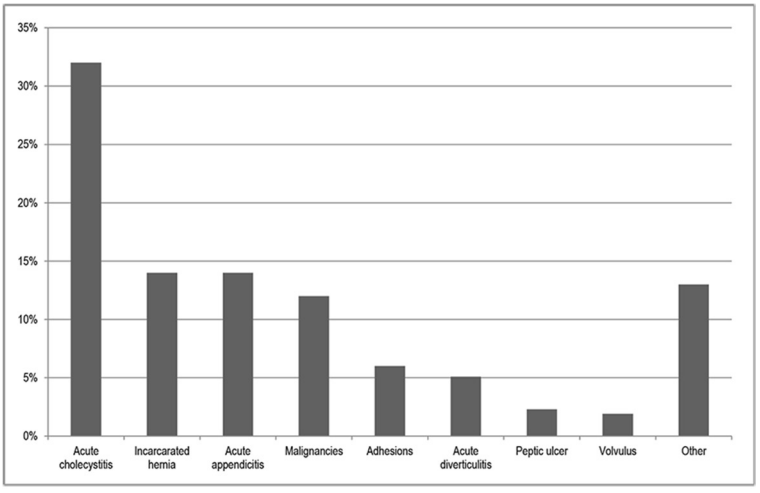

Figure 1. Distribution of gastrointestinal emergency operations in the elderly (n=430)

The overall mortality and morbidity rates were 14% and 32% respectively. Medical complications (17%; of which 56% were grade 3 or more complications according to Clavien-Dindo classification) occurred more often than surgery-related complications (15%; 59%). There were no complications directly associated with anaesthesia. Conservative care was sufficient in 78% of patients with postoperative adverse events. Reoperations were rare (7% of all patients, 21% of patients with complicated outcome), with no associated significant rise in mortality. Mortality was higher among patients with postoperative heart failure (29% of these patients died, $p=0.011$), pneumonia (39%, $p<0.001$) or sepsis (60%, $p=0.003$). Of the mortalities, one patient died during the operation (0.2%) and 14% during the 30-day follow-up. One-year mortality among operated patients was 24%. Most deaths were either infection (51% of all deaths; sepsis in 34% and pneumonia in 13% of patients) or malignancy related (28%). Table 9 presents the outcome related statistics.

Table 9. Postoperative morbidity and mortality after emergency abdominal surgery in the elderly

Variable	Occurrence	Mortality within group
Morbidity	32%	
Conservatively treated complications		
Heart failure	8%	29%
Pneumonia	5%	39%
Sepsis	1%	60%
Surgically treated complications		
Wound dehiscence	4%	50%
Mortality		
30-day mortality	14%	
1-year mortality	24%	

To estimate the risk factors behind higher mortality, a multivariate analysis was performed after bivariate correlation analysis. All the statistically significant variables (age, low BMI, previous history of malignancies, coronary artery disease, atrial fibrillation, acetylsalicylic acid medication, history of no previous medication, surgical technique, ASA score) were inserted into a cox regression analysis. Patients with increased mortality were older (HR 1.1, 1.0–1.1, p=0.014), had atrial fibrillation more often (HR 2.1, 95% CI 1.1–3.9, p=0.017), had pre-existing malignancies (HR 2.2, 95% CI 1.2–4.1, p=0.010) or were underweight (HR 4.8, 95% CI 1.9–12.3, p=0.001). ASA score III or more was associated with poor outcome (HR 4.3, 95% CI 2.0–9.2, p<0.001), as there was also an association with higher mortality after open surgery (HR 3.2, 95% CI 1.1–9.2, p=0.029).

7.2 Severe postoperative sepsis in the elderly

A total of 154 patients (73 elderly patients and 81 younger patients) fulfilled the inclusion criteria of this study. The mean ages of the elderly and non-elderly patients were 76 years (65–88 years) and 50 years (18–64 years) respectively. Females predominated in the elderly population and, unsurprisingly, pre-existing diseases increased with age. The most common indication for surgery in older patients was acute cholecystitis (22%), followed by acute diverticulitis (14%), complicated gastroduodenal ulcer disease (14%) and malignancies (11%). The anatomic focus of the sepsis was intra-abdominal in 86% of patients and pneumonia in 14% of patients. The clinical characteristics of elderly and younger patients are summarized in Table 10.

Table 10. Baseline characteristics of elderly and non-elderly patients

Variable	Elderly patients n=73	Non-elderly patients n=81
Age, mean (range)	76 years (65–88 years)	50 years (18–64 years)
Gender, female	56%	30%
BMI, kg/m^2	27 (±4.4)	27 (±5.8)
Comorbidities		
Cardiac disease	43%	28%
Diabetes	21%	10%
Chronic pulmonary disease	8%	3%
Indication for surgery		
Acute cholecystitis	22%	9%
Acute diverticulitis	14%	7%
Gastroduodenal ulcer	14%	10%
Malignancy	11%	7%
Infection focus		
Intra-abdominal	86%	77%
Pneumonia	14%	16%

Hospital and one-year mortality rates increased with age, being 15% and 22% among patients aged less than 65 years and 48% and 64% among the elderly. After successful treatment of the infection 9% of the younger patients discharged from the hospital, 17% of the discharged patients aged 65–79 years and 78% of the discharged patients aged more than 80 years died within one year. None of the patients aged 85 years or more survived longer than one year. The Kaplan-Meier survival curve of different age groups is shown in Figure 2.

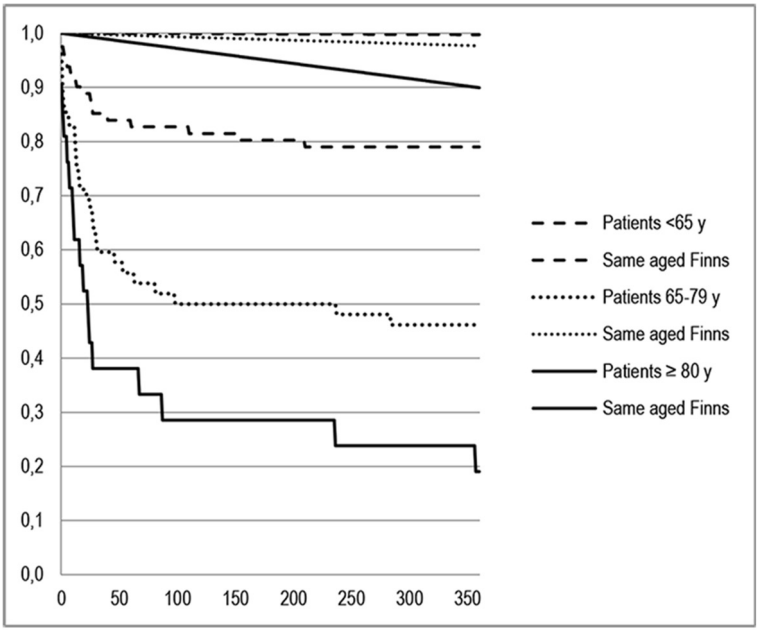

Figure 2. Kaplan-Meier curve for survival in different age groups (log rank p<0.001) compared to survival in same-aged Finns

Survivors of all age groups (n=107, 69%) were compared to non-survivors (n=47, 31%). Patients who died were older (mean age 59 years vs. 72 years, p<0.001) and suffered more often from chronic cardiac diseases (35% vs. 53%, p=0.040), renal diseases (2% vs. 11%, p=0.041), pulmonary diseases (3% vs. 11%, p=0.044) or were undergoing cancer chemotherapy (0% vs. 6.7%, p=0.008). Septic shock (p=0.267) and mechanical ventilation (p=0.085) did not increase mortality in a statistically significant way, while both were more common among patients who died. ICU-used scores (SAPS-II, APACHE-II and SOFA) were predictive of increased mortality, as there was also an association between elevated lactate levels and risk of dying.

7.3 Acute ERCP in the elderly

A total of 480 elderly patients underwent 531 ERCPs during the study period. The mean age of patients was 78 years and 52% were female. Co-existing diseases were present in 78% of patients, the most common being hypertension (56%), diabetes (25%), coronary artery disease (22%) and atrial fibrillation (22%). The clinical characteristics of study population are presented in Table 11.

Table 11. Baseline characteristics of elderly patients undergoing emergency ERCP

Variable	
Age, mean (range)	78 years (65–97 years)
Gender, female/male	52% / 48%
Comorbidities	
Hypertension	56%
Diabetes	25%
Coronary artery disease	22%
Atrial fibrillation	22%
Dementia	8%
Previous malignancy	8%
Congestive heart disease	6%
Asthma	5%
COPD	4%
Medication	
Acetylsalicylic acid medication	24%
Warfarin therapy	20%
Insulin therapy	10%
Corticosteroid therapy	6%

The most common indication for ERCP was biliary obstruction caused either by bile duct stones (56%) or malignancy (34%). The majority of malignancies were advanced and inoperable (73%). Other indications for the procedure included benign biliary obstruction (5%) and postoperative bile leak (4%). Of patients with postoperative bile leak, one had a lateral injury to the common hepatic duct (Strasberg-Bismuth D) and the rest cystic duct leak (Strasberg-Bismuth A). All these patients had undergone laparoscopic cholecystectomy. Figure 3 illustrates distribution of diagnoses.

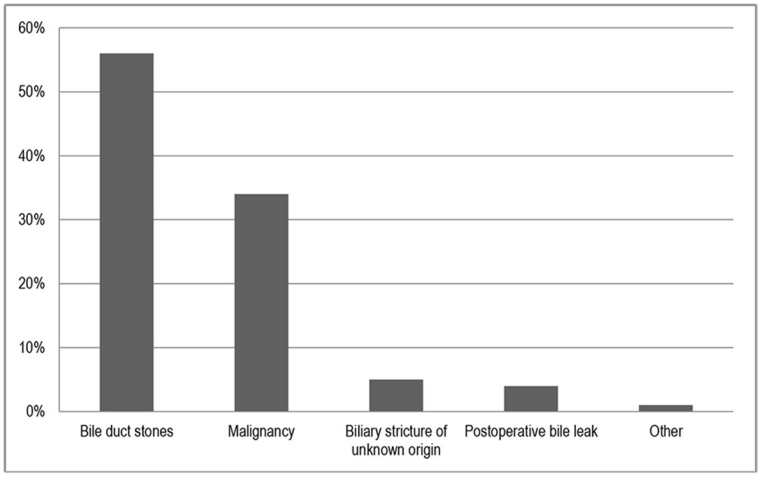

Figure 3. Indications for emergency ERCP in elderly patients (n=480)

ERCP was successful in extracting the bile duct stones in 73% of the patients in the index procedure, and in 97% of patients with an additional, scheduled ERCP. Ten patients (3%) required surgical treatment or could not be treated, most often because of poor physiological status. Malignancy-related jaundice was relieved endoscopically in 59% of patients, while the rest (40%) required percutaneous biliary drainage either immediately or later. However, among the patients with successful cannulation, release of the biliary obstruction was achieved in 84% of patients. Endoscopic procedure was sufficient for treating postoperative bile leak in 94% of patients. The success remained unproven in one patient who died of sepsis one day after the procedure. However, even in this patient, the bile drain output was reduced after the procedure. Efficiency data on the procedure is presented in Table 12.

Table 12. Efficiency of acute ERCP in the elderly

Variable	Success rate
Bile duct stones extracted (with first ERCP)	73%
Bile duct stones extracted (with additional scheduled ERCP)	97%
Decompression of malignant biliary obstruction (with first ERCP alone)	59%
Postoperative bile leak treated (with first ERCP)	94%

The overall morbidity was 3.4%, the most common complication being pancreatitis (1.7%). Three patients (0.6%) suffered from post-ERCP bleeding and one patient (0.2%) from cholangitis. Perforation was reported in one patient (0.2%) and cardiovascular or sedation-associated complications in two patients (0.4%). Only one of the complications was graded severe (pancreatitis) as it necessitated hospitalization for 27 days and percutaneous drainage. There were no procedure-related deaths. However, overall 30-day mortality was 10%; ranging from 2.7% in patients with bile duct stones to 24% in patients with malignancy. Median survival of patients with malignancy was 170 days (3–1635 days), while in patients with inoperable pancreatic malignancy it was as low as 121 days (5–997 days). Postoperative outcomes are summarized in Table 13.

Table 13. Post-endoscopic morbidity and mortality in elderly patients

Variable	
Morbidity	
Pancreatitis	1.7% (severe in one, 0.2%)
Haemorrhage	0.6%
Infections	0.2%
Perforation	0.2%
Cardiovascular and sedation -related	0.4%
Overall morbidity	3.4%
Mortality	
Procedure-related mortality	0.0%
30-day overall mortality	10%
1-year overall mortality	34%

According to our logistic regression analysis complications were significantly more common among patients with chronic obstructive pulmonary disease (OR 5.1, 95% CI 1.1–24.3, p=0.041) and difficult cannulation (OR 5.1, 95% CI 1.0–25.4, p=0.045).

7.4 Cholecystectomy in the elderly

A total of 601 elderly patients underwent emergency cholecystectomy for acute cholecystitis during the study period. The mean age of these patients was 75 years (range 65–98 years), and 53% per cent of these patients were male. The majority of patients (66%) had pre-existing diseases, of which cardiovascular diseases (54%), diabetes (13%) and pulmonary diseases (7%) were the most common. Forty-five percent of patients were assessed to be in ASA classes III or more. The clinical characteristics of study population are presented in Table 14.

Table 14. Baseline characteristics of elderly patients undergoing emergency cholecystectomy

Variable	
Age, mean (range)	75 years (65–98 years)
Gender, female	47%
Comorbidities	66%
Cardiovascular disease	54%
Diabetes	13%
Pulmonary disease	7%
Other	15%
ASA III or more	45%

The overall morbidity and mortality rates were 26% and 3% respectively. The majority of patients (69%) underwent open surgery, and this technique was preferred over

laparoscopy for patients with ASA score III or more (p<0.001). Complications occurred more often after open surgery than after laparoscopic surgery (28% vs. 19%, p=0.011), while the difference in 30-day mortality failed to reach statistical significance (3.6% vs. 1.6%, p=0.137). The higher ASA score (III or more) was predictive of morbidity (19% vs. 38%, p<0.001) and mortality (0.0% vs. 6.2%, p<0.001) in patients undergoing open cholecystectomy, while after laparoscopic procedures no similar association was found. Moreover, the outcome of ASA III or more patients undergoing laparoscopic surgery was similar to those assessed to be in ASA I–II undergoing open surgery. Table 15 illustrates procedure-related outcomes according to patients' age, ASA score, hospital type and surgical technique.

