



LUND UNIVERSITY

Open abdomen therapy with vacuum-assisted wound closure and mesh-mediated fascial traction

Bjarnason, Thordur

2014

[Link to publication](#)

Citation for published version (APA):

Bjarnason, T. (2014). *Open abdomen therapy with vacuum-assisted wound closure and mesh-mediated fascial traction*. [Doctoral Thesis (compilation), Department of Clinical Sciences, Malmö]. Department of Clinical Sciences, Lund University.

Total number of authors:

1

General rights

Unless other specific re-use rights are stated the following general rights apply:

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Read more about Creative commons licenses: <https://creativecommons.org/licenses/>

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

LUND UNIVERSITY

PO Box 117
221 00 Lund
+46 46-222 00 00

Open abdomen therapy with vacuum-assisted wound closure and mesh-mediated fascial traction

Thordur Bjarnason

AKADEMISK AVHANDLING

som med vederbörligt tillstånd av Medicinska Fakulteten vid Lunds Universitet för
avläggande av doktorsexamen i medicinsk vetenskap kommer att offentligen
försvaras i Lilla aulan, Jan Waldenströms gata 5, SUS, Malmö, fredagen 17/1
2014 kl. 13.00

Handledare: Doc. Agneta Montgomery

Biträdande handledare: Dr. Ulf Petersson och Doc. Stefan Acosta

Fakultetsopponent: Doc. Ari Leppäniemi, Helsinki University, Central Hospital,
Helsinki, Finland



LUND
UNIVERSITY

Lund 2014

Lunds Universitet, Medicinska fakulteten,
Institutionen för kliniska vetenskaper, Malmö,
Enheten för kirurgi

Organization LUND UNIVERSITY Faculty of medicine Department of clinical sciences, Malmö Division of surgery	Document name DOCTORAL DISSERTATION	
	Date of issue December 2013	
Author(s) Thordur Bjarnason	Sponsoring organization	
Title and subtitle: Open abdomen therapy with vacuum assisted wound closure and mesh mediated fascial traction		
<p>Introduction: Several life-threatening intra-abdominal conditions may be treated with open abdomen (OA) therapy. Potential complications to OA treatment include damage to the exposed bowel resulting in enteric fistulas, and inability to close the abdomen afterwards resulting in large ventral hernias. Vacuum-assisted wound closure and mesh-mediated fascial traction (VAWCM) is a novel technique for temporary closure of an OA, intended to increase the chances of subsequent delayed primary fascial closure without increasing the risk of complications. A classification system for the OA has been proposed by the World Society of the Abdominal Compartment Syndrome (WSACS), aimed at improving OA therapy and facilitating clinical research, but has not previously been evaluated.</p> <p>Aims: The aims were to study:</p> <ul style="list-style-type: none"> • Short-term clinical outcome of OA therapy with VAWCM with regards to fascial closure and factors associated with failure of fascial closure, mortality, morbidity and possible technique-related complications. • One-year clinical outcome of OA therapy with VAWCM with regards to the incidence of incisional- and parastomal hernias, abdominal wall discomfort and frequency of hernia repair operations after one year. • Validity and reliability of the 2013 OA classification system by WSACS and to propose instructions for use with the classification. • Physiological effects of vacuum therapy (VAWC) in an OA with regards to the extent of negative pressure reaching the bowel, the efficacy of the VAWC system in draining fluid from the abdominal cavity and whether paraffin gauzes can be effectively used as pressure isolation when placed between the vacuum source and the bowel. <p>Results/conclusions:</p> <ul style="list-style-type: none"> • VAWCM provided a high fascial closure rate after long-term OA treatment in mostly elderly, non-trauma patients. Technique-related complications were few and fistula incidence and mortality were similar to other studies. • Incisional hernia incidence one year after OA therapy with VAWCM was high. Most hernias were small and asymptomatic and few required surgical repair during the first year. • The validity and reliability analysis of the OA classification system by WSACS showed that each patient's most complex OA grade, worsening OA grade without later improvement, as well as development of grade C (enteric leak) or grade 4 (entero-atmospheric fistula) were associated with worse outcome (mortality and failure of fascial closure). Every effort should be made to prevent patients from ascending to a more complex OA grade, to try to repair enteric leaks and to avoid enteroatmospheric fistulas. • Negative pressure reaching the bowel during VAWC therapy was limited, regardless of negative pressure setting. Reduced therapy pressure did not lead to reduced pressure at the bowel surface. The system drained the abdominal cavity completely of fluid. Paraffin gauzes were of limited value as a means of isolation against pressure propagation. 		
Key words: Open abdomen, laparostomy, VAWC, NPWT, TNP, VAWCM, classification		
Classification system and/or index terms (if any)		
Supplementary bibliographical information		Language: English
ISSN and key title: 1652-8220		ISBN: 978-91-87651-31-1
Recipient's notes	Number of pages: 177	Price: 300 kr
	Security classification	

Signature _____ Date _____

Open abdomen therapy with vacuum-assisted wound closure and mesh-mediated fascial traction

Thordur Bjarnason



LUND
UNIVERSITY

Lund 2014

Lund University, Faculty of Medicine,
Department of Clinical Sciences, Malmö,
Division of Surgery

© 2014 Thordur Bjarnason
thordur.bjarnason@med.lu.se

Lund University, Faculty of Medicine
Doctoral Dissertation Series 2014:7
ISBN 978-91-87651-31-1
ISSN 1652-8220

Printed in Sweden by Media-Tryck, Lund University
Lund 2014



**CLIMATE
COMPENSATED
PAPER**



REPA[®]
A part of FTI (the Packaging and
Newspaper Collection Service)

