Morbidity and mortality following standardised perioperative management of patients operated with acute abdominal surgery in a high-risk emergency setting

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Abstract

Patients suffering from acute pathology in the abdomen is common throughout the world and surgical intervention can often be necessary. Those who are most seriously ill need an acute management with major abdominal surgery, the dominant procedure being an emergency laparotomy. The most common underlying causes are obstructed or perforated bowel, intra-abdominal bleeding and surgical complications. The postoperative period is associated with a high risk of complications, such as high mortality, high need for intensive care and long hospital stays. International studies from 2014 and 2017 have suggested improved post-operative outcome after standardization of the management of the patients that undergo emergency laparotomy.

The aim of the study is to implement and evaluate the intervention of a protocol-based standardised care for patients undergoing acute high-risk abdominal surgery. The objective is to investigate whether standardised perioperative care can reduce mortality and morbidity on short and long term.

During 2017 a protocol for management of patient undergoing emergency laparotomy was developed at NU-Hospital group in Trollhättan, Sweden. The study was named SMASH (Standardised perioperative Management of patients operated with Acute abdominal Surgery in a High-risk setting). Key elements in the protocol include: pre-operative communication, planning and rapid assessment with initiation of antimicrobial therapy. Furthermore, high level of competence and systematic approach in operation room as well as elevated level of post-operative care, with focus on bedside assessments and monitoring are of major importance.

The post-operative outcome after emergency laparotomy for a prospective intervention group managed according to the protocol-based standardised care was compared with a control group operated the years before the intervention was implemented. Study endpoints to investigate was 30-day mortality (primary), one-year mortality, length of stay in hospital and intensive care and surgical complications (secondary). The cohort of controls was operated during 38 months in 2014-2017 and the intervention group during 42 months in 2018-2021.

A total of 1344 patients was included in the study, 681 interventions and 663 controls. The 30-day mortality seen was 10.7% for interventions and 14.5% for controls ($p=0.045$), and one-year post-operative mortality was 19.7% and 27.8% respectively ($p=0.0005$). Length of stay in Intensive care unit was reduced to 3.1 days from 5.4 days ($p=0.007$) and in hospital the stay reduced to 10.2 days from 11.9 ($p=0.009$). Severe surgical complications were reduced to 27.3% from 37.6% ($p<0.0001$).

Adjusted analysis strongly indicate that the protocol-based standardised care improves post-operative outcome after emergency laparotomy both in the short and long term, reduce length of stay both in intensive care and in the hospital, and leads to fewer post-operative complications.

Keywords: Acute care surgery, Emergency laparotomy, perioperative management, anesthesiology

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Stor akut bukkirurgi i Sverige.

Aspekter på hur sjukvårdspersonalen med ett strukturerat omhändertagande kan påverka antalet dödsfall och andra komplikationer efter operationen.

Bakgrund och problemformulering:

Inom akutsjukvård är patienter med buksmärta och sjukdomar i bukens organ vanliga, både i form av kroniska och akuta besvär. I vissa fall består behandlingen av en kirurgisk operation. När tillståndet blir akut är det vanligt att besvären kan härledas till en blindtarmsinflammation eller gallbesvär, dessa tillstånd är inte direkt livshotande och operationen kan ofta ske med titthålskirurgi. Ibland är tillståndet allvarligare, det kan då bero på att det är totalt stopp i- eller hål på tarmen, eller att det blöder från något organ i buken. I dessa fall blir oftast patienten påtagligt akut sjuk och en stor öppen bukoperation är det enda som är livräddande. På grund av patientens akuta tillstånd är det bråttom att genomföra operationen innan ytterligare försämring sker, patientens allvarliga tillstånd innebär även stora risker med operation och sövning, vilket ställer stora krav på sjukvårdspersonalens omhändertagande av den sjuke. Det är sedan tidigare känt att dessa stora akuta bukoperationer har en hög dödlighet, ca 1 av 7 avlider inom en månad efter operationen. En fjärdedel är så svårt sjuka att de behöver intensivvård och många kan behöva nästan två veckor på sjukhus innan de är friska nog att återvända hem.

Vår inspiration och nya arbetssätt:

I Danmark och England har man i mitten på 2010-talet lyckats förbättra för patienterna som behöver stor akut bukkirurgi genom att strukturera omhändertagandet som det medicinska teamet genomför. Det har visat sig genom att man lyckats minska dödligheten efter att man infört detta arbetssätt. Inspirerade av de danska och engelska framgångarna utvecklade vi inom NU-sjukvården i Trollhättan ett strukturerat arbetssätt för omhändertagande, ett protokoll som fungerar både som en checklista och ett planeringsunderlag för teamet kring patienten. Arbetssättet infördes i februari 2018 med målet att se om det kunde bli bättre även för våra patienter. I september 2021 hade ca 700 patienter omhändertagits enligt detta strukturerade arbetssätt, i avhandlingen benämnd interventionsgrupp. För att på ett strukturerad och vetenskapligt sätt undersöka om det blivit en förbättring för interventions-patienterna jämfördes resultatet med en lika stor grupp som opererats under tre år innan det nya arbetssättet infördes, i avhandlingen benämnd kontrollgruppen.

Innan statistiska analyser genomfördes jämfördes grupperna avseende ålder, den akuta orsaken till att de behövde opereras samt vilka övriga sjukdomstillstånd de led av.

Vad blev resultatet och vad betyder det?

Hur hade det då gått för de båda grupperna? Det visade sig att de ca 700 som omhändertagits enligt det nya strukturerade arbetssättet hade en minskad dödlighet, med över 25% jämfört med kontrollgruppen. Vidare minskade den tid som patienten behövde vårdas inom intensivvården med över 40% samt den totala vårdtiden på sjukhus med i snitt nästan 2 dygn kortare per person.

Slutsatsen av denna avhandling är att det nya arbetssättet kan minska mortaliteten både på kort- och långsikt och att vårdtiden både på intensivvården och totalt kan minska.

List of papers

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. Timan TJ, Sernert N, Karlsson O, Prytz M.
SMASH standardised perioperative management of patients operated with acute abdominal surgery in a high-risk setting. BMC Research Notes. 2020;13(1)

II. Jansson Timan T, Hagberg G, Sernert N, Karlsson O, Prytz M.
Mortality following emergency laparotomy: a Swedish cohort study. BMC Surgery. 2021;21(1).

III. Timan TJ, Karlsson O, Sernert N, Prytz M.
Standardized perioperative management in acute abdominal surgery:
Swedish SMASH controlled study. Br J Surg. 2023 May 16;110(6):710-716

IV. Terje Jansson Timan, Niklas Ekerstad, Ove Karlsson, Ninni Sernert, Mattias Prytz.
One-year mortality following standardized management for emergency laparotomy: results from the Swedish SMASH study. Submitted.

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Abbreviations

LMIC	Low- and Middle-Income Countries
HIC	High-Income Country
ASA	American Society of Anesthesiology –functional status
IBD	Inflammatory Bowel Disease
UC	Ulcerative Colitis
CD	Crohn's disease
ICU	Intensive Care Unit
LOS	Length Of Stay
BMI	Body Mass Index
OT	Operating Theatre
GDFT	Goal Directed Fluid Therapy
NPWT	Negative Pressure Wound Therapy
CI	Confidence Interval
OR	Odds Ratio
EGS	Emergency General Surgery
SIRS	Patients developed Systemic Inflammatory Response Syndrome
COPD	Chronic Obstructive Pulmonary Disease
AKI	Acute Kidney Injury
MAP	Mean Arterial Pressure
PACU	Post anaesthetic care unit
NRS	The numeric rating scale
CRRT	Continuous renal replacement therapy
FTR	Failure to rescue
NELA	The National Emergency Laparotomy Audit
HIC	High-Income Countries
HDU	High Dependency Unit
IQR	Inter Quartile Range
PPU	Perforated Peptic Ulcer
EWS	Early Warning Score
ERAS	Enhanced Recovery After Surgery
CRF	Clinical Record Form
IHD	Ischaemic Heart Disease
COPD	Chronic Obstructive Pulmonary Disease
LOS	Length of Stay
ACS-NSQIP	The American College of Surgeons National Surgical Quality Improvement Program

Brief definitions

ASA Classification	The ASA (American Society of Anesthesiologists) physical status is a system to assess and communicate a patients pre-anaesthesia comorbidities, it can be helpful in predicting perioperative risks.
Hinchey Classification	Used in surgery to describe perforations of the colon due to diverticulitis.
Hartman's operation	Sigmoid resection with a colostomy and closure of the rectal stump.
Bromage scale	A clinical scale used to evaluate the motor block of epidural and spinal anaestheisa.
NELA database	The National Emergency Laparotomy Audit for patients undergoing emergency laparotomy in hospitals across England and Wales. The audit collects and presents data on management and outcome with the aim to enable improvement in quality of care.
Clavien-Dindo Classification	Widely used complications classification system for grading adverse events as a result of surgical procedures. Complications are graded on a scale from zero (no complication) to five (death).
SOFA score	The Sequential Organ Failure Assessment (SOFA) score is a systematic way to assesses the level of organ failure on critically ill patients. The score evaluates function of respiration, hemodynamics, coagulation, liver, neurology and kidneys, based on the data obtained and delivers a score from 0 to 4 as a rate of organ failure.
P-POSSUM	Portsmouth-Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity. A score based on the patient's physiological status and severity of the operation, calculates the risk of postoperative complications or death as a % risk.
Charlson comorbidity index	A score that predicts the mortality within a certain time from hospitalization for a patient who may have a range of comorbidities.

Introduction

Surgical and anaesthesiological care in hindsight

For centuries, mankind has been attempting to cure surgical diseases and surgical techniques and care have been developing continuously over the same period. The pain, which is both one of the most prominent symptoms of surgical pathology and also often a result of surgical treatment, has been a major difficulty to overcome in surgical care. The first steps in modern anaesthesia were taken by the young American dentist, William Morton, when, in October 1846, together with surgeon, John Collins Warren, he performed the first general anaesthesia(1). This important step in medical development has been followed by many others and was probably the start of an era of collaboration between surgeons and anaesthetists that is constantly being intensified, a journey that has increased patient safety, reduced post-operative complications and been able to help and cure far more patients in need of advanced medical interventions than was possible when Morton and Warren began their collaboration.

A global perspective

The development of surgery in recent decades has been extensive and has taken place at a rapid pace(2). Along with increased medical knowledge and the development of surgical techniques, more and more patients can be treated surgically(3, 4) and the surgical and anaesthesiological care are intertwined in the field of peri-operative medicine(5). The topic of the current thesis is highly specialised medical interventions in a high-spending context. At the same time, there are major inequalities in terms of the global need for surgery. It is reported that two-thirds of the world's population, about five billion people, lack access to safe surgery and anaesthesia that could cure and/or relieve a pathology that, in a more resource-filled context, would be taken for granted(6, 7). Moreover, a study from Shrime and colleagues estimate that 30% of the global health disease burden is surgical(8). Nepogodiev and colleagues reports that over 4 million people worldwide die during 30-days following surgery, making postoperative deaths the 3rd most common cause of death in the world(9).

Elective vs emergency and acute high-risk abdominal surgery

There are several differences between the patient who can wait for surgical intervention and the one who is suffering from a pathology that cannot wait. It can be crucial for the outcome that the intervention takes place promptly and the time span from decision to operate to surgical treatment is reduced to a minimum(10). In high-income countries, a clear majority of general surgical procedures are elective, i.e., for patients that can wait. Diagnoses such as cholecystectomies, hernia surgery, surgery on the colon and breast surgery are most common(11). Compared with emergency procedures, the proportion of complications is lower in elective care. Studies show an overall rate of complications of 8.8-16.8% and a mortality rate of 0.5-0.8% for elective procedures(11, 12). As healthcare strives to avoid complications, the numbers can be considered high, but they are lower than in emergency cases(13, 14).

In acute care surgery, the abdominal procedures dominate(11) and can be divided into two subgroups based on the volume of procedures and the post-operative complication rate. The interventions that are most numerous and associated with low rates of morbidity and mortality are acute cholecystectomies and appendectomies. The second group are often summarised as acute high-risk abdominal surgery, usually called emergency laparotomy, and the procedure is associated with high morbidity and mortality and includes peptic ulcer disease perforations, small bowel resections, partial colectomy and adhesiolysis(14). It is usually not the surgical procedure itself that is risky; for example, a small bowel resection in an elective surgical setting on a clinically stable patient is not a high-risk procedure. In emergency laparotomy, however, when pathology affects physiology in combination with the patient's comorbidity, everything adds up and the same small bowel resection becomes a high-risk procedure(15, 16).

The patient

Demographics

There are retrospective datasets that extensively describe the demographics of the patient who requires emergency laparotomy. In most published material from Europe and the US, a small majority of women are seen, from 51.4% up to 55.4%(13, 17-24), and one Greek study presents only 46.1% females(25). The variation in age is wide, but a mean age of 61 to 70 years is seen(13, 17-19, 22, 26). The majority often consist of elderly patients and the group aged 70 to 80 years is most common in several studies(20, 24, 27). The most common indication for surgery is bowel obstruction, followed by perforation. In larger cohorts, the two major ASA classes (American Society of Anesthesiology – functional status) are class 2 and 3(18, 19, 23, 28, 29).