Table 15. Surgical outcomes according to age, ASA score, surgical technique and hospital type

Variable		Morbidity 26%			Mortality 3.0%	
Age < 80 years / Age ≥ 80 years	24%	30%		1.8%	6.0%	(p=0.011)
ASA I–II / ASA ≥ III	19%	34%	(p<0.001)	0.3%	5.5%	(p<0.001)
Open cholecystectomy	28%			3.6%		
AGE: < 80 y / ≥ 80 y	28%	30%		2.1%	7.1%	(p=0.016)
ASA: I–II / ≥ III	19%	38%	(p<0.001)	0.0%	6.2%	(p<0.001)
Laparoscopic cholecystectomy	19%			1.6%		
AGE: < 80 y / ≥ 80 y	16%	30%	(p=0.047)	1.4%	2.5%	
ASA: I–II / ≥ III	18%	23%		0.8%	3.2%	
University hospital	23%			1.7%		
AGE: < 80 y / ≥ 80 y	22%	27%		0.4%	5.7%	(p=0.012)
ASA: I–II / ≥ III	13%	34%	(p<0.001)	0.0%	3.5%	(p=0.025)
Laparoscopic / open surgery	14%	29%	(p=0.002)	0.0%	2.6%	
Central hospital	28%			4.2%		
AGE: < 80 y / ≥ 80 y	26%	37%		3.3%	6.2%	
ASA: I–II / ≥ III	24%	34%	(p=0.045)	0.7%	7.6%	(p=0.003)
Laparoscopic / open surgery	27%	28%		3.6%	4.4%	

Older patients were at higher risk of postoperative morbidity and mortality, and had more often serious comorbidities than did younger elderly patients (p<0.001). Six percent of patients aged 80 years or more and 1.8% of patients aged 65–79 years died within one month of surgery (p=0.008). Mortality increased rapidly after the age of 90 years; and as many as 40% of these patients died within one month of the operation. Figure 4 illustrates postoperative morbidity and 30-d mortality in different age groups compared to 30-day mortality of same-aged Finns in general population.

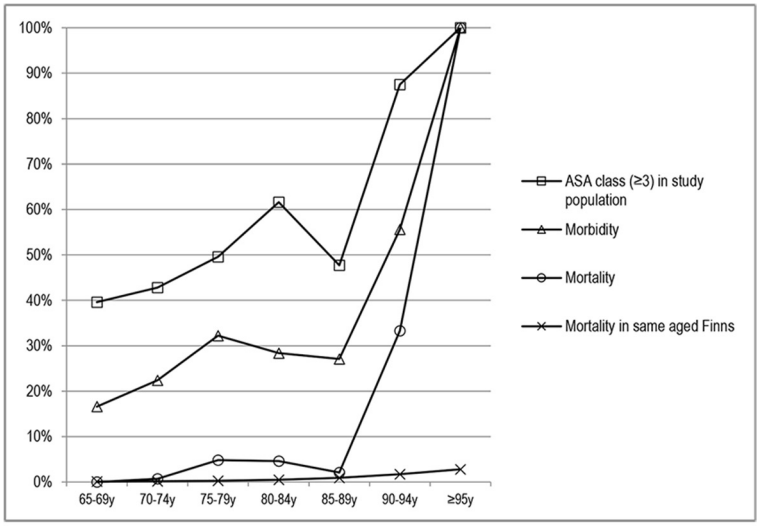

Figure 4. Age-adjusted morbidity and mortality of the study population compared to mortality of same-aged Finns.

Variables including ASA score (I–II or ≥ III), patients' age (<80 years or ≥ 80 years), surgical technique (open or laparoscopic cholecystectomy) and hospital type (central or university hospital) were entered in the multivariate analysis. According to this, only higher ASA score was predictive of increased morbidity (OR 2.1, 95% CI 1.4–3.1, p<0.001) and mortality (OR 14.7, 95% CI 1.9–114, p=0.010).

8 DISCUSSION

Abdominal emergencies cause an undeniable burden on health care services and the elderly are overrepresented in emergency admissions (Scott et al. 2016; Bruns et al. 2015; Ogola et al. 2015; Gale et al. 2014; Stewart et al. 2014). As the elderly population increases, it is likely that greater numbers of older patients will be admitted to emergency departments. Furthermore, surprisingly little is known about the incidence of gastrointestinal emergencies and the safety and efficacy of emergency operations performed on the elderly. In this thesis the focus is on the outcomes of these emergencies, and its contribution to the literature is in providing data on the incidence of gastrointestinal emergencies, associated risks and factors predisposing to adverse outcome.

First we studied emergency gastrointestinal surgical operations in the elderly and concluded that emergency surgery is still associated with significant morbidity and mortality. Almost one in six of the elderly patients undergoing surgery died within one month, and one third suffered from postoperative complications. This corroborates earlier studies, where perioperative mortality has been around 15–20% (Rangel et al. 2015; Ingraham et al. 2012; Fukuda et al. 2012; Blansfield et al. 2004; Kettunen et al. 1995). If compared to other common emergency operations, our results were poorer. For example, Panula et al. (2011) reported 10.5% 30-day mortality in patients aged 65 years or more undergoing hip fracture surgery and Avery et al. (2001) 13.5% mortality in octogenarians undergoing cardiac bypass surgery.

We emphasize that not only older age, but co-existing diseases and malnutrition have a negative and even more drastic impact on outcomes. The presence of comorbidities in operated patients has been found to be associated with higher mortality (Frenkel et al. 2014; Glance et al. 2012). However, the evidence is not consistent across all studies (Merani et al. 2014). While we failed to demonstrate improved outcomes if compared to a similar study some twenty years ago (Kettunen et al. 1995), there was a clear trend towards lower mortality in the oldest patients in our recent study. For example, in patients aged 85 years and over 30-day mortality had decreased from 43% to 21%.

Nevertheless, mortality was significantly higher than in same-aged Finns in general population. For example, 30-day mortality among nonagenarians was 17 times (1.9% vs. 33%) that of same-aged Finns. Of all patients who died, 43% experienced at least one complication. Mortality was higher among those with postoperative infectious events (e.g. pneumonia and sepsis). The importance of these complications is already well-recognized (Scarborough et al. 2016; Havens et al. 2015; McCoy et al. 2015). Consequently strategies focusing on the timely recognition and management of these events once they occur are essential to improve outcomes (Sheetz et al. 2013).

In the second study we analysed the outcome of elderly patients with severe postoperative sepsis. We concluded that the elderly had significantly higher mortality than younger adults. Almost two thirds of the elderly patients died within one year and half during the hospital stay. Corresponding outcomes have been reported in the literature, where short-term mortality has exceeded 40% (Bouza et al. 2016). Our results, however, seem to be poorer than for sepsis patients in general. For example, according to previously published study the hospital mortality of all elderly sepsis patients in the same Finnsepsis data was 6% lower (Karlsson et al. 2009). Furthermore, it needs to be recognized that while successful treatment of infection can be achieved in the majority of patients, mortality remains high long after discharge. Earlier studies have reported increased mortality up to five years (Winters et al. 2010). In this study after successful treatment of the infection elderly patients discharged from hospital were at least seven times more likely to die within one year than were same-aged Finns in general population. None of the sepsis patients aged 85 years or more survived over one year.

Not surprisingly, the most morbid oldest patients were at the highest risk. Risk-adjusting comorbidities included chronic cardiovascular, pulmonary and renal diseases. The risk was also higher in patients with ongoing cytostatic medication. The importance of pre-existing conditions is already well-identified (Kaukonen et al. 2014; Williams et al. 2004; Sarnak and Jaber 2000; Brun-Buisson et al. 1995). In addition, the ICU scoring systems were predictive of higher mortality, as has already been reported (Vincent and Moreno 2010). As these scores are routinely used for every ICU patient, they provide us with prognostic information on the outcomes. If an elderly patient does not rapidly respond to ICU care and we are considering decreasing the intensity of the treatment, these scoring systems may be practical when informing patients' relatives of the expected outcomes.

We also emphasize that improving the survival of sepsis patients is possible. Several guidelines have already focused on reducing the rate of sepsis-related deaths by standardizing the care of these patients (Dellinger et al. 2012; Sartelli et al. 2014). Recognizing infections, rapid antimicrobial therapy, appropriate resuscitation and

infection source control are all critical. Moreover, tools such as qSOFA may be practical when sepsis is suspected (Seymour et al. 2016).

In the third study we focused on acutely performed ERCP. We concluded that the procedure can be safely and efficaciously performed on older patients. The most common indication for ERCP was obstructive gallstone disease, followed by malignancy-related obstruction. These two indications accounted for 90% of all ERCP procedures. Both these indications are more common among older patients (Siegel and Kasmin 1997). Although there has been some decrease in the need of ERCP as non-invasive diagnostic methods such as MRI have replaced the need for ERCP, it is likely that population ageing will lead to increased demand for ERCP procedures in the future. In our study one in 1,000 elderly inhabitants required emergency ERCP each year.

We presented a few other important findings concerning the safety of ERCP. First, there were no procedure-related deaths, and the risk of all post-ERCP complications and especially post-ERCP pancreatitis was lower than in adult patients in general. According to previous systematic reviews the rate of post-ERCP pancreatitis has been around 3–7% in all adult patients (Silviera et al. 2009; Andriulli et al. 2007), while in this study only 1.7% of patients suffered from post-ERCP pancreatitis. Second, the risk of ERCP complications was not influenced by patient's age. For example, morbidity among patients aged 65–79 years was similar to that in older patients. Finally, our study agreed with the widely accepted correlation between postoperative morbidity and difficulty of cannulation (Halttunen et al. 2014; Enochsson et al. 2010). The importance of COPD on the contrary has not previously been identified. A higher rate of complications in this patient population may reflect problems in our practice for monitoring sedation. Appropriate pre-sedation assessment and proper patient selection, preparation and optimization of patients, as well as the availability of skilled professionals for sedation administration are key factors in providing high-quality patient care (Standards of Practice Committee 2008). Our results here might have been even better if anaesthetist led, deeper and continuous sedation had been selected for patients with chronic pulmonary diseases.

In the fourth study we found high morbidity and mortality associated with surgical treatment of acute cholecystitis in older patients. The overall morbidity and 30-day mortality rates were 26% and 3% respectively. The perioperative morbidity in elderly patients has been previously reported to be around 4–16% and mortality 0–4% (Lee et al. 2015; McKay et al. 2013; Yetkin et al. 2009; Bingener et al. 2003; Tagle et al. 1997). Mortality increased significantly with advancing age, while there was no similar increase in postoperative morbidity. As many as 6% of patients aged 80 years or more died within one month. Corresponding outcomes have been reported before (Rosenmüller et al. 2007).

The outcomes of emergency cholecystectomy were stratified by patient's age, hospital type and surgical technique without any statistically significant differences. Only ASA score was predictive of morbidity and mortality. The predictive value of this score has been already recognized (Sandblom et al. 2015). While there were no significant differences in outcomes between hospitals, there was a trend towards better outcomes in patients operated on in university hospitals. In an earlier Scottish study (Harrison et al. 2012) the results varied widely among study hospitals, and mortality was lowest in large volume centres.

We also pointed out that laparoscopic cholecystectomy may improve outcomes in high-risk patients; while in healthy patients the outcome was similar regardless of which surgical technique was chosen. Consequently, our results favour the use of laparoscopic surgery for all patients and especially for those with severe systemic diseases unless laparoscopic surgery is absolutely contraindicated. However, there is a lack of evidence to support our views, as these surgical techniques in geriatric population have not so far been studied in high-quality clinical trials. On the contrary, other less invasive methods such as percutaneous cholecystostomy have been found to be an alternative to surgery for high-risk patients (McKay et al. 2012). Overall, more research is required on surgical, less invasive and conservative treatments. It should be noted, however, that extensively conservative care may lead to more complicated presentations more often, which means more invasive and difficult operations.

There are some obvious limitations in this study. Our conclusions may have been biased as the most morbid patients may not have been referred to surgical treatment and ICU care. In addition, there is an apparent patient selection bias when we compare surgical techniques because laparoscopic surgery may not have been chosen for patients with the highest preoperative risk or for those with assumedly complicated diagnoses. Our sepsis data is outdated, and it is likely that the outcome has improved since our data was collected. For example, in 2013 lower mortality rate was reported in Finnish sepsis patients (Nisula et al. 2013). Furthermore, surgical results might have been even better, as surgical treatment of some previously hazardous conditions has undergone a major paradigm shift from surgical towards less invasive treatments. For example, for perforated diverticulitis, resection with end colostomy (i.e. Hartmann operation) has been the traditional care, but in recent years its use has been challenged by other options including resection with anastomosis and proximal diversion and laparoscopic lavage (Vennix et al. 2015; Afshar et al. 2012).

In conclusion, we have shown that acute cholecystitis disease is the most common reason for emergency gastrointestinal surgery and ERCP in the elderly. While surgery was associated with significant morbidity and mortality, ERCP proved to be a safe and efficacious procedure for even the oldest patients. Infections were a major cause

of postoperative deaths, and severe sepsis was associated with poor outcomes. The risk assessment scores represent a practical way to assess the risks inherent in operations. However, this study merely scratches the surface of this subject. Nevertheless, if the risk could be preoperatively assessed, this information could be used to tailor the whole perioperative care according to specific risk profiles. Thus we could concentrate on postoperative rehabilitation from admission onwards. Although the survival of any patient is of the utmost importance, better cognisance of patient-reported outcomes (e.g. quality of life) as an outcome measure needs to be highlighted. It is as crucial for us to focus on increasing life expectancy as it is to maintain an adequate quality of postoperative life. As the pressure on the health care system increases, novel approaches will be needed for the care of this vulnerable group of patients.

9 SUMMARY AND CONCLUSIONS

The main conclusions of the present thesis are:

1) Acute cholecystitis is the most common reason for emergency gastrointestinal surgery in elderly patients, and despite advances in operative and non-operative care and diagnostic technologies emergency gastrointestinal surgery is still associated with high morbidity and mortality. Infections account for the majority of postoperative deaths.
2) Severe postoperative sepsis causes excessive short-term and long-term mortality in older patients.
3) ERCP for acute disease is a safe and efficacious procedure in elderly patients, with no greater risks than those reported before in younger adult population.
4) High ASA score (III or more) predicts morbidity and mortality after emergency cholecystectomy, whereas the importance of older age, hospital type and surgical technique is less obvious. However, the results also favour the use of laparoscopy for all patients and especially for those with severe systemic diseases unless it is absolutely contraindicated.

10 ACKNOWLEDGEMENTS

This thesis was carried out at the Department of Gastroenterology and Alimentary Tract Surgery, Tampere University Hospital, and at the School of Medicine, University of Tampere.

I owe great appreciation to the Head of Department, Professor Teuvo Tammela for encouraging active research in the Department of Surgery.

I owe my deepest and warmest thanks to my supervisors, Professor Hannu Paajanen, Associate professor Johanna Laukkarinen, and Docent Tuomo Rantanen. Without your assistance and dedicated involvement in every step throughout the process, this would have never been accomplished. I would like to thank Hannu for his guidance in getting my scientist career started. Your determination, motivation and hard work has been an inspiration to me. I am grateful for Tuomo not only for supervising this research but also encouraging me to specialize in gastrointestinal surgery. Your advice on research as well as my life and career has been priceless. I express my special appreciation and thanks to Johanna, who has been a tremendous mentor for me. I would like to thank you for encouraging my research and for allowing me to grow both as a surgeon and as a scientist.