To my family

Contents

List of publications	9
Abbreviations	10
Thesis at a glance	11
Foreword	13
General introduction	15
From a case to a thesis	15
History of open abdomen therapy	16
Indications for open abdomen therapy	18
Open abdomen therapy – a double-edged sword	21
Temporary abdominal closure techniques	23
A word of caution	30
Vacuum therapy for fistula management	30
Late incisional hernias	31
Classification of the open abdomen (OA)	32
Vacuum-assisted wound closure with mesh-mediated fascial traction	33
Aims of the thesis	39
Patients and methods	41
Ethics and clinical trial registration	41
Overview – all studies	41
Patients – prospective cohort study (papers I–III)	41
Methods – prospective cohort study (papers I and II)	43
Methods – evaluation of the OA classification (paper III)	46
Methods and subjects – experimental study (paper IV)	52
Statistics	54
Results	57
OA therapy with VAWCM (papers I and II)	57
Validity and reliability of the OA classification (paper III)	72
	7

Physiological effects of vacuum therapy in an open abdomen (paper IV)	76
General discussions	81
Physiological effects	83
Fascial closure	83
Complications	85
Mortality	87
Incisional hernias	88
Parastomal hernias	89
Other techniques combining vacuum and traction	90
Increasing use of VAWCM	92
Open abdomen classification	93
Methodological issues	94
Lessons learned from experience in OA management	95
Conclusions	99
Future perspectives	101
Populärvetenskaplig sammanfattning (summary in Swedish)	103
Acknowledgements	107
References	109
Medicinae doctores in chirurgia, Malmö, Lund University	121
Original papers	125

List of publications

This thesis is based on the following publications, which will be referred to by their roman numerals in the text:

- I. Acosta S, **Bjarnason T**, Petersson U, Pålsson B, Wanhainen A, Svensson M, Djavani K, Björck M. Multicentre prospective study of fascial closure rate after open abdomen with vacuum and mesh-mediated fascial traction. *Br J Surg*. 2011 May;98(5):735-43.
- II. **Bjarnason T**, Montgomery A, Ekberg O, Acosta S, Svensson M, Wanhainen A, Björck M, Petersson U. One-year follow-up after open abdomen therapy with vacuum-assisted wound closure and mesh-mediated fascial traction. *World J Surg*. 2013 Sep;37(9):2031-8.
- III. **Bjarnason T**, Montgomery A, Acosta S, Petersson U. Evaluation of the open abdomen classification system by the World Society of the Abdominal Compartment Syndrome: a validity and reliability analysis. Manuscript.
- IV. **Bjarnason T**, Montgomery A, Hlebowicz J, Lindstedt S, Petersson U. Pressure at the bowel surface during topical negative pressure therapy of the open abdomen: an experimental study in a porcine model. *World J Surg*. 2011 Apr;35(4):917-23.

Papers are reproduced with permission of John Wiley & Sons (paper I) and Springer-Verlag New York (papers II and IV).

Abbreviations

AAA	Abdominal Aortic Aneurysm
ACS	Abdominal Compartment Syndrome
BMI	Body Mass Index
CI	Confidence Interval
CT	Computed Tomography
DL	Decompressive Laparotomy
EHS	European Hernia Society
IAH	Intra-Abdominal Hypertension
IAP	Intra-Abdominal Pressure
ICU	Intensive Care Unit
IPOM	Intra-Peritoneal Onlay Mesh
IV	Intra-Venous
MODS	Multiple Organ Dysfunction Syndrome
NPWT	Negative Pressure Wound Therapy (another term for VAWC)
OA	Open Abdomen
OR	Odds Ratio
PDS	Polydioxanone
PVH	Planned Ventral Hernia
SOFA	Sequential Organ Failure Assessment
TAC	Temporary Abdominal Closure
TNP	Topical Negative Pressure (another term for VAWC)
US	Ultrasound
VAC®	Vacuum Assisted Closure® (a commercially available VAWC system)
VAWC	Vacuum-Assisted Wound Closure
VAWCM	Vacuum-assisted wound closure and mesh-mediated fascial traction
WSACS	World Society of the Abdominal Compartment Syndrome

Thesis at a glance

Title	Aim	Method	Results/conclusions
<p>Paper I: Multicenter prospective study of fascial closure rate after open abdomen with vacuum and mesh-mediated fascial traction.</p>	<p>To study clinical results after OA therapy with VAWCM: in particular fascial closure, mortality, morbidity and possibly technique-related complications.</p>	<p>111 consecutive patients at four Swedish hospitals were included.</p>	<p>Fascial closure rate was high. Technique-related complications were few and serious complications were comparable to other studies.</p>
<p>Paper II: One-year follow-up after open abdomen therapy with vacuum-assisted wound closure and mesh-mediated fascial traction</p>	<p>To study clinical results one year after OA therapy with VAWCM, in particular incidence of incisional- and parastomal hernias.</p>	<p>The same patient cohort as in paper I was followed up after one year. Hernia was determined with clinical examination and CT.</p>	<p>Incisional hernia incidence one year after OA therapy with VAWCM was high. Most hernias were small and asymptomatic, few required surgical repair.</p>
<p>Paper III: Evaluation of the open abdomen classification system by the World Society of Abdominal Compartment Syndrome (WSACS): a validity and reliability analysis.</p>	<p>To study validity and reliability of the 2013 OA classification system proposed by WSACS.</p>	<p>Data from paper I was used. OA grades were compared to clinical results for evaluation of validity. Inter-rater and test-retest reliability were assessed.</p>	<p>Most complex grade, worsening grade, grade C (enteric leak) or grade 4 (entero-atmospheric fistula) were associated with worse outcome (failure of fascial closure and mortality). Inter-rater reliability was good and test-retest reliability was moderate to good.</p>
<p>Paper IV: Pressure at the bowel surface during topical negative pressure therapy of the open abdomen: an experimental study in a porcine model.</p>	<p>To study the physiological effects of VAWC therapy in an OA: in particular pressure distribution, fluid drainage and pressure isolating effect of paraffin gauzes.</p>	<p>Six pigs were prepared with an OA and VAWC. During therapy, physiological aspects were evaluated.</p>	<p>Negative pressure reaching the bowel was limited, regardless of pressure setting. The system drains the abdominal cavity completely of fluid. Paraffin gauzes do not isolate against pressure propagation.</p>