On the other hand, when the cohort undergoing surgery is based on the population in a low- and middle-income country (LMIC) setting, the demographics differ. For example, in a cohort of 286 patients undergoing exploratory laparotomy in rural Ghana, 37.4% were women and the mean age was 46.5 years. The dominant (29%) abdominal pathology was appendicitis, complicated by perforation or abscess in almost 60% of cases. The in-hospital mortality was 12.6%(30), but the mortality following appendicitis was 0.0% and the cases with the high mortality were suffering from bowel obstruction, major trauma or perforated ulcer disease.

In Europe and the US, the majority of patients seek healthcare early and appendicitis is treated with an uncomplicated laparoscopy, so laparotomy is therefore uncommon(30), while, in LMIC, patients seek medical care at a late stage, resulting in a complicated pathology and the need for emergency laparotomy. Furthermore, there is a lack of competence and a shortage of medical equipment to carry out the procedure laparoscopically(31, 32).

Incidence

In Denmark, Liljendahl and colleagues report from a nationwide register study an incidence of 27.4 primary laparotomies per 100,000 person-years for individuals over 18 years in the catchment area. The inclusion criteria were based on the surgical interventions; bowel resection, ostomy and abdominal drainage. The following were excluded: trauma laparotomies, operations performed > 72 hours after hospital admission, secondary laparotomy and elective cases. Furthermore, the incidence increased with higher age, with the highest rise seen between 50 and 80 years. However, when patients turn 89, the incidence drops. For the whole study period (2003-2014), the overall incidence fell slightly(33). With the aim of estimating the incidence of emergency laparotomy in England, Chapter and colleagues estimate that the incidence is approximately 1:1100 (this converts to 90.9 laparotomies per 100,000 in the population) based on single-centre data from Brighton, England. The defined laparotomies in the cohort were: > 18 years, all midline laparotomies and thoraco-abdominal operations. Appendectomies, vascular, gynaecological and endoscopic procedures were not included. The calculations were based on the average number of emergency laparotomies annually divided by the whole population in the catchment area(34). Using data from 99 Australian public hospitals, Burmas and colleagues have reported an annual incidence of 58.6 to 78.8 per 100,000 in the population in Australia, where the differences are between the states in the country(35).

National Swedish data on the incidence of emergency laparotomy do not exist. The local incidence in the catchment area of Northern Älvsborgs County Hospital in Sweden is 83.3 emergency laparotomies per 100,000. The defined laparotomies were adults over 18 years, all emergency laparotomies including trauma laparotomies and, in selected cases, laparoscopy. Appendectomies and cholecystectomies and vascular surgery were not included. Calculations was performed on the population in the catchment area of the hospital(19).

The underlying abdominal pathology and the effect on physiology

To further define the group of patients that undergo acute high-risk abdominal surgery, different underlying pathologies need to be defined, together with the way the pathology affects physiology. Overall, older age and increased comorbidity reduce the possibility of surviving the surgical emergency without serious complications(36).

General symptoms and diagnostics

Patients with abdominal pain constitute one of the most common symptoms in specialised care. Fagerström and colleagues showed that this accounts for 10-20% of all patients at a Finnish university hospital emergency department (ED) over a period of 26 years. However, the largest subgroup was

non-specific abdominal pain without the need for surgery(37). Furthermore, additional radiological diagnostics are also relevant. According to data from the US, of 19 million patients with abdominal pain visiting the ED every year, approximately 25% were examined by a CT scan. Ricci and colleagues studied a cohort of 9,125 cases managed in more than 1,200 US hospitals in 2015. They were all patients over 65 years of age, admitted with acute abdominal pain and undergoing emergency surgery on the day of admission. In 3.2% of the hospitals, a CT scan was not available, while over 85% of hospitals were staffed to perform CT scans around the clock. The study revealed that a delay (≥2 hours) in the assessment of the CT images by a radiologist was associated with an increased risk of complication and death(38).

Ischaemia

The mesentery and bowel can become ischaemic due to several mechanisms, the most common of which is strangulation causing ischaemia in the adhesive small bowel. This condition requires an emergency intervention to save any viable bowel before it goes into necrosis.

Mesenteric ischaemia is a very serious condition with high mortality. The intestine is able to cope with a reduction of up to 75% of circulation for several hours without being damaged due to ischaemia and this is partly due to collateral blood flow. When ischaemia occurs due to arterial embolism, hypotension or the mechanical stoppage (strangulation) of blood flow, the epithelium of the submucosa is affected first and this leads to oedema and the accumulation of intestinal bacteria, followed by bleeding. Cell death proceeds from the intestinal lumen and transmurally through the intestinal wall until the entire area is affected by necrosis. This process releases inflammatory mediators and toxic metabolites, resulting in a systemic effect and, even if the circulation is successfully reversed, the permeability of the bowel is increased, leading to the translocation of the intestinal bacteria that normally perform a barrier function in the mucosa. The end stage is necrosis and tissue death, resulting in the perforation of the bowel(39-41). Acute arterial intestinal ischaemia is fortunately uncommon(39), but the condition is associated with a high short-term mortality rate of over 55% and most of these patients suffer from post-operative complications(42). Severe abdominal pain together with haemodynamic instability and the sudden onset of symptoms is sometimes a diagnostic challenge where several serious diagnoses may be conceivable, such as abdominal aortic aneurysm and acute coronary syndrome(39).

Obstructed bowel

Bowel obstruction can be divided into the obstruction of the small bowel and the colon. In many settings, the obstructed small bowel in need of surgical treatment is the most common reason for emergency laparotomy(19, 28). The underlying pathology is often abdominal adhesions, followed by abdominal wall hernias, malignancies, abscesses, malrotations and foreign bodies. Other, less common causes of bowel obstruction are complications after diverticulitis and diverticulosis. Moreover, the inflammation in the different pathologies involved in inflammatory bowel disease (IBD) can, in rare cases, result in complete bowel obstruction. Disorders due to infections caused by tuberculosis or parasites leading to bowel obstruction are, however, rare in Sweden (43).

In most cases, adhesions are a complication after previous surgery where the peritoneum has undergone microdamage and the subsequent inflammation has led to intra-abdominal post-operative adhesions(43, 44). Adhesions occur in at least 2/3 of patients after a laparotomy and most cases are asymptomatic(45). Long-term follow-ups have shown that patients with adhesions run a high risk of hospitalisation. Management in hospital involves either conservative treatment, which is most common, or surgical re-operation on a bowel obstruction(46). Conservative treatment has been shown to be associated with a higher risk of recurrence, but, on the other hand, surgical treatment reduces recurrence but increases the risk of complications and mortality(47). Another reason to operate on an adhesive small bowel obstruction at an early stage is to shorten the time of malnutrition and to prevent the translocation of bacteria that can lead to infection and sepsis(48). For obstruction in the colon, an intra-luminal mass (cancer) is the cause of obstruction in 60% of all cases, followed by volvulus and diverticulitis. In these cases, a non-surgical approach is often not an option(49).

Inflammation

Diverticular disease and IBD are inflammatory conditions that represent common gastrointestinal diseases in developed countries(50-52). However, an inflammatory condition itself is generally not an indication for surgery, whereas the complications the condition may cause are.

If intestinal contents become stagnant in pouches (diverticula), bacterial growth and local necrosis occur and the inflammation, i.e. diverticulitis, can result in microscopic or macroscopic perforation. An uncomplicated diverticulitis is usually treated with antibiotics and can be managed without hospitalisation. However, in about 1/3 of cases, the disease is complicated and can result in perforation, fistula to another organ, abscess and bowel obstruction(53).

Complicated cases are graded from 1 to 4 according to the Hinchey classification(54) (see Figure 1). Hinchey grades 1 and 2 involve either a pericolic abscess (grade 1) or a pelvic abscess formation because of a perforation of a pericolic abscess (grade 2). These conditions are categorised as complicated but can often be treated with drainage and/or antibiotics. Hinchey grades 3 or 4 are characterised by generalised peritonitis of pus (grade 3) or faeces (grade 4) and for them a surgical intervention is essential (54).

Figure 1. Hinchey Classification	
1a	Pericolic inflammation, no fluid collection
1b	Pericolic abscess
2	Pelvic abscess formation because of a perforation of a pericolic abscess
3	Purulent peritonitis
4	Fecal peritonitis

However, the exact intervention can vary; for a patient with a fistula, surgery with primary anastomosis may be required, while an unstable septic patient can undergo a sigmoid resection with a colostomy and closure of the rectal stump (Hartmann's operation) (55). Furthermore, in 2008, Myers and colleagues suggested that rinsing the abdominal cavity with saline through a laparoscopic intervention (laparoscopic lavage) was a safe alternative for the treatment of Hinchey grade 3(56). In a systematic review and meta-analysis published in 2017, Angenete and colleagues stated that the number of re-operations decreased for the group undergoing laparoscopic lavage compared with colon resection. However, no difference in mortality and morbidity was found(57). In addition, Samuelsson and colleagues suggest, in a Swedish population-based retrospective register study, that laparoscopic lavage for purulent peritonitis with Hinchey grade 3 is a safe alternative to surgery with resection. The procedure was associated with fewer complications and shorter hospital stays but a higher risk of infections and re-admission to hospital (58).

IBD is complex and is generally divided into three groups; ulcerative colitis (UC), Crohn's disease (CD) and indeterminate colitis; in the latter, neither UC nor CD is present. The pathogenesis is not fully understood. The affected patient has an immune response and reduced diversity of the microbiome in the bowel. There is an underlying heredity, but it is also believed that factors linked to diet may be the cause. The symptoms can initially be abdominal pain, diarrhea and bleeding(59). When conservative treatment with diet and drugs is no longer enough, surgery becomes necessary. The overall surgical treatment is a wide field of elective interventions which treat complications of the disease. In some cases, emergency surgery is necessary. For example, a patient with Crohn's disease and bowel obstruction may need to undergo a resection due to a stricture in the bowel(60).

Perforations

Perforations of the bowel can be the result of blunt or penetrating trauma. The non-traumatic reasons causing a perforation are perforation secondary to obstruction, diverticular disease, IBD, ischaemia, radiation enteritis, perforated foreign body or infections(61). Perforation could also occur due to surgical complications such as an anastomosis that starts to leak and this is seen more often in the colorectal type of anastomoses. Male gender, old age, earlier radiotherapy and emergency surgery are risk factors(62).
The clinical manifestation of perforation in the gastrointestinal tract varies. What is

decisive is the type and degree of peritonitis. According to previously published data, patients who become critically ill from peritonitis are those with a colonic perforation, with a perforation due to ischaemia or those with ulcer perforation(63). In the GenOSept study by Tridente and colleagues, 977 patients from 16 countries were included. They were all admitted to the ICU after emergency laparotomy with faecal peritonitis present. The cohort had a median ICU stay of 10 days and a 28-day mortality of 19.1%(64). Consequently, there was an increased post-operative mortality risk for the patients with peritonitis(65) and they were characterised by a severe septic condition most often seen as haemodynamic instability, combined with abdominal pain(66). In these cases, antimicrobial treatment, immediate emergency laparotomy and advanced intensive care are crucial in order to save the patient's life.

Bleeding

When intra-abdominal bleeding is the primary reason for emergency surgery, the most common underlying reason in patients with haemodynamic instability is a penetrating or blunt trauma. Several causes of bleeding are conceivable, including the rupture of an intra-abdominal organ. In these cases, surgical control of the bleeding is the highest priority(67). Intra-abdominal bleeding due to a direct surgical complication is also common, but, if bleeding is detected and stopped immediately, the risk of affecting the post-operative phase is small. However, a missed bleed causes complications in terms of re-operation and prolonged care. Bleeding as an indirect reason for surgery can also occur; for instance, bleeding from a primary cancer tumour or metastases in the intestines or abdominal organs.

Abdominal surgery on the seriously ill – surgical considerations

For high-risk abdominal surgical cases, there are many considerations in terms of approach, laparoscopic vs laparotomy, and intra-operative procedures. Several factors need to be considered, from the time the patient arrives at hospital and the first resuscitation is made, the surgical assessment, diagnostics and computed tomography scan reports to the decision to operate until the first incision is made. A systematic review of 50,653 patients has revealed a significantly longer time to surgery for non-survivors than survivors after emergency laparotomy(10). In 2020, Boyd-Carson and colleagues published data from a cohort of 3,809 British patients who underwent emergency laparotomy or laparoscopy. The overall result revealed an increased risk-adjusted odds of mortality of 6% for every hour that the first incision was delayed(68). To summarise, several decisions must be taken at the same time as the pace of patient management should remain high.