I would like to express my great gratitude to all my co-authors. I am thankful for your aspiring guidance, invaluable constructive criticism and friendly advice during the research. Sincere thanks go to Sari Karlsson, MD, PhD, Antti Siiki, MD, PhD and Antti Kivivuori, MD for their work in sepsis, ERCP and cholecystectomy studies. I also warmly thank Sannamari Kotaluoto, MD, PhD, Associate professor Niku Oksala and Satuliisa Pauniaho, MD, PhD, to mention a few, and the rest of the Pancreas and Acuta research groups for their valuable comments. I express special thanks to Pekka Löppönen, MD, PhD, who was the first to introduce me to statistics. I thank Mika Helminen who kindly assisted me with the analysis and was very patient with my knowledge gaps in the area. I especially thank Virginia Mattila, for her expertise in revising my English. The official reviewers of this thesis, Docent Esko Kemppainen and Docent Jari Ovaska, need to be acknowledged for their constructive criticism and valuable comments.

I would like to acknowledge all colleagues I have had the privilege to work with and learn from during the years of surgical training. There are too many to be mentioned here. I am extremely thankful for all colleagues in Alavus, Seinäjoki and Tampere.

I owe great gratitude to my friends. Getting through this thesis required more than academic support, and I have many, many people to thank for listening to and, at times, having to tolerate me over the past few years. I owe special thanks to my golf, swim and triathlon buddies. I am very lucky to have friends like you in my life.

I express my warmest thanks to my parents Heikki and Sirpa, my sister Paula and my aunt Mari and their beloved families for their continuous support. I dedicate this book to my grandmother Maire who never stopped believing in me - her memory will be with me always.

Finally, I cannot express enough thanks to my beloved wife Sari who spent sleepless nights with me and always supported me even in the most stressful moments. Your constant support, encouragement, patience and unwavering love were undeniably the bedrock upon which the past years of my life have been built. Words are powerless to express my love and gratitude for you.

Tampere, 1 December 2016

Mika Ukkonen

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12 ORIGINAL PUBLICATIONS

World J Surg (2015) 39:2854–2861
DOI 10.1007/s00268-015-3207-1

ORIGINAL SCIENTIFIC REPORT

Emergency Abdominal Operations in the Elderly: A Multivariate Regression Analysis of 430 Consecutive Patients with Acute Abdomen

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Published online: 25 August 2015

Abstract

Background This study is intended to ascertain if outcome of acute abdominal surgery among elderly patients with acute abdominal pain have improved.

Methods Altogether 456 patients aged >65 years underwent emergency abdominal surgery between the years 2007 and 2009 in our hospital. After excluding emergency reoperations of elective surgery, a total of 430 consecutive patients were included in this retrospective audit. The key factors under analysis in this study were the occurrence of major complications and death from any cause within 30 days after the operation. In addition, we compared our results to our previously published data some 20 years ago.

Results The most common diagnoses were cholecystitis ($n = 139$, 32.3 %, incidence of 125 per 100,000 elderly persons), incarcerated hernia ($n = 60$, 13.9 %, 54/100,000), malignancy related ($n = 50$, 11.6 %, 45/100,000), or acute appendicitis ($n = 46$, 10.7 %, 41/100,000). The majority of operations (80.7 %) were performed using open technique. Of all 112 laparoscopic procedures, 25.9 % were converted to open surgery. Reoperations were rare and postoperative surgical complications were not associated with statistically significant increase in mortality, even if reoperation was needed. The 30-day mortality and morbidity rates were 14.2 and 31.9 %, respectively. Logistic regression analysis showed that patient's age ($p = 0.014$), atrial fibrillation ($p = 0.017$), low body mass index ($p = 0.001$), open surgery ($p = 0.029$), ASA grade III or more ($p < 0.001$), and previous history of malignancies ($p = 0.010$) were likely to increase mortality.

Conclusions Despite modern diagnostics and improved surgical techniques, the results of emergency abdominal surgery still have relatively high morbidity and mortality as reported in earlier studies.

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Introduction

The world population is ageing rapidly [1]. This is a global issue, and both developed and developing countries will face a significant increase in the proportion of elderly people. The number of people worldwide over 65 years of age is estimated to rise from 524 million in 2010 to 1.5 billion in 2050 [2]. Not surprisingly, an ageing world poses social, economic and health care challenges. We can study these forthcoming challenges in countries where the demographic change has already occurred or is rapidly advancing. For example, in Finland during the past two decades, the percentage of people over 65 years of age has already increased from 13.5 to 19.4 [3]. As the proportion of people older than 65 years of age has increased and the proportion of younger people has diminished, ageing has emerged as one of this country's fundamental problems.

The demographic change in the population has changed the profile of emergency abdominal surgery, where typical diagnoses in elderly patients include acute cholecystitis, incarcerated hernia, bowel obstruction and acute appendicitis [4, 5]. Of these only the last one is considered less common in older patients [6]. In addition to a rise in the number of procedures required, the recovery from surgery is also considered more often complicated in the elderly [7, 8]. Complications are more common and hospital stays are longer. Altogether, it is reasonable to assume that the demand for surgical resources will grow [9].

Despite the urgent need for knowledge in the treatment of the elderly surgical patients with acute abdomen, there are surprisingly few population-based studies [4, 5, 7, 10–12]. Our former study from one district hospital some 20 years ago reported overall morbidity (26 %) and mortality (22 %) in emergency abdominal surgery of patients >65 years of age [5]. In the present study, we were interested to ascertain whether the diagnoses or the outcomes of emergency abdominal surgery in the elderly have changed apace with the development of laparoscopic surgery, advanced diagnostic imaging and intensive care medicine.

Materials and methods

All patients over 65 years of age who underwent emergency abdominal surgery between 2007 and 2009 at the study hospital (central hospital) in Finland (annual catchment area of approximately 193,500 inhabitants, of which approximately 37,000 were elderly inhabitants) were included in this study. All emergency cases from the catchment area were referred to this hospital. The data were collected retrospectively from the electronic medical records used in the emergency department, on the surgical ward and in the intensive care unit. Endoscopic procedures and emergency reoperations after elective surgery (26 patients) were excluded. Therefore, out of 456 patients operated on, a total of 430 patients were included in the study.

Outcome

Primary outcome variables were the following: 30-day mortality and morbidity. Secondary outcome variables were time spent in hospital (days), rate of conversion from laparoscopic to open surgery and rate of reoperations required. Complications were defined and classified by using Clavian-Dindo (C-D) classification [13]. The key factors under analysis in this study were the occurrence of major complications and death from any cause within 30 days after the operation.

Statistical analysis

All statistical analyses were performed using SPSS Statistics version 22 for Windows (IBM Corp, Armonk, NY, USA). The analysis of the categorical variables was calculated with the χ^2 test and of the continuous variables with the Mann–Whitney U test. The ANOVA and Kruskal–Wallis tests were used for multiple statistical comparisons. To estimate risk factors, all the variables significant in univariate analysis were inserted into a cox regression analysis. Hazard risk (HR) and their 95 % confidence intervals (CI) were derived from the multivariate analyses. Statistical significance was set at $p < 0.05$.

Results

The clinical characteristics of patients with or without complications are summarized in Table 1. 1. A total of 430 patients were included in the study (with a median age of 76 years (range 65–96), 50.9 % men). The most common comorbidities were hypertension ($n = 221$, 51.4 %), coronary artery disease ($n = 100$, 23.3 %) and atrial fibrillation ($n = 70$, 16.3 %). Only 113 patients (26.3 %) had no co-existing diseases. Patients with complicated (either death or serious complication) and uncomplicated outcome were compared. Older age ($p = 0.007$, $p < 0.001$) and polypharmacy ($p = 0.001$, $p < 0.001$) were associated with higher risk of death and complications. The patients who died had more often a history of previous malignancies ($p < 0.001$, especially gastrointestinal malignancy $p < 0.001$), coronary artery disease ($p = 0.001$) or atrial fibrillation ($p < 0.001$, with warfarin therapy $p < 0.001$).

Table 1 Baseline characteristics according to surgical outcome

Variable	Morbidity			Mortality			Total	
	n	(%)	*p* value[a]	*n*	(%)	*p* value[b]	(*n* = 430)	
Age, mean (years, range)	77.8	± 7.2	0.007	79.9	± 6.6	<0.001	76.4	± 7.2
Sex, f/m	75	62	NS	29	32	NS	211	/219
BMI (kg/m^2)	26.8	± 4.5	NS	24.2	± 5.0	<0.001	26.4	± 4.7
Underweight (<18.50)	3	(33.3)	NS	7	(77.8)	<0.001	9	(2.1)
Normal weight (18.50–24.99)	47	(28.1)	NS	26	(15.6)	NS	167	(38.8)
Overweight (≥25.00)	57	(34.3)	NS	22	(13.3)	NS	166	(38.6)
Obese (≥30.00)	30	(34.1)	NS	6	(6.8)	0.026	88	(20.5)
Comorbidities								
None	28	(24.8)	NS	13	(11.5)	NS	113	(26.3)
Cardiac comorbidities[c]	101	(34.8)	NS	45	(15.5)	NS	290	(67.4)
Respiratory comorbidities[d]	16	(34.0)	NS	4	(8.5)	NS	47	(10.9)
Diabetes mellitus	24	(36.9)	NS	9	(13.8)	NS	65	(15.1)
Chronic rheumatic disease	7	(25.0)	NS	5	(17.9)	NS	28	(6.5)
Chronic kidney disease	5	(62.5)	NS	3	(37.5)	NS	8	(1.9)
Malignancies	20	(27.4)	NS	22	(30.1)	<0.001	73	(17.0)
Medication								
No medication	9	(18.4)	0.031	2	(4.1)	0.031	49	(11.4)
No anticoagulants	66	(29.3)	NS	28	(12.4)	NS	225	(52.3)
Acetylsalicylic acid	39	(33.1)	NS	10	(8.5)	0.037	118	(27.4)
Warfarin	29	(39.2)	NS	20	(27.0)	0.001	74	(17.2)
Other anticoagulants	5	(23.8)	NS	3	(14.3)	NS	21	(4.9)
Insulin therapy	11	(37.9)	NS	6	(20.7)	NS	29	(6.7)
Corticosteroids (per oral)	7	(25.9)	NS	7	(25.9)	NS	27	(6.3)
Polypharmacy (≥6 drugs)	76	(55.5)	0.001	42	(22.3)	<0.001	188	(43.7)
Previous abdominal surgery	37	(32.7)	NS	23	(20.4)	0.029	113	(26.3)

All the numbers in brackets are percentages

[a] Univariate analysis of patients with complications compared to patients without complications

[b] Univariate analysis of patients who died compared to patients who survived

[c] Atrial fibrillation ($n = 70$, 32.9 % mortality, $p < 0.001$), congestive heart disease, coronary artery disease ($n = 100$, 24 %, $p = 0.001$), hypertension and other cardiac comorbidities

[d] Asthma, chronic pulmonary disease, other respiratory disease

The absence of comorbidities did not statistically decrease mortality ($p = 0.341$). However, patients with no previous medication had both lower mortality ($p = 0.031$) and morbidity ($p = 0.031$). Mortality was also significantly lower in patients with acetylsalicylic acid medication ($p = 0.037$). Obesity was not associated with higher mortality; instead the surgical outcomes on underweight patients were significantly poorer ($p < 0.001$).

The most common diagnoses were cholecystitis ($n = 139$, 32.3 %, incidence of 125 per 100,000 elderly inhabitants), incarcerated hernia ($n = 60$, 13.9 %, 54 per 100,000) and malignancy related ($n = 50$, 12.0 %, 45 per 100,000). Acute appendicitis was the fourth most common reason for surgery. Of 59 patients, 46 had positive histology for acute appendicitis, while remaining 13 had normal histology ($n = 46$, 10.7 %, 41 per 100,000). Outcome varied between diagnoses. Figure 1 and Table 2 demonstrates the distribution of diagnoses.

In the 57 patients (13.3 %) who were misdiagnosed in the emergency department, the risk of complications was found to be higher. Higher ASA classification indicated higher morbidity ($p = 0.003$) and mortality ($p < 0.001$). The surgeon's experience had no effect on the outcome. Of all 112 laparoscopic procedures, 29 (25.9 %) required conversion to open surgery. Mortality in open surgery was statistically significantly higher ($p = 0.002$). Only four patients died after laparoscopic operation, all of them after cholecystectomy. The perioperative data are presented in Table 3.

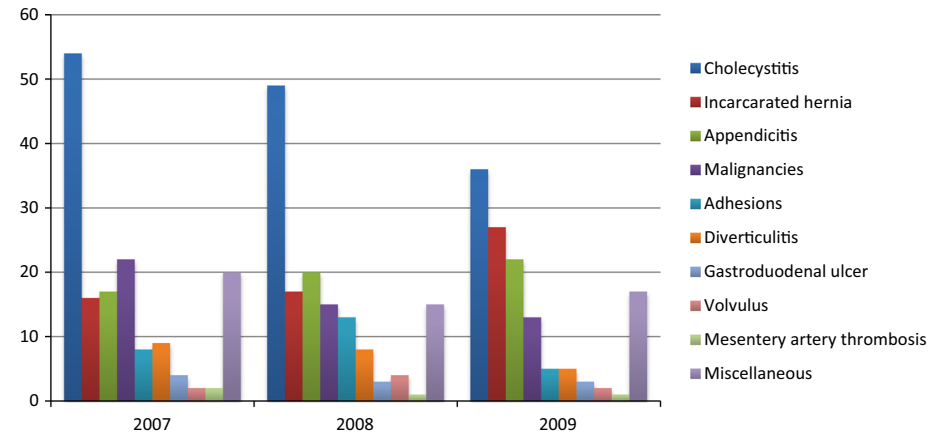

Fig. 1 Emergency abdominal operations performed between 2007 and 2009

Table 2 Major outcome and complications by procedure

Surgical diagnosis	*n*	(%)	*n*/100,000	Morbidity (%)	Mortality (%)
Acute cholecystitis	139	(32.3)	125	28.1	5.8
Incarcerated hernia	60	(13.9)	54	30.0	13.3
Inguinal	24	(5.6)	22	29.2	12.5
Femoral	18	(4.2)	16	22.2	5.6
Other	18	(4.2)	16	38.9	22.2
Malignancies	50	(11.6)	45	28.0	28.0
Large bowel	25	(5.8)	23	36.0	20.0
Palliative	20	(4.7)	18	15.0	40.0
Acute appendicitis	46	(10.7)	41	23.9	0.0
Intestinal obstruction caused by adhesions	26	(6.0)	23	61.5	15.4
Acute diverticulitis	22	(5.1)	20	50.0	36.4
Gastro-duodenal ulcer	10	(2.3)	9	60.0	10.0
Volvulus	8	(1.9)	7	62.5	25.0
Mesentery artery thrombosis	4	(0.9)	4	0.0	100
Miscellaneous	65	(15.1)	58	26.2	18.5
Total	430	(100)	387	31.9	14.2

All numbers in brackets are percentages

The overall mortality and morbidity were 14.2 and 31.9 %, respectively. Medical complications (17.2 %, C-D $\geq$ III 55.6 %) were more common than surgical complications (14.9 %, C-D III $\geq$ 59.4 %). There were no complications directly associated with anaesthesia. In univariate analysis, patients with complicated outcome were compared to patients without complications. Medical complications ($p < 0.001$) including postoperative heart failure ($p = 0.011$), pneumonia ($p = 0.001$) and sepsis ($p = 0.003$) were associated with higher mortality. Conservative treatment was sufficient in most cases. Reoperations were rare (30 patients, 7.0 %), with no associated significant rise in mortality. Of the mortalities, one patient died during the operation and the rest during the 30-day follow-up. Most common causes of death were infections and malignancy related. Tables 2, 4 and 5 presents the prevalence of postoperative complications and death.