Foreword

During my surgical training at Landspítali University Hospital in Reykjavík and at Centralsjúkhuset in Kristianstad, I became interested in laparoscopy. When I finally had become a surgeon, I joined the laparoscopy team in Malmö to pursue further training and research in the field of minimally invasive surgery. In a mysterious way, I ended up doing a thesis on maximally invasive surgery...

Perhaps, the reason is not so mysterious. In fact, minimally and maximally invasive surgery balances quite well. Among the tasks of laparoscopic surgeons at our department is to repair the abdominal wall, both with laparoscopic and open techniques. In the end, open abdomen therapy is about the abdominal wall. It certainly will be, if it cannot be closed.

When I was given the opportunity to work with very skilled coworkers on a project that involved rather dramatic surgery (and no mice) that could have significant practical implications in the care of severely ill patients, I, of course, accepted.

Do, or do not. There is no try.

– *Yoda*

General introduction

From a case to a thesis

In March 2005, a 65-year old man underwent an elective open repair of an abdominal aortic aneurysm (AAA) at Skåne University Hospital, Malmö. The operation was complicated with severe bleeding, with 18 L estimated blood loss. Postoperatively, the patient was circulatory instable and required high dose noradrenalin infusion for inotropic support and large volumes of plasma and crystalloid infusion to maintain a blood pressure > 60 mmHg. In order to maintain adequate oxygen perfusion, administration of 80 % oxygen with high peek inspiratory airway pressure on the ventilator was required. Urinary output was negligible. Intra-abdominal pressure, measured through a urinary catheter, was 45 mmHg. An acute decompressive laparotomy was performed, where 5½ L of blood were evacuated. The abdomen was left open, using the vacuum pack method. The patient was kept intubated in the intensive care unit. Renal replacement therapy was

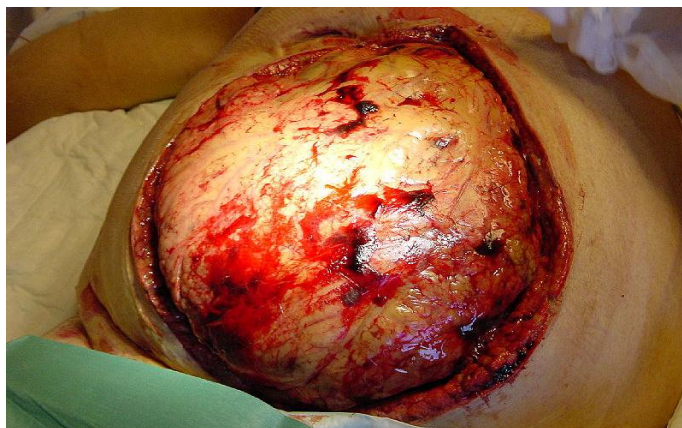


Figure 1. Decompressive laparotomy due to ACS in a 65 year old patient after open AAA repair.

initiated. Several wound-dressing changes were necessary every day due to leakage of wound fluid into the patient's clothes and bed. Nine days after the index operation, a vacuum-assisted wound closure (VAWC) dressing (see page 31) was applied instead of the vacuum pack. The pressure was set to 100 mmHg negative pressure. This resulted in improved control of fluid leakage and it was noted that the

macerated skin near the wound edges started to heal. After 20 days, the patient's maximal weight of 118 kg had decreased to 82 kg. In spite of this promising development, it was apparent that it would not be possible to close the abdomen due to the extent of lateral retraction of the fascial edges.



Figure 2. Large remaining fascial diastasis after almost 3 weeks of open abdomen therapy, indicating that abdominal closure will not be possible.

At this point, it was decided to attempt gradual medial approximation of the fascia, using a polypropylene mesh sutured to the fascial edge on each side. VAWC therapy was continued with the mesh sutured together in between the layers of the dressing. After three dressing changes with a gradual tightening of the mesh, the fascial edges could be re-approximated and sutured together in the midline. The patient was treated in the intensive care unit for 54 days with an open abdomen for 42 days. The patient was eventually discharged from the hospital and is still alive after eight years. No incisional hernia has been detected at follow-up.

This case was the inspiration for a prospective, multicenter study, evaluating the vacuum-assisted wound closure and mesh-mediated fascial traction technique for the management of open abdomens, which is the basis of this thesis.

History of open abdomen therapy

An open abdominal cavity outside of an operating theater is undesirable, both for the patient and the surgeon. It was formerly considered a surgical failure and performed as a last resort. In the last decade, however, OA therapy (also called laparostomy), has become an established surgical strategy in emergency situations. Historically, OA therapy evolved separately out of three different clinical scenarios: abdominal trauma, severe intra-abdominal infection and raised intra-abdominal pressure.