The emergency laparotomy

Damage-control surgery and source control

Damage-control surgery was first described by Stone and Colleagues in 1982. In a small clinical study of 31 patients undergoing laparotomy with the onset of severe bleeding during surgery, they were able to show that, of the 14 patients undergoing standard surgery, the bleeding was controlled in 14% of the cases and the mortality rate was 93%. In the remaining 17 patients, an abbreviated surgical approach with an abdominal tamponade and the restoration of coagulation and haemostasis before finishing the surgery with a second operation. Using the latter approach, Stone and colleagues obtained control of the bleeding in 82% of the patients and the mortality rate decreased to 35%(69). In 1993, this approach was named "damage-control" surgery(70) by Rotondo and colleagues and it has also been successfully introduced in unstable, critically ill patients who were exposed to trauma. The basic concept is to start surgery at an early stage to achieve surgical source control, the intervention must be short, focusing on what is most vital, while other surgical procedures can deliberately be left unfinished until a later stage. After source control, physiological resuscitation continues with intensive care until the patient is able to undergo definitive surgery(71-73). The damage-control concept is useful for critically ill non-trauma patients with abdominal pathology and it is particularly beneficial for acute mesenteric ischaemia, post-operative peritonitis and intra-abdominal bleeding(74). It has been shown that failure to achieve source control in abdominal sepsis increases the short-term mortality rate from 26.7% to 42.9%(75).

Open abdomen and second-look laparotomy

The post-operative open abdomen (surgery ends without the abdominal wall being permanently closed and instead negative pressure wound therapy (NPWT) is used), with the aim of reducing post-operative complications. Several indications exist, oedema in the abdominal organs making it impossible to close the abdominal wall, combined with the risk of increased intra-abdominal

pressure which can lead to abdominal compartment syndrome in the abdominal cavity, damage-control surgery due to intra-abdominal bleeding, patients in septic shock, or contamination of the abdominal cavity(76, 77). The open abdomen leads to a planned return (second-look laparotomy) to the operating theatre (OT) within 24-48 hours after index surgery(77).

The laparoscopic approach to high-risk abdominal surgery

Less invasive surgery is always preferable, but only if it effectively treats the pathology. Worldwide, as well as in Sweden, the dominant intervention for acute high-risk abdominal surgery is laparotomy with a midline incision. To be performed laparoscopically, the correct skills and equipment are needed, but this also includes the 'right' patient, with a diagnosis that is possible to manage laparoscopically. In some contexts, for example, an LMIC setting, there is a shortage of skills and equipment. Although the development of various less invasive surgical methods is continuously in progress, few abdominal pathologies are suitable for laparoscopy. In a Danish study from 2017 comprising 1,139 acute high-risk abdominal surgery patients operated on laparoscopically, 63% of patients were converted to open surgery. The most common reasons for conversion were the need for bowel resection, poor visibility and dense adhesions(78).

Pathologies such as complications after bariatric surgery with a small bowel obstruction resulting in internal herniation, adhesions, volvulus or obstruction in the jejuno-jejunostomy can be managed with an emergency laparoscopy, but there is a risk of conversion to open surgery and resection due to an ischaemic bowel(79).

Negative laparotomies

The term negative or non-therapeutic surgery applies to a scenario where the operation is performed, but no pathology is found. In emergency laparotomy management, this appears to be most common in trauma laparotomies. A Danish observational study from 2022 with 98 patients undergoing trauma laparotomy revealed that 17.3% were non-therapeutic(80). In the case of the critically ill non-trauma patient, diagnosis can also be a challenge. Consequently, to determine whether the multi-organ failure is due to an abdominal pathology and surgery is needed. In a French study retrospectively including 59 patients undergoing consecutive negative laparotomies from 1996 to 2013, 85% were managed in the ICU at the time of surgery and the postoperative mortality rate was 37%. The study also detected that 60% of the patients had a CT scan before the operation and 40% of them showed major anomalies, even though the operation subsequently turned out to be negative(81).

Anaesthesiological considerations

Pain

Post-operative pain management is important to consider after any surgical intervention. Regardless of whether the procedure is urgent or elective, major abdominal surgery is associated with a significant need for pain relief. After a laparotomy, the primary pain management is epidural anaesthesia, since it provides good pain relief and the incidence of post-operative ileus decreases(82).

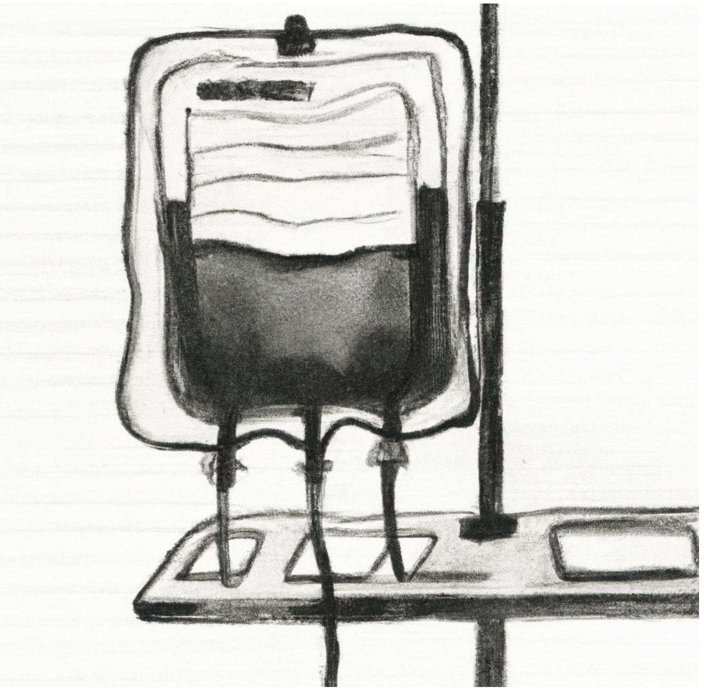
Other advantages of epidural anaesthesia include the reduction of complications. In a meta-analysis comprising 5,904 patients who underwent abdominal and thoracic surgery, the patients were randomised to either systemic or epidural pain relief and a reduction in pneumonia was seen in the group with epidural anaesthesia (O.R 0.54), as well as a reduced incidence of re-intubations(83). In a Danish study published in 2020 of 3,810 patients who underwent major laparotomy, the findings were in favour of epidural analgesia when 90-day mortality was studied. The mortality in the epidural group (n=1,296) was 23.5% and in the non-epidural group (n=2,514) 30.0% and the adjusted association was O.R 0.77 (95% CI, (0.64-0.92))(84).

For the patient with severely affected physiology

Anaesthetic management enables surgery on patients with life-threatening pathology in the abdomen. This is, however, not without its difficulties, as many of these patients' vital functions are severely affected.

Management

It is often found that patients suffer from hypovolemia and deranged electrolytes as a result of vomiting and a lack of fluid intake at the time of hospitalisation, a condition that may deteriorate further if the patient becomes septic. The group of severely ill patients may require resuscitation before surgery at an upgraded level of pre-operative care at a hospital unit with the capacity to start intensive care. The following measures may be needed pre-operatively; start antimicrobial treatment, set up an arterial line for haemodynamic and non-invasive cardiac output monitoring, start fluid resuscitation, optimise coagulation and haemostasis, re-arrange electrolyte deficits, start the transfusion of blood products and, in selected cases, have the capacity to prepare the patient with thoracic epidural anaesthesia(85). However, there are cases where quickly reaching surgical source control is so urgent that it is simply inappropriate to waste the minutes needed for an epidural in the pre-operative phase. It can instead be performed post-operatively. In different hospital settings, the best unit to perform pre-operative resuscitation as described above can vary, but it is usually done at a pre-operative centre or in an ICU setting. Totally stable patients do not require upgraded pre-operative care; instead pre-operative care performed on a surgical ward or at an emergency department until OT is ready is sufficient.



For severe emergencies, such as massive intra-abdominal bleeding or severe intestinal ischaemia(74) or sepsis(86), a short time to surgical source control is the only thing that can save the patient's life. In these very urgent cases, when there is an absolute need for rapid surgical intervention, it is necessary to perform both resuscitation and anaesthesia at the same time(86), a phase that can be characterised as damage-control anaesthesia with similarities to trauma anaesthesia. Tobin and colleagues describe the phases of trauma anaesthesia in a structured manner. The pre-induction phase comprises the prevention of hypothermia, a transfusion protocol and good control of medical equipment, followed by the anaesthesia induction with ongoing resuscitation and the use of specific drugs and doses adapted to the patient's critical condition(87). Systematic teamwork is important and some factors worth considering before high-risk anaesthesia are summarised by Higgs and colleagues in four categories regarding the intubation of critically ill patients(88). First, prepare the patient, including an upgraded level of the pre-operative care mentioned above but with the addition of optimising the patient's position for high-risk airway management. Second, prepare the equipment and optimise monitoring and equipment for airway management and drugs; ketamine is preferred for the critically ill patient(89). Next, prepare the team, focus attention on the importance of specific roles including team leader. Finally, prepare for difficulty, including a plan A, B and C for airway management and a strategy for haemodynamic management. The described scenario requires experience and many hands working simultaneously with different spectra of the patient's physiology(88).

Sepsis

Early antibiotics are a cornerstone of sepsis treatment, according to international guidelines. Another is source control and, in cases with an abdominal focus on infection, surgery is necessary to achieve source control(90). Anaesthesia in the septic patient often means that fluid resuscitation and the initiation of vasopressor infusion need to be started before the operation in order to reduce the risk of haemodynamic complications(85, 91). Ingraham and colleagues reported that more than 42% of a cohort of 67,445 unselected American emergency general surgery (EGS) patients developed systemic inflammatory response syndrome, SIRS, sepsis or septic shock(11) and, in another large American study including more than 37,000 patients undergoing emergency laparotomy, the corresponding figure was over 53%, of which 13% developed septic shock(18). A small study from Florida showed that 20% of patients requiring acute colon surgery had severe sepsis or septic shock(92).

Respiratory comorbidity

Respiratory failure is sometimes present even before anaesthesia, for different reasons. Many patients already suffer from chronic obstructive pulmonary disease (COPD). According to an American study of 234 unselected emergency laparotomies, 12% were suffering from COPD before surgery(93). A septic condition due to pathology in the abdomen can also impair lung function in a patient with low respiratory resources. A study by Hausman and colleagues compared 2,644 patients with COPD who received regional anaesthesia with an equal number of patients who underwent general anaesthesia and the result showed that the general anaesthesia group had a higher relative risk of post-operative complications, 44% (2.6% vs 1.8%, p=0.049) higher risk of unplanned intubations in the post-operative phase and 43% (3.3 vs 2.3%, p=0.038) higher risk of infections in the pulmonary tract. An overall increased risk of general post-operative morbidity was seen, even when pulmonary infections were excluded. However, no statistically significant difference was seen in post-operative 30-day mortality between the groups(94). Since patients who undergo emergency laparotomy have generally not undergone pre-habilitation and have to be under general anaesthesia, this underlines the importance of management with lung-protective ventilation during anaesthesia, ensuring good post-operative pain relief, as well as careful and active post-operative monitoring and mobilisation(95). One way of reducing ventilator-induced lung injury is to reduce the driving pressure(96) in the ventilator (explained as the difference in pressure between PEEP and plateau pressure). In a review analysing 17 randomised studies including 2,250 patients, an increased OR of 1.16 for lung injury was seen for every unit of increased driving pressure(97).

Kidney function

Acute kidney injury (AKI) is common in the group that undergo acute high-risk abdominal surgery(98) and it is defined by elevated serum creatinine or impaired kidney function(99). A British prospective multi-centre study (131 hospitals) from 2017 included 2,341 patients admitted to hospital during a period of four months due to small bowel obstruction. Of the 29.6%

(n=693) who underwent immediate surgery, 27.7% (n=192) were identified with AKI on admission(100). During the anaesthesiological management, it is important to consider AKI and maintain good haemodynamic management with good mean arterial pressure (MAP) and keep the patient euvolemic as far as possible(98).

Cardiac disease

The patient about to undergo surgery may suffer from ischaemic heart disease, congestive heart failure or left ventricular hypertrophy, conditions resulting in a pattern with cardiac frailty and an increased risk of cardiac complications. In the management of these patients, it is important to maintain a good energy balance in the myocardium and avoid hypotension, hypoxia, anaemia and circulatory failure(101). All of the above mentioned are conditions that occur in patients that undergo an emergency laparotomy.

Type 1 myocardial infarction is due to arteriosclerotic plaque that acutely cuts off blood flow in a coronary artery. Type 2 myocardial infarction is caused by an imbalance in oxygen supply to the myocardium and can be influenced by anaesthesiological strategy and resuscitation. An American study by Smilowitz and colleagues with over 4.7 million surgical patients shows that 0.82% suffered a myocardial infarction peri-operatively. In subgroup analyses, it was shown that, among the 68,680 patients who had per-operative septic shock, 9.6% were affected by a myocardial infarction, where type 1 and type 2 infarctions were evenly distributed (n=3,320 and n=3,305 respectively). A peri-operative cardiac infarction increased mortality and the length of stay in hospital(102).

Hypothermia and coagulation

Peri-operative hypothermia can appear before, during or after anaesthesia. In cases with existing hypothermia on arrival at the OT, there is an increased risk that the problem will still persist post-operatively. Peri-operative hypothermia leads to affected pharmacokinetics and increased coagulopathy with an increased risk of bleeding and a potential need for blood transfusion as a result. Post-operative consequences are prolonged care in the recovery process and an increased risk of infections at the surgical site(103).