The results were compared to those of our earlier study. The mean age was 76 years in both studies (with 49 % being female in the new data and 50 % in the older study). In the older study, more patients were considered to be ASA classes three or more. Four of the most common diagnoses were the same. Incidence of cholecystitis was higher (32 vs. 18 %) and the incidence of gastro-duodenal ulcer disease was lower (2 vs. 10 %). Overall mortality in earlier study was 22 % and morbidity 26 %. The mortality of patients aged 65–69, was 6 % in both studies. In older patients, the older study reported a higher risk of dying,

Table 3 Perioperative data and outcomes

Variable	*n*	(%)	Morbidity		Mortality	
			(%)	*p* value[a]	(%)	*p* value[b]
Misdiagnosed when admitted to hospital	57	(13.3)	(56.1)	$p < 0.001$	(19.3)	NS
Preoperative ASA						
ASA I–II	255	(59.3)	(26.3)	$p = 0.003$	(5.5)	$p < 0.001$
ASA ≥III	175	(40.7)	(40.0)	$p = 0.003$	(26.9)	$p < 0.001$
Preoperative antibiotics	409	(95.1)	(32.5)	NS	(14.7)	NS
Surgeon's experience						
Specialist	241	(56.0)	(34.9)	NS	(15.8)	NS
Other subspeciality	75	(17.4)	(33.3)	NS	(17.3)	NS
Resident	114	(26.5)	(24.6)	NS	(8.8)	NS
Surgical technique						
Open surgery	347	(80.7)	(33.7)	NS	(16.7)	$p = 0.002$
Laparoscopic surgery	83	(19.3)	(24.1)	NS	(3.6)	$p = 0.002$
Conversion required	29	(6.7)	(37.9)	NS	(3.4)	NS
Postoperative anticoagulation	302	(70.2)	(39.7)	$p < 0.001$	(18.5)	$p < 0.001$
Treatment in the ICU	48	(11.2)	(62.5)	$p < 0.001$	(31.3)	$p < 0.001$

All the numbers in brackets are percentages

[a] Univariate analysis of patients with complications compared to patients without complications

[b] Univariate analysis of patients who died compared to patients who survived

Table 4 Postoperative complications and mortality

Variable	*n*	(%)	Mortality within group	
			(%)	*p* value[a]
Morbidity	137	(31.9)		
Medical complication	74	(17.2)	(28.4)	$p < 0.001$
Heart failure	35	(8.1)	(28.6)	$p = 0.011$
Pneumonia	23	(5.3)	(39.1)	$p < 0.001$
Sepsis	5	(1.2)	(60.0)	$p = 0.003$
Surgical complication	64	(14.9)	(12.5)	NS
Wound dehiscence	17	(4.0)	(50.0)	$p = 0.001$
Conservatively treated	111	(25.8)	(19.8)	$p = 0.048$
Reoperation required	30	(7.0)	(23.3)	NS
30-days mortality	61	(14.2)		

All numbers in brackets are percentages

[a] Univariate analysis of patients who died compared to patients who survived

especially in the oldest age group (21 vs. 43 %). The mortality in ASA classes II, III or more was almost the same. The comparison between the two studies is presented in Table 6.

To estimate the risk factors behind higher mortality, a multivariate analysis was performed after bivariate correlation analysis. All the statistically significant variables (age, BMI, previous history of malignancies, coronary artery disease, atrial fibrillation (warfarin therapy), acetylsalicylic acid medication and history of no previous medication, surgical technique, ASA classification) were inserted into a cox regression analysis. The results of the multivariate analysis are shown in Table 7. Patients with increased mortality were older ($p = 0.014$), had atrial fibrillation more often ($p = 0.017$), had a previous history of malignancy ($p = 0.010$) or were underweight (BMI ≤ 18.50, $p = 0.001$). ASA grade III or more ($p < 0.001$) was associated with poor outcome, as there was also an association with higher mortality after open surgical procedures ($p = 0.029$).

Discussion

The main result of this study was that regardless of technical progress, mortality and morbidity among elderly patients requiring emergency abdominal surgery is still surprisingly high. Patient's age, low body mass index, atrial fibrillation, previous history of malignancy and the surgical technique chosen were found to increase mortality. In contrast to postoperative surgical complications, medical complications were associated with higher mortality. ASA class three or more predicted higher morbidity and mortality.

Table 5 Postoperative mortality and causes of death following surgery

Variable	65–69 years ($n = 98$)		70–84 years ($n = 270$)		Over 85 years ($n = 62$)		All patients ($n = 430$)	
	n	(%)	*n*	(%)	*n*	(%)	*n*	(%)
Malignancy related	6	(6.1)	10	(3.7)	1	(1.6)	17	(4.0)
Systemic infection	0	(0.0)	17	(6.3)	4	(6.5)	21	(4.9)
Pneumonia	0	(0.0)	5	(1.9)	3	(4.8)	8	(1.9)
Other infection	0	(0.0)	1	(0.4)	0	(0.0)	1	(0.2)
Cardiovascular	0	(0.0)	3	(1.1)	1	(1.6)	4	(0.9)
Other	0	(0.0)	3	(1.1)	3	(4.8)	6	(1.4)
Unknown	0	(0.0)	3	(1.1)	1	(1.6)	4	(0.9)
30-days mortality	6	(6.1)	42	(15.6)	13	(21.0)	61	(14.2)
In-hospital mortality	2	(2.0)	27	(10.0)	10	(16.1)	39	(9.1)
90-days mortality	7	(7.1)	61	(22.6)	18	(29.0)	86	(20.0)
360-days mortality	9	(9.2)	73	(27.0)	23	(37.1)	105	(24.4)

All numbers in brackets are percentages

Table 6 The results of surgery compared to the previous study

Variable	Kettunen et al. [5] ($n = 201$)	Our present study ($n = 430$)
Age, year (mean, range)	76 (65–98)	76 (65–96)
Sex, female	50 %	49 %
Cardiovascular disease	52 %	67 %
Diabetes mellitus	12 %	15 %
Chronic pulmonary disease	11 %	11 %
Previous history of malignancies	12 %	17 %
ASA 1–2	24 %	59 %
ASA ≥3	76 %	41 %
Diagnose: Acute cholecystitis	18 %	32 %
Diagnose: Acute appendicitis	16 %	11 %
Diagnose: Incarcerated hernia	11 %	14 %
Diagnose: Malignancy	11 %	12 %
Diagnose: Gastro-duodenal ulcer	10 %	2 %
Morbidity, *n* (%)	22 %	32 %
Mortality	22 %	14 %
Mortality in patients aged 65–69	6 %	6 %
Mortality in patients aged 70–84	22–27 %	16 %
Mortality in patients aged over 85 years	43 %	21 %
Mortality in patients with ASA I–II	4.8 %	6 %
Mortality in patients with ASA ≥III	28 %	27 %

As our study showed, fewer surgeries were required for complicated gastro-duodenal ulcer disease. In addition to incidence, deaths were also less frequent in our series. In comparison to other newer data, Soreide et al. reported similar incidence (3.8–14/100,000) and mortality (10–25 %) in their study [14]. The lower risk of complicated peptic ulcer disease might be explained by the increased use of Helicobacter pylori eradication therapy and PPI-medication.

Our study reported high mortality in patients with diverticular disease. In comparison, Lidsky et al. reported 9.7 and 17.8 % mortality and 45.5 and 44.1 % morbidity in elderly (aged 65–79) and super-elderly (aged over 80) patients [15]. Zingg et al. reported higher mortality,

Table 7 Predictors of 30-days mortality according to operation performed

Variable	Mortality		
	HR	95.0 % CI	*p* value
Age	1.05	1.01–1.10	0.014
Atrial fibrillation	2.12	1.14–3.93	0.017
Malignancies	2.22	1.21–4.09	0.010
BMI			
Normal weight	Reference group		
Underweight (BMI $\leq$ 18.50)	4.80	1.87–12.3	0.001
ASA grade III or more	4.28	2.00–9.18	<0.001
Surgical technique (open surgery)	3.23	1.13–9.24	0.029

especially after Hartmann's procedure (29.2 %) [16]. In our study, only 22 patients were operated on due to diverticulitis (incidence of 20 per 100,000 elderly persons) and all were operated on with Hartmann's procedure.

In our study, surgical treatment of acute appendicitis was safe. There were no mortalities and the complication rate in appendectomy was 23.9 %. There was no significant difference in comparison to the earlier study. Instead, it is noteworthy that 77.8 % of patients had positive histology for appendicitis, the rest being normal. The use of CT might improve diagnostic accuracy in elderly patients [17].

Although age was found to be significantly and independently associated with higher mortality, its real significance is debatable (HR 1.05, with 95 % CI 1.01–1.10). If compared to the earlier study, the results for extremely old patients seem to be getting better. This may in part be due to higher life expectancy. From 1990 to 2009, life expectancy at the age of 65 rose from 13.7 years in males and 17.7 years in females to 17.2 and 21.2 years, respectively [18]. Nevertheless mortalities occur, and they are more common in older patients. In contrast to younger patients, the importance of proper diagnosis and the treatment of post-operative infections seem to be critical, as we can see in the causes of deaths.

In our present study, more than half of the patients were considered obese, which is a much higher percentage than among general elderly population in Finland [19]. Increasing obesity may explain the higher prevalence of cholecystitis compared to that reported in the earlier study, as described in the preceding paragraphs [20]. In addition, the mortality of elderly patients undergoing cholecystectomy was surprisingly high. Kuy et al. reported 3.2 % mortality after cholecystectomy in patients aged 80 or more [21]. However, they stated that reported mortality may have been too low, because readmissions and post-discharge mortality were not captured. In another epidemiologic study on Scottish population, mortality was especially high in the elderly population and in patients who had acute causes for surgery [22]. We focused especially on emergency admissions, and mortalities were precisely documented, also including post-discharge deaths.

In addition to obesity, surprisingly polypharmacy and warfarin therapy were also more common than in general elderly population [23]. In our data, 43.7 % of patients had six or more, and 16.7 % of patients ten or more medications. In the univariate analysis, polypharmacy was associated with poorer results, but in the multivariate analysis no such association was found. Most patients with multiple medications had a disease independently associated with higher mortality, such as atrial fibrillation. Furthermore, instead of counting the total amount of medication taken we believe we should focus on medication with systematic effect, as some of the drugs used could be classified as a risk-reducing medications (for example statins) and some most likely have little to no systematic effect (for example vitamins). In our study, we did a separate analysis only for corticosteroids, different anticoagulatives and insulin therapies. More studies on this subject are needed.

As initially noted, postoperative medical complications were more common than surgical complications. Only wound dehiscence was linked to higher mortality in the univariate analysis, but in the multivariate analysis no association was found. Nevertheless, it was the most common reason for reoperation. Mortality was highest in and after open surgeries. However, there was a significant patient selection bias because laparoscopic surgery was not initially chosen for patients with the highest preoperative risk or for those with assumed complicated diagnoses.

This study was a retrospective analysis of the results of emergency abdominal surgery on the elderly. Due to the retrospective nature of the study, we were unable to gather some data, for example, on patients' lifestyles. There were also problems with documentation. Surgical complications were accurately documented, medical complications, on the other hand, were not. To gather more reliable data on medical complications for our analysis, we had to go through all the perioperative imaging and nursing reports. The mortalities, however, were precisely documented. As we discovered, the results of emergency abdominal surgery vary not only between diagnostic groups but also by the surgical technique used. There were many surgeons who were highly experienced and some with less experience of emergency abdominal surgery on the elderly. Due to this, the surgical technique chosen may have varied between patients. The same variation was also seen in the quality of perioperative treatment.

Conclusions

In conclusion, this study shows that, regardless of technical progress, postoperative morbidity is still an important problem in emergency abdominal surgery performed on elderly. Even though we had more complications in our study than in our earlier study, fewer patients died in our series.

Compliance with ethical standards

Conflict of interest The authors declare that there are no conflicts of interest.

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J Gastrointest Surg (2016) 20:1028–1033
DOI 10.1007/s11605-016-3076-4

ORIGINAL ARTICLE

Severe Sepsis in Elderly Patients Undergoing Gastrointestinal Surgery—a Prospective Multicenter Follow-up Study of Finnish Intensive Care Units

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Received: 30 October 2015 / Accepted: 4 January 2016 / Published online: 14 January 2016

Abstract
Background We aimed to evaluate the outcome of elderly patients with severe sepsis after alimentary tract surgery.
Methods A prospective study was conducted in 24 intensive care units (ICU) in Finland. Four thousand five hundred consecutive patients were admitted to ICUs and 470 patients fulfilled the criteria for severe sepsis. All patients who had undergone gastrointestinal surgery were included. The outcomes of elderly (≥65 years) and younger patients were compared. The key factor under analysis was death from any cause during the hospitalization or within 1 year after the surgery.
Results A total of 73 elderly patients (and 81 younger patients) were found to have severe alimentary tract surgery-related sepsis. The mean age of the elderly patients was 76.4 years, and 56.2 % were female. The most common indication for surgery was acute cholecystitis (21.9 %), followed by acute diverticulitis (13.7 %), and gastroduodenal ulcer (13.7 %). The anatomic site of the infection was intra-abdominal in 86.3 % of cases, the second most common being pulmonary (13.7 %). In-hospital mortality was 47.9 % and 1-year mortality 64.4 %. Of the discharged patients, 31.6 % died within 1 year. Patients who died were older and more frequently had concomitant conditions. The ICU scoring systems (APACHE, SAPS, and SOFA) and elevated lactate levels were predictive of increased mortality.
Conclusion Severe sepsis among the elderly is a rare but often-fatal infectious event. In addition to high in-hospital mortality, it is also associated with significant 1-year mortality.

Keywords Elderly patients · Sepsis · Shock · Septic · Gastrointestinal diseases · General surgery

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Introduction

Aging has emerged as one of the world's most pervasive economic and health problems. Europe currently has the highest proportion of older people in the world, and Finland is one of the most rapidly aging countries in Europe. However, aging and its consequences are not confined to Finland, Europe, or other developed countries; its effects are also apparent in developing countries. In Finland, the proportion of elderly people (>65 years old) is estimated to reach 25 % before 2030.[1] A similar trend can be observed globally. According to a report by the United Nations, nearly one person out of every six is projected to be at least 65 years old by 2050.[2]

While the proportion of elderly people increases, so does the prevalence of age-associated diseases. Gastrointestinal emergencies and malignancies are related to advancing age. Gastrointestinal systemic infections will increase

concomitantly, with more elderly patients and more surgical procedures.[3,4] While surgery-associated systemic infection is a challenging event in any patient, comorbidities, poor functional status, and polypharmacy all contribute to poorer survival especially in the elderly.[5,6] Infections are associated not only with increased mortality but also with prolonged hospital stays, increased intensive care requirements, need for additional surgeries, and increased costs.