Trauma

Packing of the liver with surgical gauzes to control traumatic bleeding, dates back to the late 19th century¹⁻⁴ and the method was further evolved in the beginning of the 20th century by Pringle, Halsted and others^{2,5,6}. In these early times, the skin and fascia were closed if possible.

Injuries causing major tissue losses of the abdominal wall were not uncommon during the World Wars, leading to difficulties closing the abdomen. Ogilvie was probably first to describe OA therapy, when he in 1940 recommended that, rather than try to close an abdominal wound under excessive tension, it should be left open: “If the edges cannot be brought together with moderate tension, say, with a gentle pull on two pairs of Ochsner’s gripping the sides, it is better not to insert stitches that will only tear out and increase the damage. Here the chief need is, again, to prevent evisceration. Gauze swabs sterilized in and impregnated with Vaseline, and not merely smeared with it, should be laid over the exposed viscera, their edges tucked well under those of the defect. The sides of the incision are brought together as well as can be with strips of Elastoplast or even with stitches over the Vaseline”⁷.

By the end of the Second World War, peri-hepatic packing began to fall out of favor due to improved surgical techniques combined with high complication rate associated with abdominal packing, notably necrosis and sepsis as well as re-bleeding on gauze removal. Surgical exploration with definitive repair at the initial operation became the mainstay of treatment until packing was re-introduced in the 1970’s⁸⁻¹⁰.

The first description of abbreviated laparotomy for source control, followed by resuscitation and subsequent re-operation for definitive repair, was published by Stone in 1983¹¹. The modern concept of damage control surgery was coined by Rotondo, Schwab et al. in 1993¹². The term originates from naval warfare, meaning provisional repairs at sea, enabling a damaged ship to stay afloat. In the beginning, the initial abbreviated laparotomy was usually closed with skin-only closure, but other methods of temporary abdominal closure soon evolved.

Infection

The aphorism “ubi pus, ibi evacua” (where there is pus, there evacuate), dates back to Celsus in the first century A.D., and is applicable to the abdominal cavity itself. The use of OA therapy to drain severe intra-abdominal infections was first used in the early 1970’s. It was described in several case studies in the late 1970’s and early 1980’s¹³⁻¹⁸ as an alternative to repeated laparotomies, peritoneal lavage or radical peritoneal debridement¹⁹. Different methods of temporary abdominal closure allowing easy access to the abdominal cavity were invented, such as zippers, slide fasteners and Velcro® analogues.

Raised intra-abdominal pressure

The physiological effects of raised intra-abdominal pressure (IAP) have been known since the middle of the 19th century²⁰⁻²² and were reported in several studies throughout the 20th century²². In 1951, Baggot described the dangers of closing an abdominal wound under tension, risking wound dehiscence or death^{23,24}. When the use of laparoscopy became widespread in the 1970's, the negative effects of high IAP due to tension pneumo-peritoneum were noticed. The first modern description of abdominal compartment syndrome (ACS) and the beneficial effect of decompressive laparotomy was published by Kron et al. in 1984²⁵, although the term itself was first coined by Fietsam et al. in 1989²⁶.

Pediatric surgeons were the first to use OA therapy on a regular basis, being faced with congenital open abdomens in the form of omphaloceles and gastroschisis. Staged repair of the abdomen, avoiding excessive increase in intra-abdominal pressure and the risk of death, was first described in 1948^{27,28}.

Indications for open abdomen therapy

There are two fundamental reasons for a surgeon to leave an abdomen open: that it cannot be closed or that it should not be closed²⁹. Indications for OA therapy (regardless of underlying disease) may be divided into five categories:

Indications for OA therapy:

- Need for more space (to prevent or to relieve raised intra-abdominal pressure)
- Need for drainage of severe infection (similarly to an abscess)
- Need to save time in a quick damage control operation of an unstable patient
- Re-operation is planned (unnecessary to close abdomen in between)
- Wound dehiscence (to improve wound condition and physiology before re-closure)

In many cases, more than one of the indications above may be present. For simplicity, underlying conditions are divided into trauma and non-trauma situations and abdominal compartment syndrome in the following chapter.

Trauma setting

The damage control concept consists of three phases: an initial abbreviated laparotomy for source control (e.g. hemorrhage and/or contamination), followed by resuscitation and then a second look operation with definitive repair when the physiology (e.g. coagulopathy) has improved^{11,12,30,31}. Leaving the abdomen open

instead of suturing the fascia and skin saves time in such situations and is also practical since the wound will be opened up again the next day³². In addition, volume of intra-abdominal contents may be increased due to general edema after fluid resuscitation, hematoma or gauze packing, and it may be impossible to close the abdomen (Figure 3). Even when closure is possible, there may be a risk of subsequent development of edema or hematoma, leading to raised intra-abdominal pressure, adding negative effects on an already strained physiological situation³³⁻³⁵.