Pulmonary aspiration

The aspiration of stomach contents is fortunately an uncommon complication, less than 1% for an unselected group of surgical patients(104), but patients with a bowel obstruction run a higher risk(105). There are several established ways to prevent aspiration: a gastric tube to empty stomach contents before surgery, the induction of anaesthesia with a rapid sequence induction and in some settings the performance of cricoid pressure during the phase from the effect of anaesthetic drugs until an endotracheal tube is secured in the airway. It has also been shown that patients suffering from pulmonary aspiration have a higher need for intensive care (56% compared with 16%) and higher in-hospital mortality (24% compared with 2%)(104).

Post-operative care

Regular recovery at the post-anaesthetic care unit (PACU) represents the first phase in post-operative recovery and covers the period from the end of surgery until discharge from the recovery ward. The second phase includes hospital care until discharge, while the third phase covers the period from when the patient returns home or to a rehabilitation centre, until normal physiology is restored.

The post-operative route in hospital can vary in different hospital settings. Several factors can affect the length of post-operative period and the level of care needed. The patient's comorbidity burden and functional level before the operation have a major impact on the clinical outcome. In addition, the clinical outcome is impacted by how serious the pathology is and the degree to which this pathology affects the patient's physiology before source control is achieved.

Studies have shown that less invasive surgical procedures, i.e. laparoscopy, can result in a shorter length of stay (LOS), due partly to less surgical stress. Nielsen and colleagues investigated a cohort undergoing acute high-risk abdominal surgery. In the laparoscopy group (n=115), the median LOS was eight days, versus 11 days for the laparotomy group (n=826). However, the total group was heterogeneous, which makes it difficult to draw definitive conclusions from the results, and the group that was converted to open surgery after an initial laparoscopy (n=198) had a median LOS of 12 days(78).

Based on scientific evidence, an epidural block at thoracic level is recommended in order to reduce the physiological stress response following emergency laparotomy. The continuous epidural infusion of local anaesthetic gives pain relief, enabling good post-operative mobilisation (dynamic mobilisation). The thoracic level of the blockade is of great importance, as an inaccurate level may result in incomplete anaesthesia in relevant segments(106). In a Danish multicentre study, 34% of all patients (n=3,810) who underwent emergency laparotomy had epidural analgesia. The adjusted odds ratio between an epidural and mortality showed a decreased risk of mortality after major laparotomy for patients with an epidural (OR 0.77)(84). Furthermore, the use of epidural analgesia with the continuous infusion of local anaesthetic with or without added opioid has the potential to reduce the use of systemic opioids, facilitate early mobilisation and reduce LOS in hospital. In addition, it has been shown to accelerate gastrointestinal recovery(107).

First phase

Recovery ward or post-anesthetic care unit

The regular tasks in the recovery ward are to manage pain and nausea, initiate and continue peri-operative medication and reduce delirium. Several evaluation scales are used, of which the numeric rating scale (NRS) to evaluate post-operative pain and the Bromage scale to evaluate the motor effect of central blocks are common in clinical practice(108, 109). Post-anaesthetic care is usually continued until the level of physiological functions is restored and care can continue at the level on a regular surgical ward. To achieve this, stable vital parameters (pulse, blood pressure, respiratory rate and level of consciousness) are required, post-operative pain needs to be under control and the patient must be able to call for help from healthcare staff in the regular surgical ward if necessary.

The regular recovery ward in a Swedish setting is not by default the appropriate level of post-operative care after emergency laparotomy, as some patients may require a higher level of post-operative care.

Intensive care unit

In an American retrospective study including 2,279 adults, all unselected surgical critically ill patients, 91.9% were admitted directly to the ICU, while 8.1% had to wait in PACU due to a lack of available ICU beds. Adjusted analyses showed higher mortality for those with delayed admission of < 6 hours to the ICU (OR 5.32)(110).

The delayed extubation from mechanical ventilation requires post-operative intensive care. In a retrospective study including 387 patients with delayed extubation who underwent acute gastro-intestinal surgery during a nine-year period, two causes were identified, post-operative shock and insufficient spontaneous breathing(111).

Sepsis in the ICU

Sepsis as a reason for intensive care is common after emergency laparotomy(18). Early resuscitation is important, but continuing the care of sepsis post-operatively is equally important. The post-operative management of a patient with intra-abdominal sepsis requires multidisciplinary care based on three foundations. First, surgical re-evaluation, with a clinical examination, open abdomen or preparedness for second-look surgery. This is followed by antimicrobial treatment with broad-spectrum antibiotics and detection with culture and PCR (Polymerase Chain Reaction). Finally, intensive care, which, in addition supports organ function, with the emphasis on analgesia, sedation, ulcer prophylaxis, thromboprophylaxis and glucose control(75). According to surviving sepsis guidelines, the management for septic shock is carried out in the ICU, including the treatment mentioned above and the following; vasopressor to prevent hypotension, fluid resuscitation including transfusion and blood products if needed and lung-protective ventilation if intubated(112).

When kidney function fails, there are several life-threatening indications for starting continuous renal replacement therapy (CRRT) in the intensive care unit; dangerously high potassium, overhydration unresponsive to diuretics, severe acidosis and uraemia or anuria. AKI induced by sepsis is common and in many critical cases there is a clear indication when CRRT is needed, but the evidence relating to the best time to initiate treatment is still under discussion(113).

Second phase

Surgical ward

The second phase of post-operative care is hospital care on a surgical ward until discharge. There are several separate goals with this care, but they all have one thing in common, getting the patient ready for discharge from hospital.

Physical mobilisation prepares the patient to be more independent. Furthermore, mobilisation plays an important part in contributing to the full recovery of function in the gastrointestinal tract so that the patient is able to drink, ingest food and defecate. In the immediate post-operative phase, multimodal analgesia with epidural anaesthesia and the addition of systemic treatment is often needed. The treatment is subsequently phased out to consist solely of an oral pain regimen.

During the post-operative surgical ward care, the patients are under observation, monitoring the vital parameters, with the aim of identifying post-operative complications, mainly to avoid failure to rescue (FTR), defined as the death of a patient after suffering one or more potentially curable complications. This highlights the importance of quickly detecting a post-operative complication and instantly acting upon it, to initiate an adequate intervention so that the patient regains their previous health status. Otherwise, there will be a severe risk of multiple complications which can result in FTR(114). This requires a high level of competence and well-established guidelines in post-operative hospital care. In a large American retrospective study of patients 65 years and older who underwent high-risk surgery (oesophagectomy, pancreatectomy and gastrectomy), Ghaferi and colleagues were able to show large differences in FTR rates. This was seen in pancreatectomies, where the probability of suffering a post-operative complication was 1.7 times higher in a low-volume hospital (38.3% in low-volume and 27.7% in high-volume hospitals), but that the probability of dying following a post-operative complication was 3.2 times higher (26.0% and 9.9% respectively)(115). This indicates that the experience and competence of hospital staff play a role in the ability to discharge patients to home, even after post-operative complications occur.

Third phase

Being discharged from hospital does not mean that an individual is fully recovered.

Re-operations and recurring problems

For some of the patients who undergo emergency laparotomy, the problem is only temporarily resolved, i.e. after a surgical solution to the acute condition, there may be a risk of complication or permanent sequelae. One example could be that adhesions occur in the abdominal cavity. A Swedish 14-year follow-up study analysed 102 patients after index surgery with a small bowel obstruction caused by an abdominal adhesion, resulting in 273 hospital admissions for recurrent bowel obstructions, of which 47.3% required further surgical intervention(46).

Post-operative outcome following emergency laparotomy

Mortality

The percentage of patients that do not survive is high in all laparotomy studies. Several retrospective data report mortality after 30 days of between 8.9 and 20.2% in an unselected group of adult patients with varying pathology in the abdomen(13, 17-25, 116-118). When the focal point is beyond the commonly analysed 30-day mortality, fewer studies present data.

One explanation could be difficulty completing follow-up evaluations due to patients being discharged from the hospital in many settings.

Nevertheless, 90-day post-operative mortality after emergency laparotomy has been shown to range from 17.8 to 26.0%(17, 22, 23, 118). One study presented one-year mortality in the range of 30.5 to 34.1%(17, 22, 33), while another study presented a two-year follow-up with mortality of 30.1%(118).

There is an interest in analysing subgroups, especially elderly patients. Norwegian, English and Danish data show 30-day mortality of 24.0 to 26.0% in patients older than 80 years(23, 24, 36) and one-year mortality of 41%(24). A large American retrospective cohort of 468,000 patients older than 65 years divided into groups according to clinical frailty(119) revealed that the patients categorised as non-frail (n=218,000) had 30-day mortality of 11.1% compared with the moderately to severely frail group (n=16,000), where the corresponding figure was 27.4%. In the long term, one-year mortality in both groups was 21.6 and 53.75 respectively(120).

Subgroups with different pathology show great diversity in mortality. For instance, a German study including patients suffering from acute mesenteric ischaemia (n=179, mean age 71 years, 51.4% females) showed in-hospital mortality of 55.9%(42). In contrast, in a British cohort from the NELA database (the National Emergency Laparotomy Audit) including nearly 10,000 patients suffering from a bowel obstruction due to abdominal adhesions that underwent an emergency laparotomy and adhesiolysis, the 30-day mortality rate was 7.2%(121).

As a result, large differences in mortality linked to the differences in intra-abdominal pathology can be seen.

Hospital stay

Patients undergoing an emergency laparotomy are sometimes more affected and need many days in hospital to recover. The mean length of stay in hospital for unselected adults in high-income countries (HIC) varies from 9.1 days to 20.1 days in different studies(22, 23, 29).

Intensive care

Within the British NELA network, the patient's risk of death is assessed through the NELA risk model(122), where high-risk patients are cared for in the ICU or the HDU (High Dependency Unit). In the NELA year 7 report from 2021 (n=21,846 from 177 hospitals in England and Wales), 56.8% of all patients were directly admitted to critical care after surgery, a decrease from the year before when 63.0% were admitted to critical care(28). The EPOCH study shows that 5,050 of 7,383 in total (69%) received critical care immediately after surgery(123). Other studies report that between 19.9% and 29.5% of cases are admitted to the ICU(20, 23, 25, 118).

Few studies report the mortality of the cohort admitted to intensive care. Vester-Andersen and colleagues report 30-day mortality of 42%(23) from a large (n=2,904) prospective Danish multi-centre study, while Ylimartimo and colleagues report 30-day mortality of 17.3% in a retrospective single-centre study (n=525)(124).

The length of stay in the ICU could be an indication of multi- or single-organ failure. The length of stay can vary in patients from only a few hours to many weeks. Vester-Andersen reports a median and interquartile range (iqr) of 94 (41-285) hours (author's calculation: converting into days = 3.9 (1.7-11.9))(23), while Ylimartimo reports 2.7 days (1.4-5.5) for survivors and 2.4 days (1.3-5.2) for non-survivors(124). In the HELAS study (a prospective multicentre Greek study, n=633), the ICU LOS was 7 (95% confidence interval 5.0-9.7)(25).

Surgical complications

There are several possible post-surgical complications after an emergency laparotomy, such as post-operative pain, surgical site infection, bleeding or leakage from an anastomosis. Complications related to anaesthesia can be nausea and vomiting, hypothermia, or respiratory failure in case of bronchopulmonary aspiration. However, complications related to the index pathology that caused surgery and its physiological consequences, e.g. sepsis, are most common.

A common way of classifying post-operative complications to surgery is the Clavien-Dindo classification (C-D) (Table 1)(125). In this classification, C-D 1-2 are less serious

Table 1. Clavien-Dindo Classification of post-operative surgical complications

Grade		Definition
Grade I		Deviations from the normal postoperative recovery (without surgical, endoscopic or radiological intervention). Allowed therapeutic drugs are: antipyretics, analgetics, antiemetics and electrolytes. Physiotherapy is allowed.
Grade II		Treatments with drugs other then allowed in grade I is required. This grade include the need for blood transfusion and parenteral nutrition.
Grade III	**a**	Surgical, endoscopic or radiological intervention due to complication, not under general anaesthesia
	b	Surgical, endoscopic or radiological intervention due to complication, under general anaesthesia
Grade IV	**a**	Single organ failure
	b	Multi organ failure
Grade V		Death of patient

complications related to pain, post-operative nausea and vomiting, prolonged treatment with antibiotics and parenteral nutrition, as well as the need for blood transfusion or the correction of electrolytes. C-D 3a and 3b are related to post-operative surgical or radiological intervention, with (3b) or without (3a) general anaesthesia. C-D 4a and 4b relate to complications generating organ failure, either single- (4a) or multi-organ failure (MOF) (4b). C-D 5 is when patients die.

Danish post-operative data after emergency laparotomy in 1,139 patients showed that 47% suffer from a complication C-D ≥ 3, the most common of which was an infection in the abdomen (19.7%), followed by pulmonary complications (19.3%)(22).

Patient management for emergency laparotomy

The management of patients undergoing acute high-risk abdominal surgery is complex. It imposes high demands on healthcare workers, including the ability to work rapidly, to prioritise actions and make decisions under stress, as well as communication between colleagues, the patient and next of kin. In the last decade, Danish and British intervention studies (see below) have found that standardised peri-operative care is able to improve the post-operative outcome. As a result, the standardisation of care has been introduced in the form of care bundles.