Severe sepsis in patients undergoing gastrointestinal surgery has not been widely studied.[7–9] In this prospective multicenter follow-up study, we aimed to evaluate the incidence and 1-year outcomes of elderly patients with severe gastrointestinal sepsis. The nationwide results of all sepsis patients have been reported earlier (Finnsepsis Study).[10] Here, we report the outcomes of elderly patients with severe sepsis related to alimentary tract surgery.

Methods

All patients over 18 years of age were screened for severe sepsis in 24 multidisciplinary intensive care units (ICUs) in 19 participating hospital districts in Finland. This included all the ICUs in the participating hospitals and hospital districts. The catchment area in the study included 3,743,265 adult inhabitants, which amounts to 90.6 % of the Finnish adult population. During the study period (November 1, 2004 to February 28, 2005), these ICUs treated 4500 patients, of whom 470 fulfilled the severe sepsis criteria. The study protocol has been published elsewhere.[10] In the present study, we included all elderly patients (aged ≥65 years) with severe sepsis who had undergone alimentary tract surgery. The outcomes were compared to those of patients who had undergone surgery but were younger than 65 years.

Severe sepsis was defined according to criteria including a systemic inflammatory response, suspected or confirmed infection, and acute organ failure.[11] The sequential organ failure assessment (SOFA) score was calculated daily to ascertain the severity of the organ failure. Acute Physiology and Chronic Health Evaluation (APACHE) II and Simplified Acute Physiology (SAPS) II scores were analyzed and used in this study for purposes of prognosis.[12,13] The patient information was collected from the Quality Consortium database (Intensium). Consent from the appropriate ethics committees was obtained from each participating hospital. Population data and 1-year mortality data were obtained from Statistics Finland. No information on causes of death was collected.

The key factor under analysis in this study was death from any cause after surgery. One-year, in-hospital, and ICU mortality rates were analyzed. Age-adjusted mortality of the study group was compared to age-adjusted mortality of general population. Indications for surgery, the baseline characteristics of the study, and the control groups were also compared. The risk factors for higher mortality were analyzed.

Unless otherwise stated, data are presented as absolute values and percentages or means with standard deviations. We used chi-square test to analyze the categorical variables and one-way analysis of variance (ANOVA) for the continuous variables. Kaplan-Meier was used to estimate survival. Statistical significance was set at $p < 0.05$. All statistical analyses were performed using SPSS Statistics version 22 for Windows (IBM Corp, Armonk, NY, USA).

Results

A total of 154 patients (73 elderly patients and 81 younger patients) fulfilled the inclusion criteria for the present study. The mean age of the elderly and non-elderly patients was 76.4 years (65–88 years) and 50.1 years (18–64 years), respectively. Fifty-six percent of the elderly and 30 % of younger patients were female. Concomitant diseases, excluding chronic liver disease, were more common in the elderly patients. The anatomic site of the infection was intra-abdominal in 86.3 % of cases, the second most common anatomic site being pulmonary (13.7 %). Almost half (47.9 %) of the infections were hospital acquired. In the elderly, ICU, hospital, and 1-year mortality rates were 24.7 % (compared to 9.9 % in younger patients), 47.9 % (14.8 %), and 64.4 % (22.2 %), respectively. The clinical characteristics of both elderly and non-elderly patients are summarized in Table 1.

Table 1 Baseline characteristics of elderly (≥65 years) and non-elderly patients (<65 years)

Variable	Elderly $n = 73$	Non-elderly $n = 81$
Age, years, mean	76.4 (±6.3)	50.1 (±11.1)
Gender, female	56.2 %	29.6 %
BMI, kg/m^2, mean	26.6 (±4.4)	27.1 (±5.8)
Cardiac disease	42.5 %	28.4 %
Diabetes	20.5 %	9.9 %
Chronic pulmonary disease	8.3 %	2.5 %
Chronic renal disease	4.1 %	3.7 %
Chronic hepatic disease	1.4 %	11.1 %
Corticosteroid medication	11.0 %	4.9 %
Cancer chemotherapy	2.7 %	1.2 %
Anatomic site of the infection, intra-abdominal	86.3 %	76.5 %
Anatomic site of the infection, pulmonary	13.7 %	16.0 %
Hospital acquired infection	47.9 %	58.0 %
ICU mortality	24.7 %	9.9 %
Hospital mortality	47.9 %	14.8 %
1-year mortality	64.4 %	22.2 %

The most common indication for surgery in elderly patients was acute cholecystitis ($n=16$, 21.9 %), followed by acute diverticulitis ($n=10$, 13.7 %) and gastroduodenal ulcer ($n=10$, 13.7 %). Mortality rates varied between diagnoses. Hospital mortality rate was decidedly lowest among patients with cholecystitis. Regardless of the low in-hospital mortality of patients with cholecystitis, 43.8 % died within 1 year. All the patients who had undergone surgery because of malignancy died within 1 year. The distributions of diagnoses and outcomes are presented in Table 2.

Of the elderly patients 71.2 % were less and 28.8 % more than 80 years old. In addition to elderly and younger patients, patients aged less than 65 years, 65 to 79 years, and over 80 years were also compared. The distribution of diagnoses differed between these groups. Younger patients had acute pancreatitis more often than did older patients, who more often had acute cholecystitis or acute diverticulitis. The comparisons between the different age groups are presented in Table 3.

Hospital and 1-year mortality rates increased with age, being 14.8 and 22.2 % among patients aged less than 65 years and 47.9 and 64.4 % among patients aged 65 years or more. One-year mortality among patients aged 80 years or more was 90.5 % (only two patients survived over 1 year). Of the discharged patients, 8.7 % non-elderly patients, 17.2 % patients aged 65 to 79 years, and 77.8 % patients aged more than 80 years died within 1 year. Mortality in general was highest among the oldest patients. None of the patients aged 85 or more survived longer than 1 year. The Kaplan-Meier curve for the survival of different age groups is presented in Fig. 1.

Survivors ($n=107$, 69.5 %) of all age groups were compared to non-survivors ($n=47$, 30.5 %). Patients who died were older ($p<0.001$) and suffered more often from cardiac diseases ($p=0.040$), chronic renal ($p=0.041$), and chronic lung disease ($p=0.044$) and were undergoing cancer chemotherapy ($p=0.008$). In addition, elevated lactate levels (≥1.6 mmol/l, $p<0.001$) in the first 24 h after admission to ICU, higher APACHE ($p<0.001$) and higher SAPS ($p<0.001$) scores were also predictive of poorer outcome. SOFA score was also higher in patients who died ($p<0.001$). Of the elderly patients, none with APACHE score over 40 or SAPS score over 100 survived. Septic shock and mechanical ventilation did not increase mortality in a

Table 2 Distribution of diagnoses and outcomes of the treatment in the elderly (age ≥ 65 year)

Diagnosis	Number	Percent	Hospital mortality (%)	1-year mortality (%)
Acute cholecystitis	16	21.9	18.8	43.8
Acute diverticulitis	10	13.7	60.0	70.0
Gastroduodenal ulcer	10	13.7	50.0	60.0
Malignancy	8	11.0	75.0	100
Intestinal obstruction	7	9.6	57.1	85.7
Mesenterial arterial thrombosis	4	5.5	50.0	75.0
Pancreatitis	3	4.1	66.7	100
Trauma	2	2.7	100	100
Incarcerated hernia	2	2.7	0.0	0.0
Esophageal perforation	1	1.4	100	100
Miscellaneous	10	13.7	40.0	40.0
Total	73	100	47.9	64.4

Table 3 Incidence of diseases and outcome of the treatment in different age groups

Variable	<65 years $n=81$	65–80 years $n=52$	>80 years $n=21$
Cholecystitis	8.6 %	19.2 %	28.6 %
Diverticulitis	7.4 %	15.4 %	9.5 %
Gastroduodenal ulcer	9.9 %	13.5 %	14.3 %
Malignancy	7.4 %	7.7 %	19.0 %
Pancreatitis	18.5 %	5.8 %	0.0 %
Trauma	6.2 %	1.9 %	4.8 %
Length of ICU stay, days, mean	8.7 (±9.3)	7.2 (±8.1)	4.5 (±4.7)
Length of hospital stay, days, mean	29.8 (±20.3)	25.6 (±36.9)	10.4 (±8.0)
Hospital mortality	14.8 %	44.2 %	57.1 %
1-year mortality	22.2 %	53.8 %	90.5 %
Post-discharge mortality	8.7 %	17.2 %	77.8 %

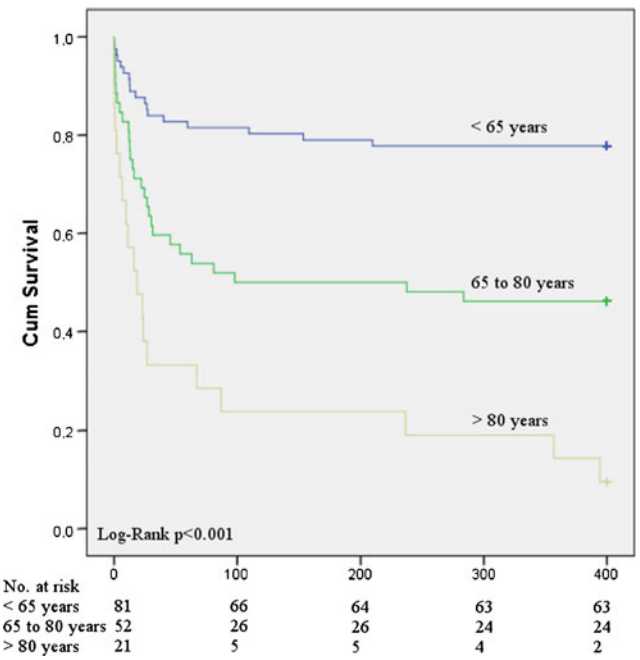

Fig. 1 One-year mortality among patients with severe sepsis according to age

statistically significant way. However, both were more common among the patients who died. The comparison between survivors and non-survivors is presented in Table 4.

Discussion

In addition to high in-hospital mortality, severe sepsis is associated with significant 1-year mortality. In earlier studies, in-hospital mortality rates in patients with sepsis generally have reportedly ranged between 20 and 60 %.[14–18] By using prospectively collected multicenter data, we were able to evaluate the short- and long-term outcome on elderly patients with severe alimentary tract surgery-related sepsis.

Our study shows that the prognosis of severe sepsis in the elderly is dismal. Both in-hospital mortality (47.9 vs. 14.8 %) and post-discharge deaths (64.4 vs. 22.2 %) were significantly more common among the elderly. When we compared our data to the annual reports by Statistics Finland, elderly patients discharged from hospital were at least seven times more likely to die within 1 year of discharge than Finns of the same age group. It is unclear why sepsis is associated with such a high post-discharge mortality. In a cohort study of 30,239 inhabitants, Wang et al.[19] have analyzed long-term mortality of 970 patients with sepsis. They found that a wide range of conditions, including cardiovascular and pulmonary diseases, caused 70 % of the registered deaths. They concluded that patients with concomitant diseases might be more susceptible to sepsis and therefore at increased risk of death. Surprisingly, when comparing our data to reports on Finnish elderly population, concomitant diseases were equally or less common than in elderly population in general.[20,21] It is therefore possible that the process culminating in death is initiated by sepsis. More studies in this subject are needed.

As already noted, both the incidence of sepsis and the associated mortality vary between indications necessitating surgery.[22,23] In our study, mortality was lowest in patients with acute cholecystitis. Despite being an easily treatable disease, 1-year mortality was still as high as 43.8 % in patients with acute cholecystitis. Riall et al.[24] analyzed Medicare data of 29,818 elderly patients with acute cholecystitis. They found 9.5 % 1-year mortality in patients aged 65 years or more who had undergone cholecystectomy (the number of patients with sepsis or severe sepsis was not reported). It is unlikely that the higher mortality in our data is attributable to the quality of perioperative care, as in Finland post-operative mortality in general is among the lowest in Europe.[25] Instead, we believe that this confirms that in elderly patients with severe sepsis, the outcome is poor regardless of treatment.

The burden of sepsis on the health care system is indisputable. Sepsis occurs in approximately 10 % of US hospital patients, but it contributes to as many as half of all hospital deaths.[26] Sepsis may originate at almost any anatomic site of infection, but alimentary tract surgery, especially emergency surgery, has been associated with increased risk for developing septic infections.[22,23] Our study enables us to provide

Table 4 Risk factors for higher in-hospital mortality in all patients undergoing surgery (surviving patients compared to non-surviving patients)

Variable	Surviving patients $n = 107$	Non-surviving patients $n = 47$	p value
Age, years, mean (min, max)	58.9 (18–87)	72.3 (44–88)	<0.001
Gender, female	39.3 %	48.9 %	0.263
Cardiac disease	35.3 %	53.2 %	0.040
Diabetes	11.2 %	21.3 %	0.100
Chronic pulmonary disease	2.9 %	11.1 %	0.041
Chronic renal disease	2.4 %	11.4 %	0.044
Chronic hepatic disease	5.8 %	8.9 %	0.485
Corticosteroid medication	6.7 %	11.1 %	0.367
Cancer chemotherapy	0.0 %	6.7 %	0.008
APACHE, mean	20.3 (±7.6)	28.6 (±9.2)	<0.001
SAPS, mean	39.4 (±13.9)	57.4 (±18.4)	<0.001
SOFA, mean	7.2 (±3.2)	10.3 (±3.7)	<0.001
Lactate, mmol/L, mean	2.3 (±2.0)	4.3 (±3.5)	<0.001
Required vasoactive medication	43.0 %	40.4 %	0.767
Septic shock	65.4 %	74.5 %	0.267
Mechanical ventilation	77.6 %	89.4 %	0.085
CPAP ventilation	25.2 %	21.3 %	0.597
Length of ICU stay, mean (days)	7.8 (±8.4)	8.7 (±8.6)	0.530
Length of hospital stay, mean (days)	21.0 (±19.7)	17.6 (±35.2)	0.447

rough estimates for the incidence of severe sepsis or septic shock. Hakala et al.[27] analyzed all fatal surgical and procedure-related complications in Finland from 2006 to 2010. By using their data, we can estimate that 0.8 % of patients undergoing gastrointestinal surgery in Finland required ICU care for severe sepsis or septic shock. Population aging will increase this burden even further. Due to aging, the number of working-aged people is diminishing while that of older people increases. This will exert continuous pressure on the health care system. As life expectancy increases, the prevalence of age-associated diseases likewise increases. The number of elderly patients requiring ICU treatment for severe sepsis can be predicted to further increase in the future.[15,18]

In our study, mortality was significantly higher among older, multi-morbid patients. The mortality was higher in patients with comorbidities including cardiac, chronic pulmonary, and chronic renal diseases. The risk was also higher in patients on cancer chemotherapy. The importance of age and comorbidities has been reported in several studies.[15,19,28–32] Patients who died also had higher lactate levels on admission to the ICU. The prognostic value of raised blood lactate levels has already been well established.[33] The scoring systems used in the ICUs (APACHE, SAPS, and SOFA score) predicted higher mortality. Martin et al.[15] found a high risk of death among patients with organ failure. They analyzed hospital discharge data on over 10 million cases of sepsis in the USA and found that patients with no organ failure or with organ failure had respectively a 15 and 70 % of mortality. In contrast to earlier studies, we found no statistically significant increase in mortality in patients with either septic shock or those requiring mechanical ventilation while in the ICU.[17,34]

In our study, infection resulted from surgical complications or was caused by the infection necessitating surgery. Several sets of guidelines have been published for both preventing post-operative infectious complications as well as treating septic patients.[35–37] These guidelines have included instructions for resuscitation, use of prophylactic antibiotics, pre-operative screening for microbes, source control in septic infection, and scheduling of surgery. It is known that rapid diagnosis, proper treatment with both antibiotics and supportive therapy, and also source control are crucial.[35] Sepsis should be diagnosed early, preferably in primary health care or outpatient clinics.[38] Antibiotic treatment should be initiated immediately when sepsis is detected and blood cultures are taken.[35] However, physiological aspects and poor cooperation often make diagnosis difficult in the elderly.[32,39,40] When there is a suspicion of sepsis, imaging studies may reduce diagnostic delay. The source of the infection should be controlled using the appropriate methods. Azuhata et al.[8] emphasized the importance of delay by stating that the source control should be performed within 6 h of the detection of sepsis unless septic shock is present, in which case pre-operative stabilization may be necessary.