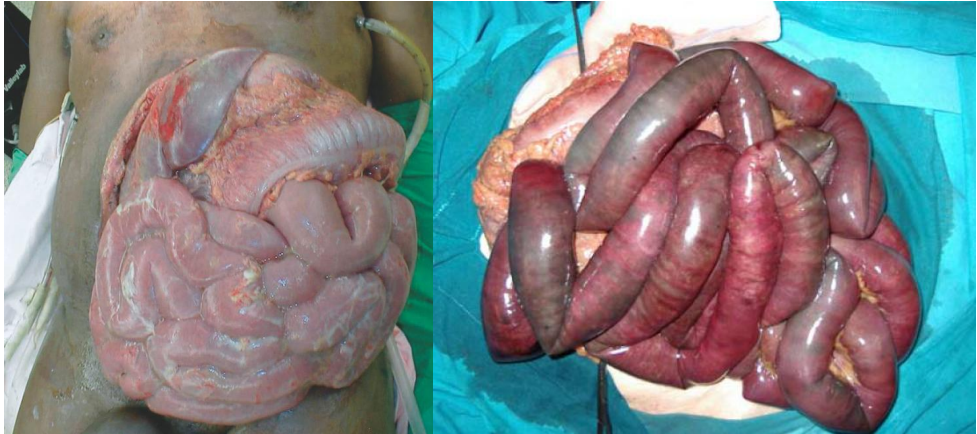


Figure 3. Closure of abdomen is not possible due to (left) visceral edema and retroperitoneal hematoma after blunt trauma and (right) retroperitoneal tumor (left: Miller et al.³⁶ © William & Wilkins; right: Ortega-Deballon et al.³⁷ © Springer, reproduced with permission).

Non-trauma setting

Intra-abdominal infection may be so severe that it requires open drainage, similar to an abscess^{13-15,17,18}. In an unstable, septic patient, it may be appropriate to adhere to the damage control protocol and perform a quick operation for source control and postpone definitive surgery (e.g. anastomoses or stomas) until the physiology has improved^{29,38}. Fluid resuscitation due to septic shock may result in general edema, further increasing IAP.

Ruptured AAA may cause a large, space-occupying retroperitoneal hematoma, increasing IAP. Many patients present with hypovolemic shock and require massive fluid resuscitation, leading to edema. After endovascular repair, where the abdomen remains closed, it is especially important to be aware of the lethal process of raised IAP and maintain a low threshold for decompressive laparotomy^{34,39,40}.

Intra-abdominal or retro-peritoneal space occupying lesions, such as tumors or spontaneous hematomas (Figure 3) are other reasons for increased IAP.

In case of bowel ischemia, restrictive surgery is warranted in order to salvage marginally circulated but possibly viable bowel, especially if early revascularization

is performed. Definitive resection and anastomosis is then delayed, and OA therapy applied in the interval until the second look operation^{34,41}.

Wound dehiscence is emerging as an indication for OA therapy. The cause of dehiscence is often more than a simple technical failure. It is frequently a complex situation with severely compromised healing in catabolic patients with deep infections and/or multiple organ dysfunction. Under such circumstances, temporary OA therapy with eradication of infection and restoration of nutritional status is preferable to immediate closure attempts⁴².

Intra-abdominal hypertension and abdominal compartment syndrome

Intra-abdominal hypertension (IAH) is defined as an intra-abdominal pressure (IAP) of 12–20 mmHg and may cause a wide spectrum of negative pathophysiological effects on the human body (Figures 4 and 5).

IAP above 20 mm Hg together with a new organ dysfunction represents abdominal compartment syndrome (ACS)³³⁻³⁵. This may occur in any of the situations described above (primary ACS). It may also be caused by massive fluid resuscitation and/or capillary leakage due to an extra-abdominal condition, such as sepsis, cardiac arrest or burns (secondary ACS)^{43,44}. Persistent or recurrent ACS may occur despite surgical decompression (tertiary ACS).

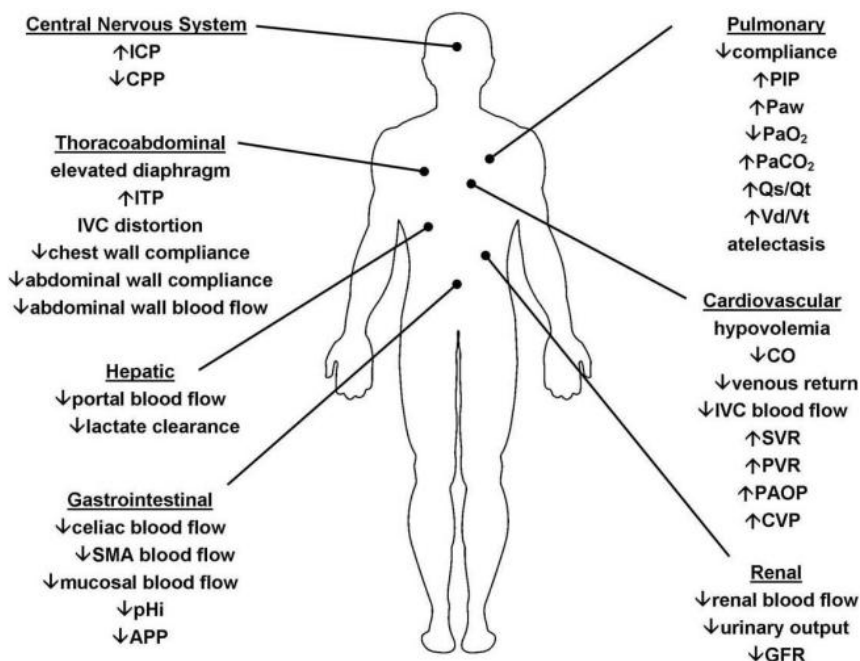


Figure 4. Pathophysiological implications of intra-abdominal hypertension (Cheatham⁴⁵, open access)

The first line of treatment for raised intra-abdominal pressure is non-operative, with e.g. nasogastric decompression, neuromuscular blocking agents, percutaneous drainage of intra-peritoneal fluid collections and diuretics to remove edema. If non-operative management is unsuccessful, decompressive laparotomy with subsequent OA therapy should be initiated early, in order to improve survival⁴⁵⁻⁴⁸. Subcutaneous fasciotomy has been described as an alternative to decompressive laparotomy, in similarity with techniques used for compartment syndrome of the extremities^{49,50}. This technique may decrease IAP sufficiently and thereby help improving deranged physiology, but at the cost of a ventral hernia.