Care bundles for acute high-risk abdominal surgery

PULP – Peptic Ulcer Perforation trail (2011)

Möller and colleagues were the first to introduce a peri-operative care protocol. The focus was a selected group (n=117) with a perforated peptic ulcer (PPU) undergoing surgery during a two-year period (2008-2009) in seven Danish surgical departments and managed according to the protocol (including 33 different actions). Outcome was compared with a register-based cohort of controls (n=1,325). The 30-day mortality in the PULP study group was 17.1% compared with 27.0% among controls(126).

ELPQuiC – the Emergency Laparotomy Pathway quality improvement Care (2015)

This British study introduced a care bundle for emergency laparotomy at four hospitals including six actions (evaluation of Early Warning Score (EWS)), start of antibiotic treatment, fewer than six hours from the decision to operate to the first incision, goal-directed fluid therapy in the operating theatre, a high level of per-operative competence and intensive care after surgery. The hospitals included historical controls (n=299) for three months prior to the introduction of the ELPQuiC protocol. From December 2012, all consecutive patients were included in the intervention group (n=427) for eight months. The 30-day mortality rate was 10.5% following the introduction of the standardisation and 14.0% for controls(127).

AHA – Acute high-risk Abdominal (2017)

The AHA study implemented a nine-point standardisation of care starting in June 2013, including all adult patients requiring an immediate laparotomy or laparoscopy. In February 2015, 600 patients were included in the intervention group with a 30-day mortality rate of 15.5% compared with the mortality in the retrospective control group, 21.8% (n=600, operated on from January 2012 until September 2012)(128).

ELC – the Emergency Laparotomy Collaboration (2019)

This multi-centre prospective study involving 28 hospitals in the United Kingdom introduced a standard of care using the same bundle as the ELPQuiC study(127). The ELC project started in June 2014 and prospective inclusion in the baseline group was initially performed for 15 months (n=5,562), followed by inclusion in the post-ELC group (intervention group) in months 16-39. The follow-up lasted 30 days, until the patient died or until discharge from hospital. The 30-day in-hospital mortality (primary endpoint) was 9.8% for the baseline group and it decreased to 9.0% during the first year of post-ELC and further decreased to 8.3% during the last months of ELC(29).

EPOCH – Enhanced Peri-Operative Care for High-risk patients (2019)

The study aimed to investigate the effect of quality improvement pathways for emergency abdominal surgery. Through a Delphi consensus process, 37 actions were identified as components in a standardised quality improvement protocol. From March 2014 to October 2015, patients over 40 years of age undergoing open acute high-risk abdominal surgery were included in this multi-centre (93 UK hospitals), stepped-wedge, cluster, randomised study. The different hospitals were randomised to start the quality improvement protocol on one of 15 different dates during the study period, resulting in a usual care group (controls, n=1,393) and a quality improvement group (interventions, n=1,210). The primary outcome was 90-day post-operative all-cause mortality. In the outcome analysis, no statistical differences between groups were seen(123).

Rationale for the SMASH study

Before implementing a new strategy based on a standardised protocol for patients in need of acute high-risk abdominal surgery, it is mandatory to learn from previous studies and experiences. As previously mentioned, the medical environment and healthcare system differ from country to country and it is therefore of major interest to evaluate and analyse the result of the implementation in a Swedish context in a scientific way. Furthermore, before introducing this new care bundle, thorough work needs to be done to create a well-coordinated organisation including all the involved healthcare staff and clinics.

Why repeat what others have done?

From an international point of view, it is well known that this patient group as a whole is severely affected by complications(18, 23, 24, 116) and there was no reason to assume that the situation was any different in Sweden. However, in a Swedish context, a standardised protocol had not previously been studied. Little demographic, management and outcome data on unselected patients who undergo emergency laparotomy existed, not even reliable data on how many primary emergency laparotomies are performed every year. Only small studies with selected emergency laparotomy patents existed(46, 129).

Aim

The overall aim of this thesis is to implement and evaluate protocol-based standardised care (the intervention) for adult patients undergoing acute high-risk abdominal surgery, also called emergency laparotomy.

Primary endpoint

The study investigates whether protocol-based standardised care is able to reduce mortality in the short term (30 days).

Secondary endpoints

As secondary endpoints, the study explores whether the intervention affects long-term mortality (90 days and one year), length of stay in hospital, the need for intensive care, length of stay in the intensive care unit and the number and degree of surgical complications.

Methods

This single-centre study included all consecutive adult (>18 years) patients undergoing acute high-risk abdominal surgery during the study period (August 2014 to September 2021). Acute high-risk abdominal surgery was defined as emergency laparotomy, emergency laparoscopy of internal herniation and laparoscopic lavage of perforated diverticulitis Hinchey grade 3. The degree of urgency for all surgeries was six hours or less to the first incision. All laparotomies that had an urgency of more than six hours, planned re-operations, i.e. second-look laparotomies, cholecystectomies, appendectomies, operations not performed by the surgical clinic and children (<18 years) were excluded.

During the study period, all patients were prospectively included in the intervention group. The management was performed with the support of protocol-based standardised care, the intervention. The post-operative outcome for the intervention group was then compared with retrospectively collected data from a control group, operated on in the same hospital during the period before the intervention was introduced.

Intervention group

The study prospectively included 725 acute high-risk abdominal operations, representing 681 unique individuals during approximately 42 months, from 25 February 2018 to 3 September 2021. All the included cases were managed according to protocol-based standardisation with an activated clinical protocol.

Control group

In total, 710 operations were included in the retrospective control group. They represented 663 unique individuals who underwent surgery during 38 months in the period from 20 August 2014 to 20 October 2017 (see Figure 2)(130). The inclusion criteria were the same as for the intervention group. During the study period for the controls, there was no standardised management for the patients who underwent acute high-risk abdominal surgery at Northern Älvsborg County Hospital (NÄL), NU Hospital Group, Trollhättan.

Figure 2. Study structure for the cohort of control and the intervention group

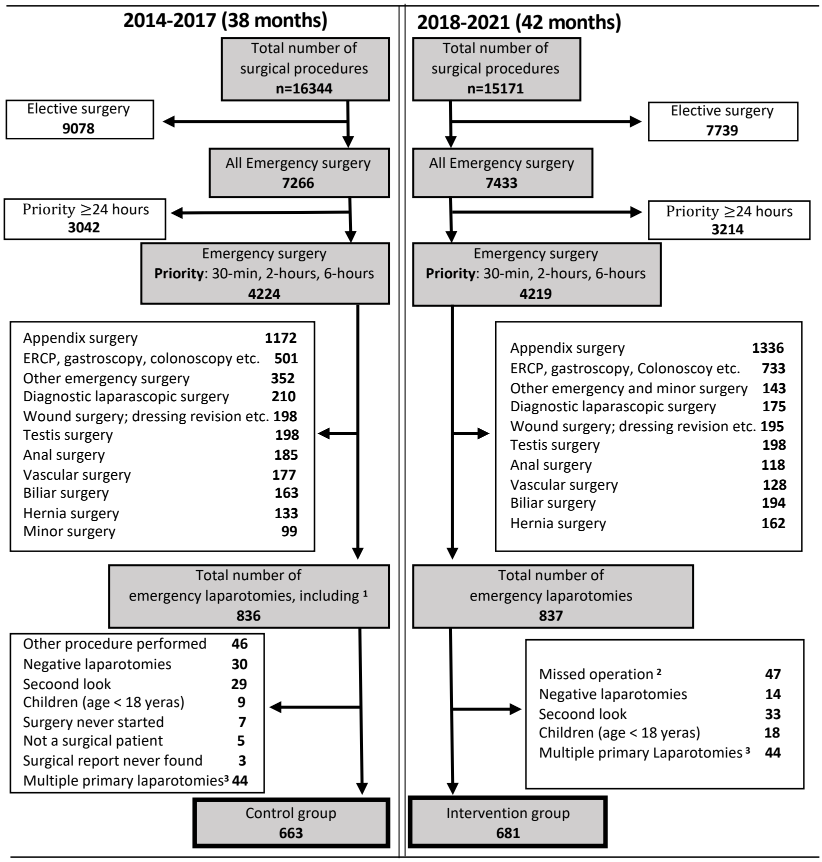


Figure 2. Show the exclusion/inclusion process. The total number of surgical procedures performed during the two study periods. The 38 months for the cohort of controls (20 August 2014 to 20 October 2017) and a little bit more than 42 months for the intervention group (25 February 2018 to 3 September 2021). 1=the laparotomies that had a different procedure-code initially. 2 = standardised protocol never used. 3=One individual can only be included once.

The SMASH protocol

When deciding to operate, the standardised protocol was activated. The form functioned both as a clinical record form (CRF) for the study and as a checklist for the involved healthcare workers at the surgical clinic, emergency department, operating theatre ward, department of anaesthesia, recovery ward, intensive care unit and regular surgical ward. The paper protocol in its physical form followed the patient through hospital care to discharge from hospital. After hospital discharge, the standardised protocol was saved in the electronic database connected to the hospital medical journal.

The standardised protocol is shown in Figure 3(130).

Figure 3.

VÄSTRA GÖTALANDSREGIONEN
NU-SJUKVÅRDEN

Akut Laparotomi

Detta kliniska formulär följer patienten från beslut operation är taget till det att patienten skrivs ut från sjukhus.

När patienten skrivs ut skall formuläret till:
Kontaktperson: Mattias Prytz, Överläkare
mattias.prytz@vgregion.se tel: 010-4353523

Operationskort:
JAH00 Akut laparotomi
Viktigt! Tillägg **JAH01** vid laparoskopi.

Angelägenhet:
- ☐ Urakut
- ☐ 2 timmar
- ☐ 6 timmar

KLISTERLAPP PATIENTDATA

Preoperativt-Kirurgläk ansvar

Opanmälan: datum__________tid_______

- ☐ Senaste **Kirurgbedömning** bedside innan opanmälan. Klockan:_______
- ☐ Reoperation efter elektivt ingrepp
- ☐ Kirurgin inleds laparoskopiskt

Nedanstående genomförs **omgående** efter att beslut om operation tagits.

- ☐ **Antibiotika** Givet klockan _______ Vid sepsis- andra dos efter 4 tim.
- ☐ **NEWS-skattning** Journalförs i melior. Poäng: _____
- ☐ **Blodgas** med laktat
- ☐ **Kemlabb**. Blodstatus, EL-status, CRP, Procalcitonin, blodgruppering bastest. OBS! Akut analys.
- ☐ **KAD** (tempgivande)
- ☐ **Ventrikelsond**
- ☐ Ställningstagande och planering av den fortsatta **preoperativa vården i samråd med ansvarig anestesiolog**. (Alla faktorer som kan försena opstart skall elimineras, inkl dusch.)

Nedanstående genomförs **skyndsamt** och skall vara genomfört innan operation.

Ställningstagande till vårdbegränsningar. Anges nedan om begränsningar finns.
- ☐ Ja
- ☐ nej

- ☐ **Anhörigkontakt**. Anledning om ej kontakt______________________________

Komorbiditet

- ☐ KOL
- ☐ Ischemisk hjärtsjukdom
- ☐ Hjärtsvikt
- ☐ Diabetes
- ☐ Njursvikt
- ☐ Obesitas
- ☐ Rökare
- ☐ Inget av ovanstående

Peroperativt- Anestesiläk ansvar

- ☐ **Anestesiolog bedömning** bedside

Klockan ___________ ASA-klass:_____

Anestesiklar:__________Anestesistart:_______

Operationsstart:_______Operationslut:_______

- ☐ **Thorakal EDA** Om EDA ej anläggs anges anledning nedan:_________________________
- ☐ **Artärkateter**
- ☐ **Noradrenalin**
- ☐ **RSI induktionmedel**.
  - ☐ Ketanest
  - ☐ Propofol
- ☐ **CVK** Bör framförallt övervägas då behov av postop vård på IVA finns.

Målstyrd vätsketerapi

- ☐ **CardioQ**
- ☐ **Lidco-Rapid**
- ☐ **PPV**
- ☐ **Annat ___________________________**

Beslut om postop **vårdnivå** samråd kir-anest.

- ☐ Postop **UVA**
- ☐ Post **IVA** Främsta anledning till Postop-IVA __________________________________ __________________________________

Anestesiologisk komplikation med postoperativ betydelse
- ☐ Ingen komplikation
- ☐ Aspiration
- ☐ Annat____________________________

Peroperativ Kompetens Kirurgi
- ☐ ST
- ☐ Specialist
- ☐ Överläkare

Peroperativ Kompetens Anestesi
- ☐ ST
- ☐ Specialist
- ☐ Överläkare

Postoperativt- UVA-SSK ansvar

Postop start: datum_______ tid_______

Postop slut: datum_______ tid_______

Nedanstående genomförs på UVA/IVA innan rond med anestesiolog.

- ☐ **Övervakning** standard
- ☐ **Temp _______ grader.**
- ☐ **Kemlabb,** Litet IVA-status
- ☐ **Blodgas** (reg i melior)
- ☐ **Aktiv tempreglering**
- ☐ **VAS vid ankomst:__________**

NEWS-skattning, Poäng:______ Innan **utskrivning** från UVA, journalförs i melior.

VAS vid utskrivning:_________

Postoperativt- Anestesiläk ansvar

Efter ca **30 minuter** på UVA/IVA.