Our study has some limitations. First of all, the size of the study population sample was relatively small. Second, we included only patients treated in the ICU. This may have caused bias, as some of the patients may have been restricted from admission to the ICU or may have been treated in intermediate care or post-operatively on the recovery ward. Third, the large number of post-discharge deaths may also be explained by restrictions on treatment during or after the ICU stay. These may, for example, have included possible readmissions to the ICU. Finally, not all the ICUs in Finland participated in the study. However, 90.6 % of the Finnish population lived at the time of the study in the catchment areas of attending hospitals. We therefore consider that the nationwide treatment of sepsis patients in Finnish intensive care units was accurately represented in the study population. The data was moreover obtained by daily prospectively monitoring patients during the course of the study. This enabled us to obtain precise data. The data was also gathered after the discharge.

In conclusion, severe sepsis is a rare but often-fatal event in gastrointestinal surgery performed on elderly patients. As comorbidities are more common and functional status not optimal, elderly patients are at higher risk of adverse outcome. Rapid diagnosis and appropriate treatment are crucial. As the detection of sepsis is time-wise critical, new approaches are needed for detecting septic events as early as possible. Guidelines for both preventing and treating severe sepsis are needed. In the case of elderly patients, the probable benefits and possible risks of the treatment need to be assessed carefully when making decisions on how to proceed. Decisions should not be based solely on age; functional capacity and comorbidities must also be included in decision-making.

Acknowledgments The authors would like to acknowledge all the researchers and study nurses taking part in the Finnsepsis Study at the participating hospitals (hospital: researcher, study nurses): (1) Satakunta Central Hospital: Vesa Lund, Marika Vettenranta, and Päivi Tuominen; (2) East Savo Central Hospital: Markku Suvela, Sari Hirvonen, and Anne-Marja Turkulainen; (3) Central Finland Central Hospital: Raili Laru-Sompa and Tiina Kirkhope; (4) South Savo Central Hospital: Heikki Laine, Aki Savinen, and Pekka Kettunen; (5) North Karelia Central Hospital: Sari Karlsson, Jaana Kallinen, and Vesa Parviainen; (6) Seinäjoki Central Hospital: Kari Saarinen, Johanna Kristola, and Niina Tuominen; (7) South Karelia Central Hospital: Seppo Hovilehto, Sari Melto, and Marjut Repo; (8) Kainuu Central Hospital: Tuula Korhonen, Ulla Koponen, and Kirsti Pomell; (9) Vaasa Central Hospital: Pentti Kairi and Marianne Ström; (10) Kanta-Häme Central Hospital: Ari Alaspää and Elina Helminen; (11) Lappi Central Hospital: Outi Kiviniemi and Tarja Laurila; (12) Middle Pohjanmaa Central Hospital: Tadeusz Kaminski and Tea Verronen; (13) Kymenlaakso Central Hospital: Jussi Pentti and Seija Alila; (14) Helsinki University Hospital: Ville Pettilä, Marjut Varpula, Marja Hynninen, Elina Kolho, Marja Pere, and Maiju Salovaara; (15) Helsinki University Hospital (Jorvi): Tero Varpula and Mirja Vauramo; (16) Helsinki University Hospital (Peijas): Rita Linko and Kimmo Kuusisto; (17) Tampere University Hospital: Esko Ruokonen, Pertti Arvola, Minna-Liisa Peltola, Anna-Liina Korkala, and Jani Heinilä; (18) Kuopio University Hospital: Ilkka Parviainen, Seija Laitinen, Elina Halonen, Mirja Tiainen, and Heikki Ahonen; (19) Oulu University Hospital: Tero Ala-Kokko, Jouko Laurila, Tarja Lamberg, and Sinikka Sälkiö;

and (20) West Pohja Central Hospital: Jorma Heikkinen and Kirsi Heinonen.

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Dig Dis Sci (2016) 61:3302–3308
DOI 10.1007/s10620-016-4283-2

ORIGINAL ARTICLE

Safety and Efficacy of Acute Endoscopic Retrograde Cholangiopancreatography in the Elderly

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Received: 20 March 2016 / Accepted: 16 August 2016 / Published online: 26 August 2016

Abstract
Background Endoscopic retrograde cholangiopancreatography (ERCP) is a frequent procedure in elderly patients.
Aims We aimed to determine the safety and efficacy of acute ERCP in older patients.
Methods A prospectively managed, hospital-based registry containing all ERCP procedures and complications at a tertiary referral center was used to form the study population, which consisted of consecutive elderly (≥65 years) patients undergoing acute ERCP during the 5-year study period. Indications, details, outcome, and complications of the procedure were analyzed in relation to patient age, gender, and co-morbidities.
Results A total of 480 elderly patients (median age 78; range 65–97; 48 % men) underwent 531 ERCPs during the study period. The most common indications were bile duct stones (56.1 %) and biliary obstruction caused by malignancy (33.7 %). Successful stone extraction was achieved in 72.8 %, and with an additional, planned ERCP in 96.6 % of the patients. Post-ERCP complications developed in 3.4 % of the patients. These included pancreatitis in 1.7 %, hemorrhage in 0.6 %, and duodenal perforation in 0.2 % of the patients. One of these (0.2 %) was considered severe as this patient required invasive treatments and prolonged hospital stay. The risk of complications was associated with chronic obstructive pulmonary disease and difficult cannulation. Procedure-related mortality was zero, but overall 30-day mortality was 10 %, being 24 % in the patients with malignancy.
Conclusions ERCP can be safely and efficaciously performed on elderly patients. The high mortality should be taken into consideration when selecting therapeutic options.

Keywords Endoscopic retrograde cholangiopancreatography · ERCP · Morbidity · Mortality · Aged · Elderly

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a routinely used diagnostic and therapeutic technique for biliary and pancreatic diseases. Typical indications, such as biliary obstruction caused by biliary stones or malignancy, are more common in elderly patients [1]. In spite of some decline in the need for ERCP as noninvasive diagnostic methods (such as MRI and endoscopic ultrasonography) might have replaced ERCP in some cases [2], population aging may increase demand as the typical indications become more common.

ERCP remains the riskiest routinely used endoscopic procedure, and elderly patients have depleted resources to recover from any operations, especially if the outcome is complicated. Therefore, the possible benefits and risks need to be carefully assessed for every patient. In terms of performing acute ERCP on elderly patients, little is known about the safety and efficacy. Our aim was to study the role and risk factors for ERCP in elderly patients in a prospective setting in a Finnish tertiary hospital.

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Methods

A prospectively managed, hospital-based registry containing all ERCP procedures and complications in Tampere University Hospital (average catchment area during the study period was 496,000 inhabitants, of whom 93,000 elderly people) was used to form the study population. This consisted of all consecutive patients undergoing acute ERCP at the age of over 65 years between January 2010 and December 2014. ERCP was considered acute when it was performed during a period of hospitalization beginning with an acute admission.

The following information was prospectively collected and registered: indication for ERCP, all procedures performed, difficulty of cannulation, outcome of the procedure, post-ERCP complications, and other adverse events. Patients' medical records were retrieved and reviewed for comorbidities. Cannulation was considered difficult if it either took more than 5 min, if there were more than five cannulation attempts on the papilla, or if the pancreatic duct was cannulated more than twice [3]. The medical director of Tampere University Hospital approved the protocol for the registry.

The primary outcome was incidence of procedure-related complications or death. The secondary outcome was the success of the procedure. The success rate was defined according to achievement of the pre-procedural goal set. ERCP complications (pancreatitis, hemorrhage, cholangitis, and perforation) were defined and classified according to Cotton et al. [4], and were prospectively recorded for 30 days after the procedure. Procedure-related mortality and overall 30-day mortality were extracted from the hospital records and the Population Register Centre.

All the ERCP procedures were performed by experienced endoscopists in this high-volume center. During the study period, five endoscopists performed majority of the operations (85 %), while the total number of ERCPs at the study hospital during the study period was approximately 2000. A single dose of intravenous antibiotics (i.v. cefuroxime 1.5 g; Orion Pharma, Finland) and an anti-inflammatory suppository (diclofenac 100 mg; Voltaren, Novartis, Finland) was administered to all patients before ERCP. Most ERCP procedures were performed under conscious sedation according to the local practice. The patient was sedated with i.v. midazolam (Dormicum, Roche Pharma AG, Germany) together with oxycodone (Oxanest, Takeda, Austria) and monitored by the endoscopy team. Duodenal peristalsis was reduced by administering i.v. hyoscinebutylpromide (20–40 mg; Buscopan, Boehringer Ingelheim, Germany) or i.v. glucagon (0.3 mg; Glucagen, Novo Nordisk, Denmark). Patients were monitored by pulse oximetry, and supplementary oxygen was provided when needed.

All statistical analyses were performed using SPSS Statistics version 22 for Windows (IBM Corp, Armonk, NY, USA. Differences among different patient cohorts were determined by using the Fisher's exact test for categorical variables, and for non-categorical variables with the Mann–Whitney U test. Variables of potential significance (p value ≤ 0.10) were entered into a multivariate analysis (logistic regression analysis, enter method). Statistical significance was set at $p < 0.05$. Multiple statistical comparisons were performed using multivariate logistic regression analysis (binary logistic regression, enter method).

Results

A total of 480 patients underwent 531 ERCPs during the study period. The median age of patients was 78 years (range 65–97) and 48 % of patients were men. Fifty-one patients underwent multiple ERCPs (41 patients underwent two, and five patients three procedures). The most common comorbidities were hypertension ($n = 299$, 59.3 %), coronary artery disease ($n = 114$, 21.5 %), atrial fibrillation ($n = 114$, 21.5 %), and diabetes ($n = 132$, 24.9 %). Only 106 patients (22.1 %) had no co-existing diseases. The clinical characteristics of patients are summarized in Table 1.

The two most common indications for ERCP were presence or suspicion of bile duct stones ($n = 298$, 56.1 %) and biliary obstruction caused by malignancy ($n = 179$, 33.7 %). The most common sites for malignancy were pancreas ($n = 101$, 56.4 %) and biliary tract ($n = 40$, 22.3 %). The majority of the malignancies (72.7 %) were inoperable, with the most common reason being advanced disease (86.2 %). Ten percent of the procedures were performed for other indications. These included bile leak after cholecystectomy ($n = 22$, 4.1 %) and benign biliary strictures ($n = 28$, 5.3 %). Of patients with bile leak, one had a lateral injury to the common hepatic duct (Strasberg–Bismuth D) and the rest cystic duct leak (Strasberg–Bismuth A). Figure 1 presents the distribution of diagnoses.

The procedures included sphincterotomy ($n = 388$), balloon extraction ($n = 354$), and lithotomy ($n = 180$) as the most common maneuvers. Cannulation was graded difficult in 172 cases, and despite multiple attempts and different techniques, 97 cannulation attempts (18.3 %) eventually failed in the index ERCP. The most common reason for cannulation failure was tumor growth ($n = 49$, 50.5 %). Procedure-related characteristics are presented in Table 2.

Table 1 Baseline characteristics of elderly (age ≥65 years, $n = 531$) patients undergoing acute ERCP

Variable	All patients *n* (%)	Patients with complications *n* (%)	*p* value
Age, years (mean, range)[a]	77.6 (65–97)[b]	77.0 (65–97)[c]	0.691
Gender, f/m	278 (52.4)/253 (47.6)	9 (3.2)/9 (3.6)	0.513
Hypertension	299 (56.3)	10 (3.3)	0.566
Coronary artery disease	114 (21.5)	5 (4.4)	0.339
Atrial fibrillation	114 (21.5)	1 (0.9)	0.073
Heart failure	33 (6.2)	0 (0.0)	0.309
Other cardiovascular disease	36 (6.8)	1 (2.8)	0.652
Asthma	26 (4.9)	2 (7.7)	0.218
COPD	21 (4.0)	3 (14.3)	0.030
Diabetes	132 (24.9)	5 (3.8)	0.477
Chronic kidney disease	12 (2.3)	1 (8.3)	0.342
Chronic rheumatic disease	19 (3.6)	0 (0.0)	0.513
Previous malignancy	44 (8.3)	0 (0.0)	0.205
Dementia	43 (8.1)	3 (7.0)	0.172
ASA medication	129 (24.3)	7 (4.9)	0.189
Warfarin therapy	106 (20.0)	2 (1.9)	0.268
Other antiplatelet medication (i.e., clopidogrel)	4 (0.8)	2 (50.0)	0.006
Insulin therapy	53 (10.0)	1 (1.9)	0.448
Corticosteroids	29 (5.5)	0 (0.0)	0.358

[a] Mean age (and range) of all patients[b] and patients with complications[c]

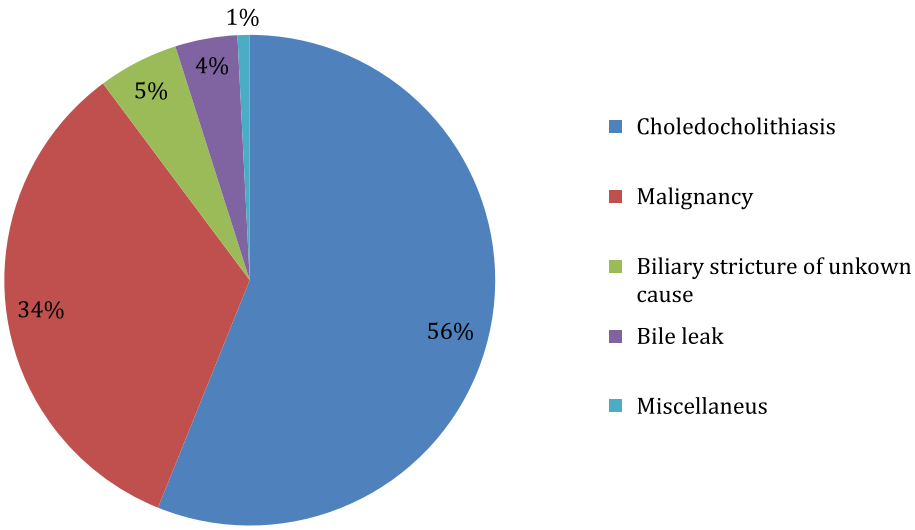

Fig. 1 Indications for acute ERCP in the elderly (age ≥65 years, $n = 531$)