Figure 5. A patient with a tense abdomen, developing abdominal compartment syndrome.

Open abdomen therapy – a double-edged sword

OA may be the only feasible treatment in certain surgical emergencies and undoubtedly saves lives^{51,52}. At the same time, there are serious complications accompanying OA therapy that need to be considered, such as ventral hernias, enteric fistulas and difficult wound care.

Planned ventral hernia

As soon as OA therapy is initiated, adhesions start to form between the viscera and the inside of the abdominal wall. At the same time, intrinsic forces of the oblique

abdominal wall muscles cause each side to retract laterally. If not prevented, the abdominal wall will soon become fixed and impossible to close (frozen abdomen).

If the fascia cannot be closed at the end of OA therapy, the only option may be a “planned ventral hernia”, i.e. a healed wound despite non-closed fascia. The most common method to accomplish this is to promote granulation on the bowel surface followed by split-thickness skin grafting (Figure 6). Since OA therapy usually includes a full length laparotomy for optimal effect, the resulting hernias can be very large, requiring extensive reconstructive hernia surgery to repair.

Factors leading to a frozen abdomen:

- Adhesions between viscera and abdominal wall
- Lateral retraction of abdominal wall due to intrinsic muscle retraction



Figure 6. Planned ventral hernia, awaiting reconstruction one year after OA therapy.

Enteroatmospheric fistulas

Without protective cover, the bowel is exposed to the physical elements, evisceration, desiccation and manipulation during dressing changes. Furthermore, there is a risk of damage from harmful toxins in contaminated wound fluid⁵³. An enteric fistula, opening up among exposed bowel loops may be extremely difficult to manage and carries high risk of mortality (Figure 7).

Patients receiving OA therapy often suffer from severe illnesses such as bowel ischemia, sepsis, multiple organ dysfunction syndrome (MODS) and general catabolic state, which may increase the risks of enteric fistulas even further.

Increased survival due to OA therapy might result in more patients being at risk during a longer period of time, which in turn might lead to increased prevalence of fistulas. The presence of bowel anastomoses or other suture lines, gastrostomy catheters or nutritional jejunostomy catheters may also increase the risk of leakage and fistula formation.

The technique used for temporary abdominal closure (TAC) is another factor for consideration, due to different physical properties of the dressing.

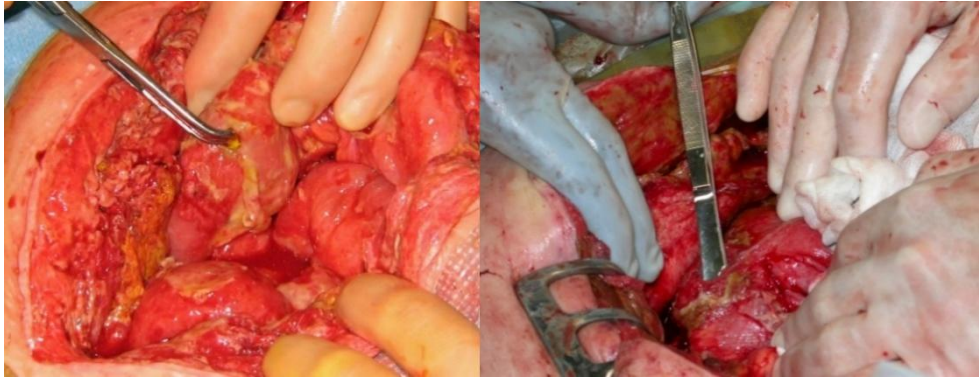


Figure 7. Enteroatmospheric fistula in an open abdomen (left: Töttrup⁵⁴ © Springer, reproduced with permission; right: own figure).

Risk factors for an enteroatmospheric fistula:

- OA therapy itself (exposed bowel, manipulation during dressing changes)
- Underlying disease (bowel ischemia, MODS, catabolism, suture lines, feeding tubes)
- TAC method (physical properties)

Difficult wound care

Large amount of wound fluid may be produced in the abdominal cavity, especially in the presence of infection and/or edema. Fluid losses up to several liters per day may lead to difficulties in upholding fluid balance. It may also lead to frequent, cumbersome dressing changes with skin maceration – “a nursing nightmare”⁵⁵.

Temporary abdominal closure techniques

Several difficulties need to be overcome when dressing the open abdomen. The intra-abdominal contents need to be covered in a way that helps maintain a physiological environment as close to normal as possible, by removing excess

wound fluid, toxins, debris and bacteria. The dressing must also be able to handle large quantities of wound fluid. The bowel needs to be prevented from evisceration and protected from mechanical damage. Importantly, it should facilitate subsequent closure when an OA is no longer necessary⁵⁶. Several different TAC methods have been described and the most common ones will be described below.

Ideal temporary abdominal closure should:

- Prevent evisceration and protect bowel.
- Maintain physiological wound environment
- Handle large quantities of wound fluid
- Facilitate fascial closure at the end of OA therapy

Skin-only closure

Rapid closure of skin can be achieved using a running suture or towel clips (Figure 8). This technique was commonly used in the early days of damage control surgery.

Even though the fascia is open underneath the skin, it does not create much extra space for expansion, and increased abdominal tension may in worst case result in ACS. Tension of the skin may result in necrosis of the wound edges and fluid leakage between closing points may require frequent dressing changes. Another important drawback is the formation of adhesions and if the abdomen is not closed within a few days, it becomes a frozen abdomen.