Rond med anestesiolog: Genomgång av behandlingsmål klockan:______________
Patient rondas **varannan timme** om inte vitalparametrar visar en helt stabil patient.

Målstyrd vätsketerapi postop
- ☐ **Lidco-Rapid**
- ☐ **CardioQ**
- ☐ **Annat___________________**
- ☐ **Ingen**

Postop **Smärtbehandling**
- ☐ EDA
- ☐ PCA
- ☐ TAP
- ☐ PainBuster
- ☐ Annat_____________________.

Fortsatt postoperativ vård:
- ☐ Vårdavdelning
- ☐ IMA
- ☐ IVA

Postop vård-avd: Avd ssk ansvar

Ankomst avdelning: datum_____ Tid_____

- ☐ NEWS vid ankomst. Poäng:_____
- ☐ NEWS 2 h efter ankomst Poäng:____
- ☐ NEWS 4 h efter ankomst Poäng:____
- ☐ NEWS 8 h efter ankomst Poäng:____

Vid klinisk försämring tas kirurgkontakt.

NEWS 1 gång/pass så länge ansvarig kirurg ser behovet.
News-skattning avslutas datum_________

Granskad av:

Fynd och åtgärd vid op: ____
____

Postop komplikation Kirurgläk ansvar

Bör ej fyllas i för tidigt, ca 1 v. postop.

Postoperativ komplikation har uppstått som: Datum:_____________
- ☐ 1) Behandlas med farmaka: Antiemetika, antipyretika, analgetika, diuretika och/eller elektrolyter
- ☐ 2) behandlas med farmaka som ej nämns ovan (exv blodtransfusion eller TPN)
- ☐ 3a) Kräver kirurgisk, endoskopisk eller radiologisk intervention
- ☐ 3b) Kräver kirurgisk, endoskopisk eller radiologisk intervention i full narkos
- ☐ 4a) Kräver IVA eller IMA-vård pga singel organsvikt
- ☐ 4b) Kräver IVA eller IMA-vård pga multiorgansvikt
- ☐ 5) Leder till att patient avlider

Interprofessional collaboration

The development of the SMASH care bundle went through several stages. First, a group was formed with three surgeons and three anaesthesiologists who were given a mandate to decide on the various measures that would be included in the SMASH care bundle. The process included analysing current science, studying the historical incidence of emergency laparotomy at NÄL (at the start, the local incidence was unknown), while a plan on how to introduce the intervention in practice was created. All the staff who were going to be involved in work on the protocol received information and training. They included anaesthetists and intensive care doctors, surgeons, nurses on the surgical ward recovery ward, the ICU staff and the nurses at the operating theatre. In total, it took about a year and a half before the intervention was ready to start.

When the study was ongoing, an interprofessional review group consisting of a surgeon, an anaesthesiologist, a nurse from each of the three surgical wards, a nurse from the ICU and recovery ward and an anaesthesia nurse followed the implementation of the protocol. At a monthly meeting, the interprofessional group audited the past month's laparotomies, reviewing each individual case and monitoring to ensure that the intervention was followed by checking the completed paper protocol and comparing it with the computerised hospital record and the computerised surgery planning system. After each monthly review, feedback was given to the respective departments at the hospital about what worked and what could be improved. A total of 42 review meetings were carried out by the interprofessional group before it was dissolved as the last prospective patient was included in the study.

Statistical methods

On inclusion, each patient's medical record data were scrutinised in both groups. During this phase of processing and analysing, all the data were de-identified. For categorical variables, n (%) is presented. The adjusted odds ratio is analysed by GENMOD(131) with the GEE model with binary outcome and link function logit adjusted for age, intestinal ischaemia, faecal, purulent/other peritonitis, chronic obstructive lung disease, ischaemic heart disease, congestive heart failure, chronic renal failure, diabetes, obesity, smoking, ASA classification, gender and cancer. The odds ratio is analysed by GENMOD with the GEE model with binary outcome and link function logit. For comparisons between groups, Fisher's exact test (lowest 1-sided p-value multiplied by 2) was used for dichotomous variables. The confidence interval (CI) for dichotomous variables is the asymptotic Wald confidence limits with continuity correction. Fisher's Non-Parametric Permutation Test for continuous variables and the chi-square test were used for unordered categorical variables. Statistical analyses were performed using SAS® v9.4 (Cary, NC).

Results

Study I

Study 1 is a description of the SMASH study as a scientific study. It includes a detailed description of the basic method and the different phases of the study(132).

No data or scientific results are presented.

Study II

A retrospective study that outlines demographic, management and outcome data relating to the 710 consecutive emergency laparotomies for the cohort of controls in the SMASH study.

The data showed that, during the study period, the patients undergoing surgery at NÄL had a mean age of 65.6 years and 46.6% were male. The mean LOS in hospital was 12 days and three hours. The LOS in intensive care for the 23.8% patients admitted to the ICU at any time during the post-operative hospitalisation was five days and 10 hours. Serious post-operative complications according to Clavien-Dindo were seen in 37.0% of all cases. The postoperative outcome analysis revealed that 30-day and one-year mortality was 14.2 and 26.6 respectively.(19).

Study III

This study investigates and presents the main results of the SMASH study, including the primary endpoint analysis but also covering other short-term outcomes related to the operation.

During the study period of 42 months between 2018 and 2021, a total of 681 unique patients were included in the intervention group. In total, 47 patients were missed, when the clinical protocol was not activated or could not be found post-operatively, as shown in Table 2.

Table 2. Missed cases

Variable	**All cases (n=47)**
Mean age (years)	56.4
Females	19/47 (40.4%)
Males	28/47 (59.6%)
Missed cases per year	
2018 (10 months)	16/47(34%)
2019 (12 months)	11/47 (23.4%)
2020 (12 months)	13/47 (27.7%)
2021 (8 months)	7/47 (14.9%)
Mortality	
Death within 30 days	8/47 (17.0%)

The definition for a patient to be considered missed was if the clinical protocol could not be found and reviewed by the interprofessional group during the study period, or if a protocol existed but several measures to be performed are not fulfilled. For categorical variables n/N (%) is presented.

The study thoroughly explores the differences in post-operative outcome between the prospective intervention group, where peri-operative management was carried out according to the standardised clinical protocol, and the retrospective cohort of controls.

The demographic data showed a mean age of 67.7 years in the intervention group compared with 66.0 for controls. Among interventions, 46.5% were males and 45.6% were controls (see Table 3).

Table 3. Demographics and Baseline Characteristics

Variable		Intervention (n=681)	Control (n=663)	p-value
	Age	67.6 (16.8) 71 (18; 97) n=681	66.0 (17.5) 69 (18; 96) n=663	0.083
Gender	**Male** **Female**	317 (46.5%) 364 (53.5%)	302 (45.6%) 361 (54.4%)	0.75
	BMI (body Mass index)	26.2 (5.5) 25.4 (12.8; 47.8) n=429	25.6 (5.6) 24.7 (11.1; 67.5)n=594	0.070
Comorbidity	**Chronic obstructive lung disease** **Ischemic heart disease** **Congestive Heart Failure** **Diabetes** **Chronic renal failure** **Obesity** **Smoking** **No comorbidity**	67 (9.8%) 95 (14.0%) 44 (6.5%) 84 (12.3%) 26 (3.8%) 99 (14.5%) 80 (11.7%) 357 (52.4%)	54 (8.1%) 80 (12.1%) 59 (8.9%) 76 (11.5%) 30 (4.5%) 82 (12.4%) 86 (13.0%) 333 (50.2%)	0.32 0.34 0.11 0.68 0.61 0.28 0.55 0.45
ASA-classification[1]	**ASA 1** **ASA 2** **ASA 3** **ASA 4** **ASA 5**	48 (7.0%) 254 (37.3%) 280 (41.1%) 79 (11.6%) 20 (2.9%)	72 (10.9%) 222 (33.5%) 264 (39.8%) 94 (14.2%) 11 (1.7%)	0.44
Diagnosis at surgery	**Peritonitis** **No peritonitis** **Purulent** **Faecal** **Other**	 532 (78.1%) 38 (5.6%) 59 (8.7%) 52 (7.6%)	 489 (73.8%) 42 (6.3%) 48 (7.2%) 84 (12.7%)	0.015
	Intestinal ischemia	91 (13.4%)	76 (11.5%)	0.33
	Ileus **No ileus** **Small intestine** **Colon** **Missing**	 273 (40.3%) 304 (44.9%) 100 (14.8%) 4	 277 (42.0%) 314 (47.6%) 68 (10.3%) 4	0.049
	Trauma	15 (2.2%)	20/661 (3.0%)	0.44
	Bleeding	33 (4.8%)	41/659 (6.2%)	0.33
	Perforation **No Perforation** **Colon** **Small intestine** **Ventricle** **Anastomosis** **Missing**	 469 (69.5%) 87 (12.9%) 62 (9.2%) 37 (5.5%) 20 (3.0%) 6	 460 (69.4%) 57 (8.6%) 72 (10.9%) 56 (8.4%) 18 (2.7%) 0	0.027

1= American Society of Anesthesiologists (ASA) Physical Status Classification.
For categorical variables n/N (%) is presented. For continuous variables Mean (SD) / Median (Min; Max) / n= is presented. For comparison between groups Fisher´s Exact test (lowest 1-sided p-value multiplied by 2) was used for dichotomous variables and the Mantel Haenszel Chi Square test was used for ordered categorical variables and Chi Square test was used for non-ordered categorical variables and the Fisher´s Non Parametric Permutation Test was used for continuous variables. 2022-10-24 TablesSpec.sas

The primary endpoint of the SMASH study, 30-day mortality, was 10.7% for interventions and 14.5% for controls (p=0.046) (Table 4). The mean hospital stay was 10.2 and 11.9 days for the intervention group and controls respectively (p=0.007). A decrease in the number of patients who were directly admitted (never discharged to a regular surgical ward) to intensive care from the operating theatre or from the recovery ward was seen, with 19.5% and 21.9% respectively (p=0.26). The duration of stay in intensive care for the intervention group was 3.12 days, while it was 5.40 days for controls (n=0.007). Patients suffering from serious complications (C-D 3b-5) decreased from 37.6% to 27.3% (p<0.001)(130).

Table 4. Primary efficacy analysis

Variable	Intervention (n=681)	Control (n=663)	GEE adj. OR (95% CI) / p-value	GEE unadj. OR (95% CI) / p-value	Fisher´s prop. diff. (95% CI) / p-value
Death within 30 days	73 (10.7%)	96 (14.5%)	0.69 (0.47-0.99) 0.0446	0.71 (0.51-0.98) 0.0383	3.8 (0.1; 7.5) 0.046

For categorical variables n (%) is presented. Adjusted Odds ratio is analysed by GENMOD with GEE model with binary outcome and link function logit adjusted for Age, Intestinal ischemia, Faecal, Purulent/Other, Chronic obstructive lung disease, Ischemic heart disease, Congestive Heart Failure, Chronic renal failure, Diabetes, Obesity, Smoking, ASA classification and Gender.

Odds ratio is analysed by GENMOD with GEE model with binary outcome and link function logit. For comparison between groups Fisher´s Exact test (lowest 1-sided p-value multiplied by 2) was used for dichotomous variables. The confidence interval for dichotomous variables is the asymptotic Wald confidence limits with continuity correction. 2022-10-24 TablesSpec.sas

Study IV

This study was designed to investigate the one-year mortality rates for the patients managed according to a standardised protocol and compared with historical controls. In addition, a subgroup analysis of different age groups was carried out. The post-operative outcome, in both the short and long term, for the age groups is also presented(133).

All 1,344 patients in the SMASH study were divided into subgroups based on age, 18-40 years, 41-60 years, 61-75 years and 76 and older.

The result from Study IV showed a three-month post-operative mortality of 14.1% for the intervention group and 20.8% for controls (p=0.0016). The one-year mortality was 19.7% and 27.8% respectively (p=0.0005).

The post-operative outcome for the different age groups (18-40 years, 41-60 years, 61-75 years and 76 -older) is also presented. The biggest group was the 76 and older (interventions n=260 and controls n=240). For this group of elderly, a decrease in one-year mortality was seen with 29.6% for interventions and 43.8% for controls (p=0.004).

Discussion

Opportunities and challenges in protocol-based standardised care

The peri-operative management in acute high-risk abdominal surgery is complex and involves specialists from different hospital departments. Standardising an advanced acute intervention that can take place at any time and requires interprofessional speedy co-operation is challenging. In peri-operative medicine in general, it is quite common to standardise procedures, but these are often elective in nature and can be directed at specific timepoints to ensure the correct skills are present. In this context, there is room for teamwork to improve, implement a clinical plan for the procedure, prepare medical equipment and inform the patient and their relatives what is going to be done. Much of this is more complicated to fulfil in the acute setting, like the management of the emergency laparotomy patient, with a known high risk of severe post-operative complications. A fact that leaves scope for improvement.

Implementation of the SMASH protocol

When protocol-based standardised care is going to be implemented in a specific setting, it is important to adapt to the prevailing situation. One way is to learn from previous studies when it comes to what has been shown to be beneficial to the patient and, based on this, modify and adjust these measures to match the new settings where the protocol is going to be implemented.