Successful extraction of bile duct stones was achieved in 72.8 % of the patients in the acute index ERCP procedure and with additional scheduled ERCPs in 96.6 % of the patients. Ten patients (3.4 %) required surgical treatment or could not be treated, most often because of poor physiological status. Endoscopic procedure was successful for treating acute malignancy-related jaundice in 59.4 % of patients, while 40.0 % of patients required percutaneous biliary drainage. Among the patients with successful cannulation, a successful release of biliary obstruction was achieved in 83.6 % of cases. Out of these, 16 % later required percutaneous drainage. All the bile leaks were caused by surgery. Endoscopic procedure was sufficient for treating bile leak in 93.8 % of patients. The success remained unproven in one patient who died of sepsis a day after the procedure. However, even with this patient, bile

Table 2 Maneuvers during ERCP in the elderly (age ≥65 years, $n = 531$)

Variable	Number of maneuvers *n*	Patients with complications *n* (%)	*p* value
Sphincterotomy	388	15 (3.9)	0.261
Balloon extraction	354	13 (3.7)	0.438
Lithotomy	180	9 (5.0)	0.120
Stenting	176	7 (4.0)	0.395
Pancreatic duct brushing	106	4 (3.8)	0.507
Double-guidewire-assisted cannulation	61	5 (8.2)	0.104
Pancreatic sphincterotomy	58	7 (12.1)	0.006
Precut sphincterotomy	54	2 (3.7)	0.569
Common bile duct brushing	29	2 (6.9)	0.261
CRE dilatation	24	0 (0.0)	0.425
Endoscopic retrograde pancreatography	15	2 (13.3)	0.089
Biliary duct dilation	10	1 (10.0)	0.331
Pancreatic duct dilatation	6	0 (0.0)	0.844
Biopsy of the papilla	1	0 (0.0)	0.972
Rendezvous cannulation technique	1	0 (0.0)	0.972
Spyglass endoscopy	1	0 (0.0)	0.957

All numbers in brackets are percentages

drain output was significantly reduced after the procedure. In three patients, sphincterotomy (with no stenting) was sufficient for treatment. The others were treated with both sphincterotomy and stenting. Procedure-related outcome is presented in Table 3.

Complications occurred in 3.4 % of the patients. The most common complication was pancreatitis ($n = 9$, 1.7 %). One of these (0.2 %) was severe. The patient was hospitalized for 27 days and required percutaneous drainage of a post-pancreatitis pseudocyst, but was eventually cured. Three patients (0.6 %) had post-ERCP bleeding (all classified as moderate, requiring transfusion of less than 4 units of blood and no invasive treatments). Only one patient (0.2 %) had mild post-ERCP cholangitis. In one case (0.2 %), there was a slight leak of contrast from the CBD during the procedure, but no treatment was required. Cardiopulmonary and sedation-related complications were registered in three patients (0.6 %; allergic reaction to anesthetics in one patient, atrial fibrillation in one patient, and stroke in one patient), and one patient suffered from esophageal perforation ($n = 1$, 0.2 %; treated with stenting). There were no significant differences in postoperative morbidity in according to patients' age (Table 4).

Procedure-related mortality was zero. One patient died within the same day after the ERCP, but in the autopsy, no signs of ERCP complication were found; the cause of death (both immediate and underlying cause of death) was malignancy. One-month and 1-year mortality rates were 10.0 % ($n = 53$) and 33.5 % ($n = 178$), respectively. There was a significant difference between diagnoses: 1-month mortality of patients with bile duct stones was 2.7 %, compared to 23.5 % in patients with malignancy ($p < 0.001$). Median survival of patients with malignancy was 170 days (3–1635 days) overall and 144 days (3–1195 days) in patients with inoperable malignancy. Patients with pancreatic malignancy deemed inoperable

Table 3 Success rate of acute ERCP in elderly patients according to age (age ≥65 years, $n = 531$)

Aim of the procedure	%
Extraction of bile duct stones (279 patients)	
Extracted in the index ERCP	72.8
Successfully extracted with ERCP (including patients with additional procedure)	96.6
Decompression of biliary obstruction caused by malignancy (165 patients)	
Successfully treated with ERCP	59.4
Required percutaneous biliary drainage	40.0
Treatment of postoperative bile leak (16 patients)	
Managed with ERCP	93.8
Success of the treatment remained unproven	6.3

Table 4 Post-ERCP complications in elderly (65–79 years) and very elderly (more than 80 years) patients with no statistically significant difference in the outcomes ($p > 0.05$)

Complication	65–79 years ($n = 306$) *n* (%)	≥80 years ($n = 225$) *n* (%)	All patients *n* (%)
Pancreatitis	5 (1.6)	4 (1.8)	9 (1.7)
Hemorrhage	2 (0.7)	1 (0.4)	3 (0.6)
Perforation	1 (0.3)	0 (0.0)	1 (0.2)
Infection	0 (0.0)	1 (0.4)	1 (0.2)
Cardiovascular and sedation-related complication	2 (0.7)	0 (0.0)	2 (0.4)
Procedure-related mortality	0 (0.0)	0 (0.0)	0 (0.0)
1-month mortality (all patients)	24 (7.8)	29 (12.9)	53 (10.0)
1-month mortality (patients with gallstones)	0 (0.0)	8 (3.6)	8 (2.7)
1-month mortality (patients with malignancy)	23 (19.2)	19 (8.4)	42 (23.5)
1-year mortality	93 (30.4)	85 (37.8)	178 (33.5)

had a median survival of 121 days (5–997 days, one patient alive). Of the patients with malignancy, 46 (25.7 %) were alive a year after the ERCP. Table 4 presents the prevalence of post-ERCP complications and deaths.

Complications were more common in patients with chronic obstructive pulmonary disease ($p = 0.030$), post-operative bile leak ($p = 0.034$) and less common in patients with malignancy-related biliary obstruction ($p = 0.006$). Complication risk increased also after pancreatic sphincterotomy ($p = 0.006$) and if the cannulation was considered difficult ($p = 0.003$). In multivariate analysis (binary logistic regression analysis, enter method), chronic obstructive pulmonary disease ($p = 0.041$, OR 5.1, 95 % CI 1.1–24) and difficult cannulation ($p = 0.045$, OR 5.1, 95 % CI 1.0–25) were found to be independent risk factors for post-ERCP complications (Table 5).

Discussion

No prospective results of ERCP performed in acute circumstances in the elderly have so far been reported. In this study, a prospective hospital database was used to analyze the outcome of ERCPs performed on elderly patients after acute admission. We found that procedure-related complications were rare; ERCP was in most cases performed safely and efficaciously. Chronic obstructive pulmonary disease and difficult cannulation were independent risk factors for post-ERCP complications in this patient population. Procedure-related mortality was zero, but overall 30-day mortality was 10 %, being 24 % in the patients with malignancies.

The need for ERCP is heavily age dependent. The two typical indications, biliary obstruction caused by either bile duct stones or malignancy, accounted 90 % of all procedures performed in our series. As stated before, both indications increase with age [1]. In our study approximately 115 per 100,000 elderly inhabitants (aged 65 years or more) required acute ERCP each year. According to Statistics Finland, during the study period, the proportion of elderly people in our district rose from 17.5 to 19.8 % (+14,058 elderly inhabitants). This change is not only a characteristic of our district but also is a global trend [5]. Although there has been some decrease in the need for ERCP as noninvasive diagnostic methods, such as MRI and endoscopic ultrasonography, have replaced ERCP as a diagnostic procedure [2], there will presumably be an increase in the need for therapeutic and acute ERCPs in the future as the older population grows.

In our study, all the ERCPs were performed in an acute setting, meaning that patients were admitted to hospital from the emergency room. In this setting, ERCP seems to be safe in the elderly, and even safer than reported in earlier studies: post-ERCP complications developed in 3.4 % of the patients. An earlier meta-analysis of 21 prospective studies (also including non-acute procedures)

Table 5 Risk factors independently associated with increased risk of complications in elderly patients (age ≥65 years) undergoing acute ERCP

Variable	Complications		
	OR	95 % CI	*p* value
Chronic obstructive pulmonary disease	5091	1067–24,288	0.041
Difficult cannulation	5138	1038–25,420	0.045

reported 6.9 % morbidity in all adult patients [6], while prior studies on the elderly have reported 2.5–8.4 % morbidity rates [7–14]. As shown before, in our study, pancreatitis was the most common complication (1.7 %) [15]. According to a systematic review of post-ERCP complications in the elderly [16] the risk of post-ERCP pancreatitis ranges from 1.2 to 1.8 % depending on patient's age. In our data, the outcome was similar regardless of age; very old patients (aged 80 years or more) had similar outcomes than elderly patients (aged 65–79 years). It has been suggested that elderly people are at lower risk of post-ERCP pancreatitis than their younger counterparts, but at a similar risk of other complications. In contrast to this, in our study, all the typical complications (hemorrhage in 0.6 % and duodenal perforation in 0.2 %) were also less common than previously reported [17].

Interestingly, there were no deaths directly associated with the procedure. Earlier studies on the elderly have reported similar, but somewhat poorer outcomes, with procedure-related mortality varying from 0.6 to 1.6 % [7–9]. Despite the zero ERCP-related mortality, 10 % of the patients in our study died within 1 month of the procedure. Not surprisingly, the mortality was highest in patients with malignancy and lowest in patients with bile duct stones. Regardless of this, mortality was higher among patients with bile duct stones than among elderly Finns on average. When compared to annual reports by Statistics Finland, these patients were two to six times more likely to die within 1 year than their elderly counterparts. The significance of bile duct stone disease is debatable as there was also a high incidence of comorbidities, such as diabetes and coronary artery disease, which may explain the higher mortality in the study group.

We identified risk factors for complicated outcome. Difficult cannulation increased the risk of post-ERCP complications, as shown before [17–19]. In our study, the risk of pancreatitis was almost sevenfold (4.1 vs. 0.6 %) in patients with whom cannulation was difficult. The same was evident in other complications. Only two patients with non-difficult cannulation had subsequent complications. It should be noted that there is no globally accepted definition of difficult cannulation. In this study, we used the definition of the Scandinavian Association for Digestive Endoscopy, which includes time, cannulation attempts and pancreatic guidewire passages [3]. Complications were also more common in patients with chronic obstructive pulmonary disease.

In our study, ERCP was an excellent therapeutic procedure for treating acute biliary obstruction in the elderly. Most of the bile duct stones were retrievable in the index operation. For patients undergoing difficult procedures and with unretrievable stones, we recommend a safer approach using temporary stenting and delayed elective endoscopic stone removal. Seventy percent of the remaining stones were removable in secondary ERCP in our series, and 96.6 % of stones were removable with ERCP.

In patients with malignancy-related biliary obstruction, endoscopic stenting, if successful, provided effective long-term palliation. However, in this study, failure seemed to be surprisingly common. In most cases, cannulation failed because of tumor growth (in some cases only EGD was performed). In case of successful ERCP, several guidelines recommend using plastic stents in patients with short life expectancy and self-expanding metal stents in patients with longer life expectancy or poor physiological status contraindicating surgical treatment [20]. The main advantage of plastic stents has been considered to be their low cost. On the other hand, a recent study by Walter et al. [21] stated that higher initial costs of self-expanding metal stents are covered by longer functional time. Therefore, they concluded that self-expanding metal stents should be used for palliation in all patients, regardless of estimated survival. Further studies or updates to existing guidelines on this subject are needed. In contrast to metastatic disease, in patients with operable malignancy, there is a broad consensus that the possible risks and benefits in placing the stent should be carefully assessed, as ERCP and its possible post-procedural complications should not delay the imminent surgery [20, 22].

ERCP was moreover an excellent procedure for the treatment of cystic duct leakage in elderly patients. In one patient, the success of the procedure was undeterminable, but the rest healed after the ERCP procedure. Elderly patients have not been studied before in this regard. However, similar results have been reported in earlier studies focusing on all patients undergoing ERCP due to postoperative bile leak [23, 24]. According to the Guidelines by the European Society of Gastrointestinal Surgery, ERCP should be attempted if no transection of the CBD exists [20]. The guidelines recommend using a plastic stent without sphincterotomy or sphincterotomy alone in selected patients. During the procedure, associated lesions and obstacles should also be detected and treated. The stent should be removed within 1–2 months.

This study has a few limitations. First, the study was a single-center study with limited population. The small number of post-ERCP complications makes it difficult to compare treatment modalities. Several options are available and should be considered case-by-case depending on the severity and nature of the complication. More studies on this subject are definitely needed. The main strength is the prospective nature of the study. This is the first prospective study reporting results in this precise setting. All the ERCPs in the health care district were performed in the study hospital and all the complications, techniques, maneuvers and such were precisely documented. We were also able to access data on post-discharge events.

In conclusion, this prospective study shows that ERCP can indeed be performed safely on elderly patients. The most common complication is pancreatitis, which in comparison to earlier reports, and especially in comparison to younger cohorts, seems to be less common. Nevertheless, complications occur even in the oldest patients and therefore, the probable benefits and possible risks of the procedure need to be carefully assessed. In our series, the procedures were performed by high-volume endoscopists using appropriate techniques, which may partly explain the excellent results. The high 30-day mortality in patients with malignancies should be taken into consideration when selecting therapeutic options such as stents.

Acknowledgments This study was financially supported by the Competitive Research Funding of the Pirkanmaa Hospital District, Finland.

Compliance with ethical standards

Conflict of interest All authors disclosed no financial relationships relevant to this publication.

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The impact of hospital type, surgical technique, ASA score and patient's age on surgical outcomes in elderly patients undergoing emergency cholecystectomy

Running title: Cholecystectomy in the elderly

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Keywords: Cholecystectomy; Cholecystectomy, laparoscopic; Cholecystectomy, open; Morbidity; Mortality; Aged

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Abstract

Background: While the treatment of younger adults with acute cholecystitis (AC) may be straightforward, limited evidence is available on the treatment of the most morbid elderly patients.

Methods: We aimed to find out if patients' age, the American Society of Anesthesiologists (ASA) physical status classification, surgical technique and hospital type have an impact on the outcome in elderly patients operated on for AC. The study comprised consecutive elderly patients (aged≥65 years) undergoing emergency open (OC) or laparoscopic cholecystectomy (LC) in six study hospitals in Finland.