According to definitions proposed by the World Society of the Abdominal Compartment Syndrome (WSACS) in 2013, skin-only closure is no longer an OA³⁴.



Figure 8. Towel clip closure (Sugrue et al.⁵⁷ © Elsevier, reproduced with permission).

Bogota bag

Bridging of the skin with an empty plastic infusion bag or x-ray cassette cover is both fast and cheap and allows visual inspection of the viscera (Figure 9). The technique was introduced in the literature by American trauma surgeons Feliciano and Mattox after visiting San Juan de Dios Hospital in Bogotá, Colombia^{32,58}. The invention has been credited O. A. Borráez, who as a surgical resident at the same hospital in 1984 used a sterilized front side of an empty 3L urology irrigation bag to temporarily close the abdomen after a trauma laparotomy^{59,60}. The Bogota bag (or bolsa de Borráez), is probably the most commonly used TAC device in the world, due to its simplicity and low cost^{61,62}.

Disadvantages with this technique include abdominal fluid being retained underneath the bag risking raised intra-abdominal pressure, as well as adhesion formation leading to a frozen abdomen. Recent amendments include an intra-abdominal sheet as an adhesion barrier and vacuum suction^{60,63}.

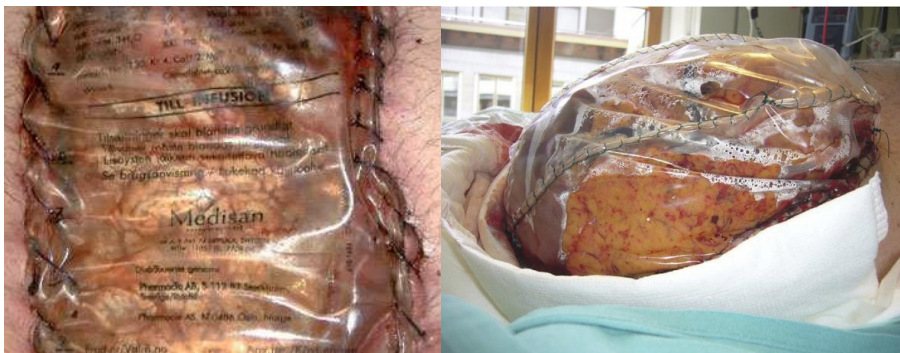


Figure 9. Bogota bag (left: © Martin Björck; right: Mayer et al.⁶⁴ © Mosby, reproduced with permission).

Meshes, sheets, zippers, slide fasteners and sandwich technique

A variety of other techniques have been described for bridging the abdominal gap in an OA, both home-made systems and commercially available devices. Some use meshes, absorbable or non-absorbable, permanent or temporary. Others include sheets of silicone or other material, some with a zipper or slide fastener to facilitate re-exploration (Figure 10). Some of the early versions did not allow for expansion of abdominal volume, such as early zipper or slide fastener models^{64,65}.

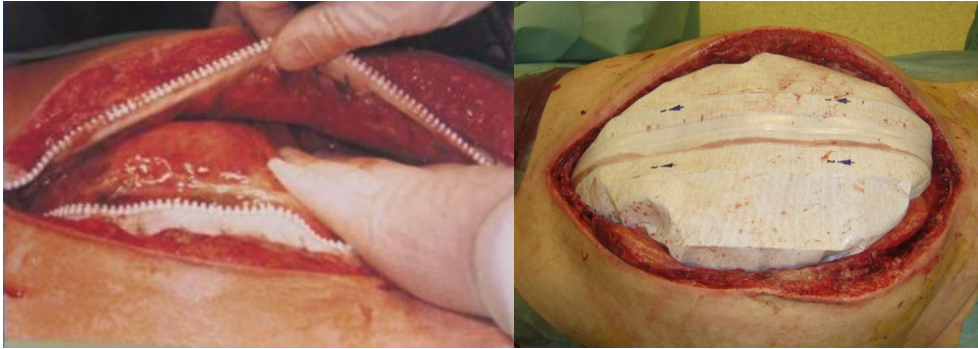


Figure 10. Left: Zipper (Wittman et al.⁶⁵ © Springer, reproduced with permission); right: Slide fastener. Mayer et al.⁶⁴ © Mosby, reproduced with permission).

In 1986, Schein et al. described the sandwich technique, using continuous suction, which was aimed at removing wound fluid, pus or fistula secretion⁶⁶. The sandwich itself consisted of a polypropylene (Marlex™) mesh to bridge the fascial defect, suction tubes in the middle and air-tight polyurethane drape (Op-Site™) above (Figure 11). The mesh was intended to be permanent but could be opened up on demand. In later descriptions, an absorbable mesh was used instead of a permanent one²⁹.

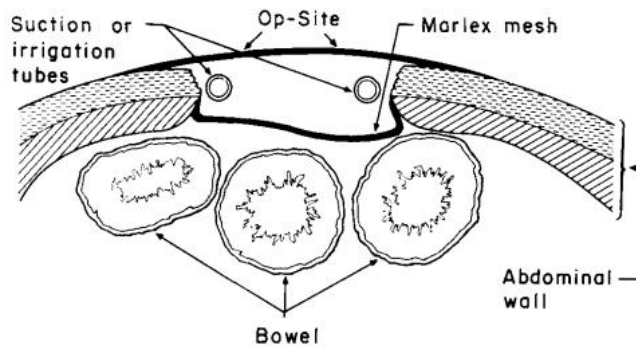


Figure 11. Sandwich technique (Schein et al.⁶⁶ © Wiley, reproduced with permission).