Another aspect of the implementation is exemplified by the team behind the EPOCH study(123) which presented a 37-point quality improvement protocol and offered education and training to the participating hospitals, based on the fact that each local team was allowed to identify prioritised elements for their context(134). Introducing protocol-based standardised care without local anchoring and adaptation to the prevailing situation may increase the risk of failure due to a lack of agreement and may instead create a contradiction between the measures in protocol-based standardised care and professional autonomy(135).

One way to evaluate the implementation at NÄL is to investigate the number of cases in which the clinically responsible surgeon failed to activate a protocol following a decision to operate. Table 2 shows that this occurred 47 times in 42 months (1.1 per month). According to Figure 2(130), it can be deduced that 18.4 patients were operated on every month during the intervention study period. Consequently, 6% of patients were missed and the protocol-based standardised care was activated in 94% of the cases, which can be regarded as an acceptable level and indicates that the implementation was carried out with some success.

In previous intervention studies, all the consecutive patients appear to be included during a specific period, regardless of the degree of adherence to the protocol. In the Danish AHA study, no data on adherence are available(128). In the PULP study, the ELPQuiC study, the ELC study and the EPOCH study, adherence to the protocol is reported as a percentage for each individual measure in the standardisation(29, 123, 127, 128). Previous intervention studies did not categorise missed cases and one explanation could be that data in the protocol were not secured in a way enabling a retrospective review. Furthermore, in the SMASH study, the protocol served as a checklist during the whole intervention process. This might be one reason why the missed cases category does not exist in prior studies.

To further evaluate the implementation of the SMASH protocol, adherence needs to be evaluated. Adherence to the protocol was as follows(130): the per-operative competence level was elevated. A larger number of senior consultants for both surgeons and anaesthesiologists were active in the management. The time to the first incision was generally shortened by 35 minutes (0.58 hours, 3.22 for interventions and 3.80 for controls). Over 94% of all intervention patients received peri-operative antibiotics, 13% more compared with controls. Goal-directed fluid therapy (GDTF) was used in 77.6% of all intervention patients (it was not possible retrospectively to collect data for the control group). An arterial line for haemodynamic monitoring and repeated blood gas analyses was used in 84.9% of all intervention patients and 36.8% of controls. The use of epidural anaesthesia increased from 67.0% to 71.1%.

Not all measures in the SMASH protocol are analysed for adherence to the intervention. Data not analysed in the present study are the immediate (on decision to operate) measurement of vital signs (EWS), the insertion of a nasogastric tube and urine catheters, as well as extended chemical blood analyses with arterial blood gas. In addition, pre-operative information to the patient and next of kin, a pre-operative physical bedside assessment by the responsible surgeon and anaesthesiologist, a post-operative bedside assessment by the anaesthesiologist and extended blood chemical analyses with arterial blood gas and, finally, postoperative upgraded patient monitoring (EWS) on the surgical ward were not yet analysed either.

Incidence

Few studies investigating the outcome after emergency laparotomy report the incidence as well. How common is a patient in need of an emergency laparotomy in the population? To be able to answer, the selection and the population need a definition. This includes the selection and the procedures that are included in the somewhat vague concept of emergency laparotomy? Then, what is the size of the population within the catchment area served by the healthcare system? Should the population as a whole count? In many cases, this can be complicated.

One way to calculate the incidence is to use the data in local or national registers. However, there are some limitations such as incomplete or missing data in the registration. Furthermore, the total number of included centres and patients are crucial and the demographics could differ both between and within countries.

In a Danish study, Liljendahl and colleagues presented an incidence of 27.4 primary emergency laparotomies per 100,000 individuals(33), while a British study from Chapter and colleagues (34) reports 1:1,100 (authors' calculations 90.9 emergency laparotomies per 100,000 individuals) and an Australian national study(35) reports an incidence of between 58.6 to 78.8 per 100,000 in the population, depending on the state in the country. Data from NÄL(19) in southwestern Sweden report 83.3 emergency laparotomies per 100,000 individuals. The wide variation in incidence could be explained by definitions of the population, as well as the selection of interventions. In the Danish material, Liljendahl defined emergency laparotomy as the operations where drainage, ostomy or bowel resection were performed. This definition excludes several subgroups that are normally referred to as emergency laparotomy, such as bowel obstruction due to abdominal adhesions, which is the most common group in many studies. On the other hand, Liljendahl excluded children (<18 years), which is reasonable when defining a procedure only performed on adult patients. In contrast, Chapter and colleagues included all midline laparotomies on adult patients and children living in the hospital catchment area. The published data from NÄL include children in the population. The widespread incidence of emergency laparotomy is likely due to the lack of a clear definition of the intervention and different definitions of the population.

Outcome

Mortality

The 30-day, 90-day and one-year post-operative mortality seen in the SMASH study was 10.7%, 14.1% and 19.7% for the intervention group and 14.5%, 20.8% and 27.8% respectively for controls. The post-operative mortality differs largely between countries even though the socio-economic conditions are considered to be similar. This is exemplified by comparing data from the Danish National Patient Register on 15,680 patients undergoing surgery from 2003 to 2014, revealing a 30-day mortality of 19.5%(33), with the British study from Oliver and colleagues which reports data with 39,903 patients undergoing surgery between 2013-2015, with 30-day mortality of 11.3%(136). In a study from Australia by Burmas and colleagues including 20,388 patients undergoing surgery in 99 hospitals nationwide, all acute high-risk abdominal operations, trauma laparotomies, including paediatric surgery but excluding laparoscopic appendectomies and cholecystectomies, the hospital mortality was 5.2%(35). The explanation for the difference is likely multifactorial, e.g. differences in patient management and thereby the quality of the care provided, the selection of patients and outcome measurements. Liljendahl and colleagues excluded a large group of patients, those that underwent surgery for bowel obstruction due solely to abdominal adhesions, where mortality is generally low. This may explain the higher mortality in the Danish cohort. Oliver and Colleagues include laparotomies with a lower degree of urgency in their cohort, operations with an urgency to surgery with up to 24 hours are included. In the SMASH study, only operations with an urgency of maximum 6 hours are included.

The Australian study included children (0-18 years), who have been shown to have low mortality(137). Furthermore, in the mortality analysis, the follow-up is based on the LOS in hospital (mean 13.9 days) and not for 30 whole days(35). Both of these factors probably led to reduced mortality for Burmas and colleagues.

However, even though the study design is similar and the countries are considered comparable in terms of a socioeconomic and northern European context, a difference in mortality is seen between the Danish AHA study and the SMASH study. The mortality in the AHA study intervention group was 15.5% and 21.8%, for historical controls, while, in the SMASH study, it was 10.7% and 14.5. One explanation could be the difference in the selection of patients, where the AHA study excluded all internal hernias owing to gastric bypass surgery (n=134 for interventions and n=149 for controls), while those operations are included in the SMASH study. Since this group is known to have low mortality(138), the higher mortality in the AHA study compared with the SMASH study might be a result of this.

The reason why a patient expires post-operatively is likely due to several factors, the degree of difficulty in pathology combined with a post-operative complication and reduced physiological reserves to deal with the condition that occurs. This has been studied by Ferraris and colleagues including 1,956,002 patients who underwent various surgical operations, children and trauma excluded. Severe complications (defined according to the ACS-NSQIP (the American College of Surgeons National Surgical Quality Improvement Program); wound, cardiac, renal, CNS and pulmonary including thromboembolic events, i.e. pulmonary embolus, sepsis, and bleeding) were reported for 10.6% (n=207,236) of all patients, of whom 10.5% (n=21,731) died. When the patients were divided into five NSQIP-classified groups based on the calculated probability of suffering a post-operative complication, the group with the greatest risk of complications accounted for 88% of all deaths(139).

Length of stay

The main goal for standardisation is to improve care for the patients. The quality should not be evaluated by counting how many days a patient spends in hospital after surgery. However, for the healthcare system, it is of value, because hospital resources can be saved. A cost-efficacy analysis is not a part of the present thesis. However, if the number of days in hospital decreases, along with decreased mortality, this could indicate that resources have been used wisely.

The post-operative LOS in hospital in the SMASH study was 10.2 days for interventions and 11.9 days for controls, a decrease of 16%. LOS in hospital differs between studies and data are registered in different ways. Many studies from North America and Europe report about 10 days (9.07 to 11.0) in hospital (23, 127, 128). In the British NELA year 8 report, a reduction in LOS of 12 to 10 days on average was seen(27). It is worth mentioning that the ELC study(29), based on data from 29 hospitals in the UK, reported an LOS of 20.1 days for the baseline group and 18.9 days after standardisation. It should be noted that the NELA only reports LOS for survivors, while the SMASH study includes all patients in its LOS analysis (non-survivors as well). By excluding patients who die in hospital, the total LOS will be affected. What determines the effect is whether non-survivors die shortly after the index operation or if this happens after a very long hospital stay. Including both survivors and non-survivors in the analysis of LOS will reflect the reality as it actually is.

Intensive care

In the SMASH study, an almost 40% reduction in LOS in intensive care was seen, with a mean of 3.2 days for interventions and 5.4 days for controls. Patients with failure in one or more vital organ functions, or for other severe medical reasons, run the risk of deterioration needs to be managed in intensive care. However, this is a very heterogenous group and the length of stay, outcome and the medical intervention needed in the ICU vary widely.

The British NELA network reports that 52.1% of all the patients in year 8 (n=22,132) were directly admitted to intensive care post-operatively. The NELA RISK calculator is used pre-operatively to calculate the risk of death within 30 days for the patients and the data show that 78.3% of all high-risk patients were admitted to intensive care(20). The data also show a larger proportion of post-operative patients in intensive care after introducing the NELA in the UK but also higher compared with 16% in Denmark(23) and 19.5% in the SMASH study(130).

The definition and levels of care in the peri-operative process differ between countries, as well as within countries, which is explained by different healthcare systems and differences in hospital settings. This complicates the ability to compare the results from different studies.

A patient that is considered stable enough to leave the first phase of recovery for care on a regular surgical ward will be discharged from recovery or the ICU. If the patient deteriorates on the ward and again requires intensive care, this is categorised as "re-admission to ICU" and has been shown to be associated with high mortality. The NELA reported that 3.5% of high-risk patients needed to be re-admitted to intensive care with a 30-day mortality of 32%(27). In Danish data, "ward before ICU admission" is reported to be 5.1% with a 30-day mortality of 44%(23). In data from the SMASH study, a re-admission rate of 3.2% for interventions and 4.5% for controls was seen, but the mortality rate was never published for this subgroup. To summarise, patients re-admitted to the ICU and their mortality is interesting as an outcome and has the potential to reflect the ability of the healthcare system to deal with complications. This also applies to the SMASH study, which has not yet published the mortality for this group.

Focus on the patient

Demographics and comorbidity

Data from the present study were collected from a retrospective review of patient records for the control group and prospective registration for the intervention group. The collected variables were smoking, obesity, diabetes, heart failure, ischaemic heart disease (IHD), COPD (Chronic Obstructive Pulmonary Disease) and chronic renal failure(130). The baseline characteristics are similar in both groups (intervention and control) when comparing demographics, comorbidity and ASA classification (see Table 3).

As the first intervention study in Sweden, a significant reduction of 32% in one-year mortality for the elderly managed according to a standardised protocol have been presented(133). As an alternative to age and comorbidity, clinical frailty has been shown in recent years to be an important variable to assess in the context of major surgery(91), but it was not commonly used at the time the SMASH study was designed in 2017. In 2010, Makary and colleagues showed that a higher degree of frailty leads to an increased risk of post-operative complications and length of hospital stay. In Makarys study, the patients who are categorised as frail have reduced physiological reserves to cope with major surgery. It is suggested that this group is more easily identified by classifying the frailty score than by other methods of pre-operative risk assessment(140). The SMASH study has shown a high mortality rate among elderly patients who undergo laparotomy and the outcome for the elderly group has improved after the introduction of protocol-based standardised care. However, no classification of frailty was made in the SMASH study and it would be interesting to evaluate how standardised care has affected the outcome for the frail patients in the SMASH study.

Patient experience

Extensive quantitative data sets relating to the post-operative outcome after emergency laparotomy can be found in the literature. What is it like, however, to be a patient undergoing emergency laparotomy? This is a question that few have attempted to answer. In 2021, Park and colleagues published a qualitative interview study of 15 patients who underwent laparotomy in New Zealand. Several themes relating to the patient experience have been highlighted following an analysis of the interviews(141).

Fear and uncertainty; the patients could experience that they underwent several diagnostic procedures and that healthcare personnel presented several possible differential diagnoses. However, there was an understanding of the difficulty involved in making the correct diagnosis, together with gratitude when a correct diagnosis was finally found.

In-patient communication and information need; the majority felt that they were treated with respect, that the staff took the time to answer their questions without making "false promises". At the same time, however, almost all of them felt that they did not receive enough pre-operative information and that the procedure may have been routine for the staff but not for them. Some of the older patients had difficulty taking in information due to their critical condition.

Post-operative concern and emotional outcome; in the acute post-operative phase, they all experienced worsening pain or being unwell after surgery. Several experienced unclear messages on what was required of them to be fit for discharge from hospital. In the longer term, they often described having difficulty enjoying life because of worrying about their condition. A third described a strong negative impact on their lives and the fact that they were still horrified by their experience, while others described a changed philosophy of life where they tried not to worry so much about the future. Overall, the majority were of the opinion that healthcare paid a great deal of attention to their physical well-being and much less to the psychological aspects(141).