Results: A total of 601 elderly patients (mean age 75 years; range 65–98 years; 47% female) underwent surgery for AC. Sixty-six percent had pre-existing diseases; OC was preferred over LC in patients with severe comorbidities ($p<0.001$). The overall morbidity and 30-day mortality rates were 26% and 3.0% respectively. Mortality increased rapidly after the age of 90; 40% of nonagenarians died within one month of the surgery, while mortality was 2.1% in patients aged 85 to 89 years. The results were stratified by patients' age, hospital type and surgical technique without any significant differences. Higher ASA score (III or more) was independently associated with higher morbidity and mortality. However, there was a decreasing trend towards lower morbidity and mortality among patients undergoing laparoscopic surgery.

Conclusions: Older age, hospital type and open surgical technique were not associated with poorer outcomes, whereas higher ASA score predicted both morbidity and mortality. However, the results favor the use of LC over OC in all eligible patients, especially for those with severe systemic diseases without any absolute contraindication for laparoscopic surgery.

Introduction

Acute cholecystitis (AC) is the most frequent reason for emergency gastrointestinal surgery in older patients (1–3). As this population constantly grows, an upsurge in demand for treatment of AC is to be expected. While urgent surgery is most often considered, alternative, less-invasive and non-operative strategies such as conservative treatment with antibiotics only or percutaneous drainage have been proposed for high-risk patients (4–6).

The surgical treatment of AC has undergone a major paradigm shift from open cholecystectomy (OC) to laparoscopic cholecystectomy (LC) and to immediate surgery instead of delayed surgery (7–8). Although the treatment of healthy adult patients with calculous AC is usually straightforward, some controversies exist on the treatment of the most vulnerable patients. Currently OC is principally reserved for cases in which LC is contraindicated or fails, leaving fewer surgeons with experience in the procedure required for the most challenging cases (9).

For the above mentioned reasons we decided to study surgical treatment of AC in elderly patients. The data was retrospectively collected from the six study hospitals during an era when LC exceeded OC in popularity in emergency procedures, while previously LC had been preferred over OC for years in elective surgery. Both morbidity and mortality of patients was analyzed in accordance with patient and procedure-specific factors, including patients' age, the American Society of Anesthesiologists (ASA) physical score, surgical technique and hospital type.

Materials and methods

The data consisted of all consecutive elderly patients undergoing emergency cholecystectomy for AC during a four-year study period (2007 to 2010) in six study hospitals in Finland. These included four tertiary referral centers (two university hospitals and two central hospitals) and two small-volume secondary care hospitals. The catchment area of these hospitals ranged from 40,000 to 260,000 inhabitants. Smaller hospitals were focused on day unit surgery; however, some emergency cases (all with no serious comorbidities) were referred to these hospitals from tertiary care emergency units.

The data were retrieved from patients' medical records and population based statistics from Statistics Finland. Patients were classified according to the ASA classification (10). Postoperative adverse events were graded according to the Clavien-Dindo (C-D) classification (11). The surgical outcome was analyzed in relation to patient's age, ASA score, surgical technique and hospital type.

All statistical analyses were performed using SPSS Statistics version 22 for Windows (IBM Corp, Armonk, NY, USA). Differences among patient cohorts were determined using the Fisher exact test for categorical variables, and for non-categorical variables the Mann-Whitney U test. Multivariate analysis (logistic regression analysis, enter method) was performed to identify independently significant variables. Statistical significance was set at $p<0.05$.

Results

A total of 601 older patients underwent emergency surgery for AC in six study hospitals. The mean age of patients was 75 years (range 65–98 years), and 47% were female. The majority (66%) had co-existing diseases, the most common being chronic cardiovascular disease (54%), diabetes (13%) and chronic pulmonary disease (7%). Forty-eight percent of patients were assessed to be in ASA classes III or more. The majority of patients (96%) underwent surgery in tertiary referral centers (51% in central hospitals and 45% in university hospitals), while only 3% of patients were operated on in district hospitals (these patients were referred from local university hospital). The overall morbidity and 30-day mortality rates were 26% and 3.0% respectively. The baseline characteristics of study population are presented in Table 1.

During the study LC was preferred over OC more often in university hospitals (65% vs. 73%, p=0.015). Both morbidity (23% vs. 28%, p=0.127) and mortality rates (1.7% vs. 4.2%, p=0.057) were lower in university hospitals. A comparison between university and central hospitals is presented in Table 2.

The outcomes of patients aged 80 years or more and younger are compared in Table 3. Not surprisingly, co-existing diseases were more common among the older patients (p=0.001). There was a trend towards higher morbidity in older patients (24% vs. 30%, p=0.073), and as many as 6.0% of patients aged 80 years or more died, while mortality among younger patients was 1.8% (p=0.008). The mortality of older patients was higher among ASA III or more patients (3.3% vs. 10.1%, p=0.024) and in patients undergoing open surgery (2.1% vs. 7.1%, p=0.016). If compared to Finns of the same age the mortality of operated nonagenarians was more than 20-fold. Figure 1 illustrates the 30-day mortality of the study population compared to 30-day mortality of same aged Finns.

Patients undergoing OC had more often serious systemic comorbidities and higher ASA scores than those undergoing LC (p<0.001). Overall morbidity was higher after OC than LC (28% vs. 19%, p=0.011). In patients with mild pre-existing systemic diseases there were no significant differences in morbidity (19.3%

vs. 17.6%, p=0.415) and mortality (0.0% vs. 0.8%, p=0.422) regardless of which technique was used, while in ASA III or more patients both mortality (6.2% vs. 3.2%, p=0.294) and morbidity (38% vs. 23%, p=0.019) were higher after open surgery. Only one of the patients assessed to be ASA classes I or II died. Table 4 illustrates the differences between OC and LC in elderly patients.

Multivariate analysis was performed to identify independently significant variables (Table 5). ASA grade III or more was associated with poor outcomes, including higher mortality and morbidity.

Discussion

The incidence of gallstone disease increases disproportionately in older adults. While early LC has become the gold standard for the surgical treatment of AC (7-8, 12), it is not as obvious how the oldest and most morbid patients should be treated. Especially in octogenarians with AC, the first treatment option may often be too conservative. Here we note the high morbidity and mortality associated with the surgical treatment of AC in the oldest patients. Older age, open surgical technique and hospital type were not significantly linked with poor outcomes, while high ASA score (III or more) predict morbidity and mortality.

Previously the advantages of LC have included decreased incisional pain, shorter hospitalization and faster functional recovery (7). In accordance with previous assumptions, the high percentage of open surgery in oldest patients may have been due to an unwarranted fear of cardiovascular laparoscopy-related complications (13). However, positive outcomes (i.e. rapid mobilization) are likely to outweigh the possible negative effects (14). In this study we report morbidity and mortality concurring with earlier reports (15-20). We demonstrated a similar rate of complications in previously health patients regardless of which surgical technique was chosen, as reported in earlier studies (7). Yet we found that morbidity and mortality among the ASA score III or more patients undergoing LC approached morbidity and mortality among those with no or mild systemic disease undergoing either kind of surgery for AC. The results favor the use of LC over OC in all eligible patients, especially for those with severe systemic diseases without any absolute contraindication for laparoscopic surgery.

In this study hospital type had no significant impact on morbidity and mortality. However, there was a trend towards lower morbidity and mortality in patients undergoing surgery in university hospitals. Previous studies have reported better outcomes in high volume centers (21). This may be a reflection of better quality of care of critically ill patients (22). In addition, 24h availability and higher quality of radiological services may lead to timely recognition and appropriate treatment of acute diseases and postoperative complications in larger centers. Finally, there has been a shift towards increasing the availability of abdominal surgeons during on-call hours. This has already been adopted in the largest centers. Consequently, surgeons skilled in laparoscopy surgeons are available during on-call hours in these centers.

Aging seemed to have a negative influence on surgical outcome in our study. However, chronological age alone should not determine the type of surgery. More importantly, concomitant conditions should be taken into account more precisely. It should be noted that if elderly patients are treated extremely conservatively, there will eventually be more complicated gallstone disease which means more invasive and difficult surgical treatment. Yet again, this study suggests that older and especially multi-morbid older patients are likely to benefit from minimally invasive techniques. These may include not only laparoscopic procedures, but also percutaneous drainage, endoscopic retrograde cholangiopancreatography and conservative treatment. Research on this vulnerable group of patients needs more emphasis. More high quality clinical trials are definitely needed.

There are some obvious limitations in this study. First of all, this was a retrospective study. It is likely that some of the adverse events (especially those with no or low clinical significance, e.g. conservatively treated surgical site infections) may not have been accurately captured. However, complications requiring major interventions were precisely known. Therefore, we decided to analyze C-D 1–2 and C-D 3–4 complications separately. We were also able to register post-discharge events as well, an aspect which may have decreased the reliability of some earlier studies (23). Finally, there is an obvious patient selection bias in this study, as the most morbid patients may have been restricted from laparoscopic surgery. This may explain some of the poorer results after OC than after LC.

Conclusion

The occurrence of postoperative complications or death after emergency cholecystectomy may more often reflect the severity of pre-existing diseases than the merits of surgical technique, older age or hospital type. There was a trend towards better outcomes among patients undergoing laparoscopic surgery; the results favor the use of laparoscopy if there is no absolute contraindication for this type of surgery.

Disclosures

None of the authors has any personal or professional conflict of interest regarding the submitted manuscript.

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Table 1. Baseline characteristics (n=601)

Variable		
Age, mean (range)	75.2 years	(65–98 years)
Age group		
Aged 65 to 79 years	434	(72.2%)
Octogenarians or older	167	(27.8%)
Gender, female	285	(47.4%)
Co-existing diseases	398	(66.2%)
Cardiovascular	326	(54.2%)
Pulmonary	41	(6.8%)
Diabetes	79	(13.1%)
Other	87	(14.5%)
ASA physical status		
ASA I-II	296	(52.1%)
ASA ≥ III	272	(47.9%)
Hospital type		
University hospital	273	(45.4%)
Central hospital	308	(51.2%)
District hospital[1]	20	(3.3%)
Open surgery	414	(68.9%)
Morbidity	153	(25.5%)
Mortality	18	(3.0%)

1 These patients were referred from university hospital

Table 2. Surgical treatment of the elderly with AC in university and central hospitals (n=601)

Variable	University hospital[1] n=293		Central Hospital n=308		p-value	
Age, mean (range)	74.6 y (65-93 y)		75.8 y (65-98 y)		0.030	
Gender, female	48.3%		46.8%		0.384	
ASA physical status ≥ III	48.1%		47.6%		0.487	
Open surgery	64.5%		73.1%		0.015	
Morbidity, (C-D 3-4)	23.2%	(5.8%)	27.6%	(3.9%)	0.127	(0.184)
Aged < 80 years	22.0%	(5.8%)	25.6%	(3.8%)	0.220	(0.223)
Aged ≥ 80 years	27.1%	(5.7%)	32.0%	(4.1%)	0.310	(0.450)
ASA I-II	13.2%	(3.9%)	24.3%	(6.3%)	0.010	(0.262)
ASA ≥ III	34.0%	(7.8%)	34.4%	(2.3%)	0.529	(0.035)
Open cholecystectomy	28.6%	(6.3%)	28.0%	(4.4%)	0.492	(0.260)
Laparoscopic cholecystectomy	13.5%	(4.8%)	26.5%	(2.4%)	0.020	(0.325)
Mortality	1.7%		4.2%		0.057	
Aged < 80 years	0.4%		3.3%		0.028	
Aged ≥ 80 years	5.7%		6.2%		0.586	
ASA I-II	0.0%		0.7%		0.486	
ASA ≥ III	3.5%		7.6%		0.113	
Open cholecystectomy	2.6%		4.4%		0.240	
Laparoscopic cholecystectomy	0.0%		3.6%		0.086	

1 Patients operated in regional district hospitals included in analysis

Table 3. Cholecystectomy in elderly patients aged less than 80 years and more than 80 years

Variable	Aged 65–79 years n=434		Aged 80 years or more n=167		p-value	
Gender, female	44.6%		55.1%		0.013	
ASA physical status ≥ III	43.9%		58.9%		0.001	
Open surgery	66.1%		76.0%		0.011	
Morbidity (C-D 3-4)	23.7%	(4.8%)	29.9%	(4.8%)	0.073	(0.585)
ASA I-II	17.5%	(4.7%)	22.6%	(6.5%)	0.230	(0.387)
ASA ≥ III	32.2%	(5.5%)	38.2%	(4.5%)	0.201	(0.494)
Open cholecystectomy	27.5%	(6.3%)	29.9%	(3.1%)	0.350	(0.141)
Laparoscopic cholecystectomy	16.3%	(2.0%)	30.0%	(10.0%)	0.047	(0.039)
Mortality	1.8%		6.0%		0.008	
ASA I-II	0.4%		0.0%		0.791	
ASA ≥ III	3.3%		10.1%		0.024	
Open cholecystectomy	2.1%		7.1%		0.016	
Laparoscopic cholecystectomy	1.4%		2.5%		0.516	

Table 4. Open and laparoscopic cholecystectomy in elderly patients (aged ≥ 65 years)

	Open surgery n=414		Laparoscopic surgery n=187		p-value	
Age, mean (range)	75.6 y (65–98 y)		74.4 y (65–93 y)		0.040	
ASA physical status ≥ III	55.1%		33.2%		<0.001	
Morbidity (C-D 3-4)	28.3%	(5.3%)	19.3%	(3.7%)	0.011	(0.271)
ASA I-II	19.3%	(5.3%)	17.6%	(4.8%)	0.415	(0.540)
ASA ≥ III	37.6%	(6.2%)	22.6%	(1.6%)	0.019	(0.019)
Mortality	3.6%		1.6%		0.137	
ASA I-II	0.0%		0.8%		0.422	
ASA ≥ III	6.2%		3.2%		0.294	

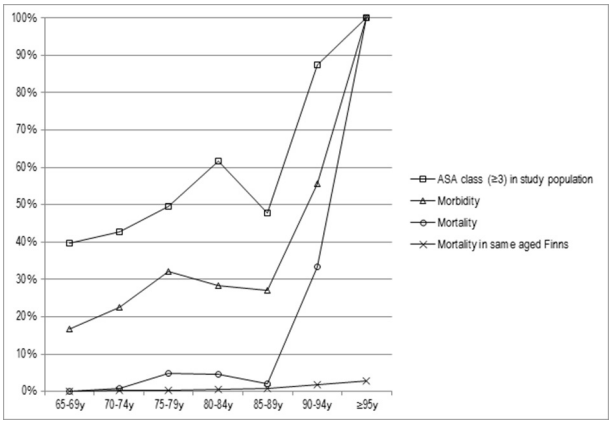

Figure 1. Proportion of ASA score III or more patients, 30-day postoperative morbidity and mortality in different age groups and 30-day mortality in same aged Finns

Table 5. Risk factors associated with increased morbidity and mortality

Variable	OR	95% CI	p-value
Morbidity			
ASA score III or more	2.1	1.4–3.1	<0.001
Octogenarians or older	1.3	0.8–1.9	0.271
Open cholecystectomy	1.4	0.9–2.2	0.098
Central hospital	1.3	0.9–2.0	0.141
Mortality			
ASA score III or more	14.7	1.9–114	0.010
Octogenarians or older	2.7	0.9–7.5	0.064
Open cholecystectomy	1.2	0.3–4.4	0.790
Central hospital	2.2	0.8–6.7	0.148