In a questionnaire study comprising 68 patients who underwent emergency laparotomy in the UK, Jones and colleagues found that patient satisfaction was strongly associated with good communication, which by extension creates confidence in the clinical teams. In addition, they concluded that many patients were disturbed by loud noise on the surgical ward(142).

Very few qualitative studies have focused on patients who undergo emergency laparotomy or healthcare professionals who work with it. The ethnographic sub-study in EPOCH is an exception. Together with the implementation of the EPOCH protocol, a prospective ethnographic study was conducted at six hospitals. The results showed that there was good commitment to the protocol among healthcare workers, but that resources and time were lacking when it came to introducing the intervention(123, 134).

Pre-operative patient information

Despite the urgency when a patient requires an emergency laparotomy, there are strong reasons to inform the patient and preferably his/her next of kin about outcome and complications. The risk of mortality should be discussed, as well as other outcomes such as the possible need for intensive care and the patient's attitude towards it, as well as limitations in care efforts, such as do not resuscitate (DNR).

In a retrospective study aiming to evaluate "failure to inform" comprising 76 patients who underwent laparotomy, the pre-operative mortality risk was calculated with P-POSSUM. In 34.8% (n=24) of the cases, mortality was discussed with the patient. The informed patients were older (median 77.5 years versus 65.5) and had a higher mortality risk. Only 18.4% (n=14) of relatives were informed(143).

Few studies that explore failure to inform exist and this may be due to a lack of documentation or the difficulty involved in retrospectively generating reliable data. Other reasons might be that the responsible surgeon or anaesthesiologist does not take the time to inform, does not feel prepared or comfortable in the situation, or is not trained for it and thereby lacks strategies for the discussion. If this is common, it is problematic and an area for improvement. Regardless of the underlying reasons for failure to inform, an opportunity to improve is to include this in standardised protocols. One way to start is to carry out a risk assessment for everyone who is going to undergo an emergency laparotomy. In the UK, 86.8% of all patients were preoperatively assessed for the risk of mortality in the last report(27). Martin and colleagues also show in their study entitled Pathway to professionalism how important it is to have a pre-operatively calculated risk in communication with the patient and his/her family, as well as with other hospital staff(134). In the SMASH protocol, risk assessment is not included, while informing the patient is included and the surgeon is urged to take a stand on possible limitations in the level of care and to contact the next of kin. Analyses of failure to inform have not yet been carried out.

Protocol-based standardisation and its effect

The standardisation of care for emergency laparotomy in the SMASH study appears to save lives, but how?

Protocol-based standardised care includes many measures and it is challenging to identify one specific measure that has a major impact on patient outcome. If a single action had a considerable effect, it could be assumed that this would have been known at an early stage, but, in a complex clinical situation like the management of emergency laparotomy, it is not likely.

When a healthcare worker who knows the work is being reviewed and evaluates/modifies his/her efforts, which can result in improved output, this phenomenon is commonly called the Hawthorne effect and should be taken into account in all studies. However, attributing the Hawthorne effect alone to the significant improvement in mortality and morbidity occurring in the SMASH study is likely to oversimplify things. Instead, complicated medical interventions to be performed in teams need clear instructions and evaluations. Improvements in management are made on many levels, at both individual and group level. In the first place, the SMASH protocol probably does not improve what is already working well. Instead, the effect of protocol-based standardisation is to raise the level of the team's and individuals' performance when it is poor. This means that it is likely that the function of the protocol is to improve the lowest level of management and thereby reduce the complications.

ERAS for emergency laparotomy

In 2001, the first steps were taken for what later became the Enhanced Recovery After Surgery (ERAS) Society. The Swedish surgeon, Olle Ljungqvist, and the Scotsman, Ken Fearon, met at a conference on nutrition. This meeting led to a survey of peri-operative patient care and an insight into the major differences between surgical centres. The idea to produce guidelines based on best practice was the start of ERAS, which has since grown into a worldwide movement with ERAS guidelines for a wide range of specialities, such as colorectal surgery, liver surgery, aortic surgery, pancreatic and duodenal surgery, orthopaedic knee and hip replacements, caesarean section, breast surgery, heart surgery and so on. What has so far characterised the ERAS guidelines is that, until recently, only elective surgery was the focal point.

In January 2021, Carol Peden and colleagues published part 1 of the ERAS guidelines for emergency laparotomy(91). The first part focuses on the diagnosis, rapid assessment and optimisation of patients. In 2023, parts 2 and 3 were published. Part 2 deals with intra- and post-operative care(144), while part 3 is a review of organisational aspects and general considerations for managing the emergency laparotomy patient(145).

Methodological considerations and limitations

Length of study

The SMASH study includes patients from August 2014 to September 2021 and compares the post-operative outcome, a study period of more than seven years. Over time, factors other than those introduced in protocol-based standardised care may develop or change, a process that can also affect the outcome. Consequently, the possibility cannot be excluded that the result of the current study could be influenced by factors outside the standardisation that the SMASH protocol implies. This effect is likely to increase over time.

Missed cases

Failure to activate the clinical protocol occurred for 47 patients. No in-depth analysis of these patients' post-operative outcomes has been performed. Table 4 shows a different gender distribution (females 40.4%), a lower mean age (56.5 years) and higher 30-day mortality (17.0%) than in the SMASH study as a whole. Compared with the previous international intervention studies, the SMASH study differs in terms of the procedure of excluding missed cases. However, it is important to point out that the cohort of missed cases differs from the SMASH study's intervention group in terms of both demographic structure and post-operative outcome. These patients could influence the analyses of the post-operative outcome if they were included in the intervention group.

All operations or unique individuals

Complete outcome data on the intervention and control group are analysed for the cohort known as "unique individuals", but this has also been done for the "all operations" cohort, where a patient may be operated on several occasions during the study period due to recurring problems. As the supplementary data to Study 3 show, the study outcome was similar in both groups, showing statistically significant values in the adjusted analyses. The decision to publish the cohort of "unique individuals" in Study 3 was based on the fact that other studies tend to exclude patients with multiple surgeries and to include all operations involved in a much more complex statistical method. However, it should be noted that, when the SMASH study group chose to publish the data for unique individuals in Study 3, this was a deviation from the original study plan.

Demographics and physiological vital signs

No comorbidity score was used in the SMASH study, enabling comparisons between the groups within the study as well as other studies. The Charlson comorbidity index is a validated index that is able to define specific comorbidities and predict the mortality risk(146). The SMASH study also failed to register in the dataset the degree to which the patients were seriously ill on admission or, when a decision to operate was made, sepsis and organ failure in particular were not registered. It would be of value to identify the critically ill with the aim of performing a subgroup analysis of their post-operative outcome. The patients could, for example, have been evaluated with the SOFA score (Sequential Organ Failure Assessment) designed to assess critical illness and clinical conditions such as sepsis(147).

Ethical aspects

The current study was not conducted as a randomized controlled trial. The development of protocol-based standardised care was based on a review of scientific studies and best practice available at that time and then adapted to the context at NÄL county hospital. Previous studies were in favour of a standardised protocol (127, 128), which explains why randomisation was considered unethical.

Only data already collected by the health care system during medical care of the patient are used. The size of the cohorts is such, that it will not be possible to trace an individual patient from published data. The regional ethical review board in Gothenburg approved the study and informed consent from the included patients was not considered necessary (EPN Dnr: 868-17).

Scores to predict outcomes

Different scores predicting outcomes after major surgery are validated and are frequently used in clinical practice. The outcome after using these assessment tools is either the risk of complications or the risk of death after surgical intervention. The most common are P-Possum, the NELA RISK calculator and the ACS-NSQIP calculator(148). Several other studies use the predicted risk of death and compare it with the observed post-operative mortality in the scientific analyses. However, this was not available in the SMASH study and, as a result, comparisons with other datasets could not be performed.

Surgical complications

In the SMASH study all patients were classified according to the Clavien-Dindo score for surgical complications. However, in the SMASH study the score was not adapted to an acute context involving critically ill patients. In 2014, Mentula and colleagues showed that Clavien-Dindo can be used for emergency surgical patients but suggested that grade 4 complications should consider pre-existing organ dysfunction and only register new onset of organ dysfunction(149). The registration of Clavien-Dindo in the SMASH study was not performed according to Mentula and colleagues' suggestion and, as a result, the number of Clavien-Dindo grade 4 complications could therefore be higher in both groups.

Outcome analysis for the future

Days alive out of hospital

During the last few decades, most study outcome analyses have usually been based on mortality in the short and long term, followed by the length of hospitalisation, the need for intensive care and other post-operative surgical complications and the SMASH study is no exception. This package of outcome measurements focuses more on the hospital's measurable performance and has several potential weaknesses. It does not give a complete picture of the patient's post-operative situation and measurements of quality of life are missing. There are several potential ways to measure post-operative quality of life and most are qualitative methods. A quantitative alternative, Days Alive Out of Hospital (DAOH) has recently been discussed as an outcome measurement. DAOH is defined as the number of days spent outside hospital during a defined post-operative period (30, 90, 180 or 365 days) counted from the time of surgery. A high number is an indicator of a life outside hospital care, i.e. a measurement of quality of life. DAOH=0 is the result of two things, that the patient either died or was hospitalised, during the defined measurement period.

In a British study, Spurling and colleagues retrospectively included 78,921 operated patients from 181 hospitals over a four-year period (2013-2017). The total 30-day mortality was 11%, while the median value $DAOH_{30}$ was 16 days. For the 8.7% who underwent laparoscopic surgery, a $DAOH_{30}$ of 22 was seen, compared with 15 for the 91.3% who underwent open surgery. The ASA-4 and ASA-5 groups each had a median of 0(150).

The general use of $DAOH_{30}$ or $DAOH_{90}$ has the potential to be an important complement to the current package of outcome analyses for acute high-risk abdominal surgery, to provide a better understanding of the patients who are discharged from hospital without being re-admitted.

No-LAP and impact on outcome

There is a group of patients not previously described: those that had a clear indication to operate but where the laparotomy was never performed. This group of patients has been categorised as No-LAP. Only a few publications have focused on the No-LAP population. The first is by McIlveen and colleagues, who, in 2019, in a prospective single-centre study over 14 months in 2015-2016, included 314 consecutive patients eligible for emergency laparotomy, where the No-LAP population consisted of 32%. Among the 68% who underwent surgery, 30-day mortality was 13% compared with 63% in the No-LAP group and, for the cohort (n=314) as a whole, 28.7% was seen. In both groups, the most common indications for surgery were obstruction (25%), ischaemia (24%) and perforation (21%) (151). In 2022, Ebrahim and colleagues presented prospective Danish data including 252 consecutive patients followed for a period of 10 months; of these 8.3% were No-LAP. The reported 30-day mortality was 9% for those undergoing surgery, 95% for No-LAP and 16% for the whole cohort. The indication for surgery for the Danish No-LAP patients was perforation (38%), ischaemia (38%) and obstruction (24%)(152). There is reason to believe that the No-LAP population has an impact in several ways, not least on mortality, as the two small studies indicate.

Conclusion

The SMASH study investigates the effect on post-operative outcome following standardised peri-operative management for emergency laparotomy.

- The results show that 30-day mortality fell by over 26%, a trend that proved to be sustained as one-year mortality fell by over 29%.
- The number of days in hospital was reduced by 1.7 days on average, a decrease of 16%.
- The length of stay in intensive care fell by more than 40%, from five days and 10 hours to three days and five hours on average.

In conclusion, the study shows that undergoing emergency laparotomy in Sweden is associated with severe complications, high mortality in both the short and long term, long hospitalisation and an extensive need for intensive care in the post-operative period. However, a standardised protocol for management has clear potential to reduce mortality and complications.

Future perspectives

Acute high-risk abdominal surgery is a very large topic. A number of aspects remain to be scientifically explored, using both qualitative and additional outcome analyses.

- Evaluating the experiences of emergency laparotomy management from the patient's point of view is of great interest and importance. The same thing applies to healthcare workers' valuable experiences related to following a standardised protocol in clinical work.

- One interesting alternative to traditional 30-day mortality as the primary outcome is to analyse 72-hour and 90-day mortality. This approach has the potential to distinguish the number of the deaths that occur close to the index operation, a very critically ill group of patients, and to compare this group with the patients that survive for more than 90 days, a period where most patients have been discharged from hospital.

- Failure to rescue (FTR) would be interesting to analyse in order to evaluate the ability to detect and manage patients with surgical complications.

- Days Alive Out of Hospital, $DAOH_{30}$ and $DAOH_{90}$, as the post-operative outcome has the potential to reflect the degree to which patients recover enough to be able to be discharged from hospital.

- The patients that have a clear indication for surgery, but in whom, for various reasons, no laparotomy was performed, the No-LAP population. Both the outcome for these patients and the different reasons behind the decision to refrain from surgery are important to evaluate for this population.

- One of the great challenges of our time in global health care, is to offer safe surgery and anaesthesia to everyone. Perhaps adapted protocols with standardised clinical peri-operative care are a way to go for healthcare systems in medium and low resource settings.

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