The sandwich technique had the disadvantage of not being adjustable for abdominal expansion but instead requiring multiple fascial manipulations. Using a permanent mesh in contact with bowel was later shown to increase the risk of fistula formation⁶⁷⁻⁶⁹.

All of the abovementioned techniques had the disadvantage of adhesion formation and fixation of the abdominal wall, with a frozen abdomen as the end result for most patients.

Wittman patch™

In 1990, Wittmann et al. described a technique using plastic sheets, sutured to the fascia on each side and closed in the midline using a Velcro®-like material (artificial burr). This allowed for adjustment of the intra-abdominal volume and for moderate traction to be applied to the fascia (Figure 12)⁶⁵.

Drawbacks with this technique include absence of a barrier against formation of intra-abdominal adhesions and suboptimal drainage of fluid between the non-permeable plastic sheets. Later modifications included addition of suction drains⁷⁰. As with other commercially available devices, an additional disadvantage is the higher price compared to a generic mesh. The device was originally marketed in USA only, but has been available in Europe since 2012.



Figure 12. Wittmann patch™ (www.starsurgical.com © Starsurgical Inc., reproduced with permission).

Retention sutures

Other methods of OA management applying traction to the fascia have been described, such as the shoe lace method by Häggmark (Figure 13)⁷¹.

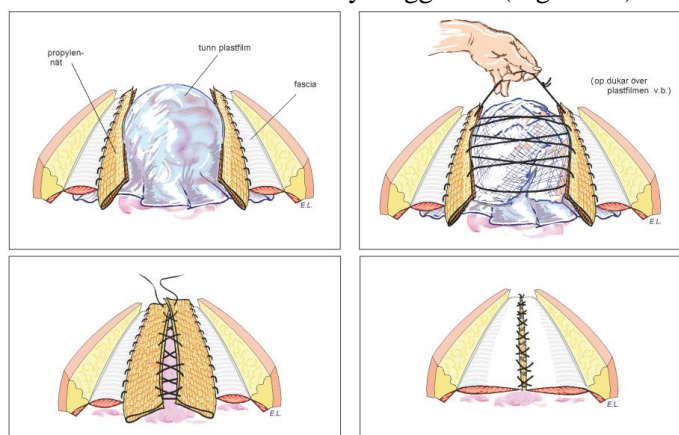


Figure 13. Retention sutures using mesh (© Häggmark & Linnander⁷¹, reproduced with permission)

Vacuum pack

In 1995, Barker and colleagues presented the vacuum pack (or vacpac), which was a major advancement in OA management⁷². A polyethylene sheet was placed intra-abdominally, acting as a pressure barrier and preventing adherence of the viscera to the abdominal wall. Surgical towels were placed between the wound edges with surgical drains on top and the wound was then covered with air-tight plastic dressing. The drains were coupled to a vacuum source set to 100-150 mmHg negative pressure (Figure 14).

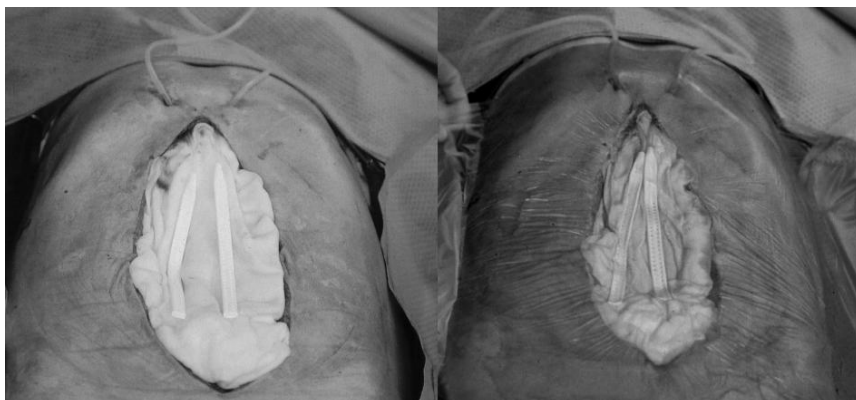


Figure 14. Vacuum pack (Barker et al.⁷³ © Lippincott Williams & Wilkins, reproduced with permission).

A disadvantage of the vacuum pack method is that the negative pressure is not calibrated so the actual pressure delivered to the wound is unreliable. In our experience, there were frequent problems with fluid leakage alongside the drain entrances as well as maceration of the skin. Furthermore, the intra-abdominal sheet, at least according to the original description, was rather small (10 × 10 inches) and perhaps not adequately preventing adhesions between the intestines and the abdominal wall. Lastly, negative pressure alone was insufficient in counteracting lateral retraction of the abdominal wall in some patients.

Vacuum assisted wound closure

A novel therapy for treatment of chronic wounds, called Vacuum Assisted Closure®, was described by Argenta and Morykwas in 1997^{74,75}. With this technique, calibrated negative pressure is distributed in the wound by means of a polyurethane sponge. The device was patented in 1991 and licensed to KCI Inc. Several generic terms have been proposed as an alternative to the original registered

trademark, such as vacuum assisted wound closure (VAWC), negative pressure wound therapy (NPWT) or topical negative pressure (TNP).

Although V.A.C.® was not designed for use in OA wounds, studies soon emerged, describing modifications of the vacuum pack method with the patented V.A.C.® sponge and/or negative pressure unit^{36,76-78}.

In 2003 the Abdominal V.A.C.® was introduced, containing all items necessary for VAWC therapy of an OA in a single kit (Figure 15).

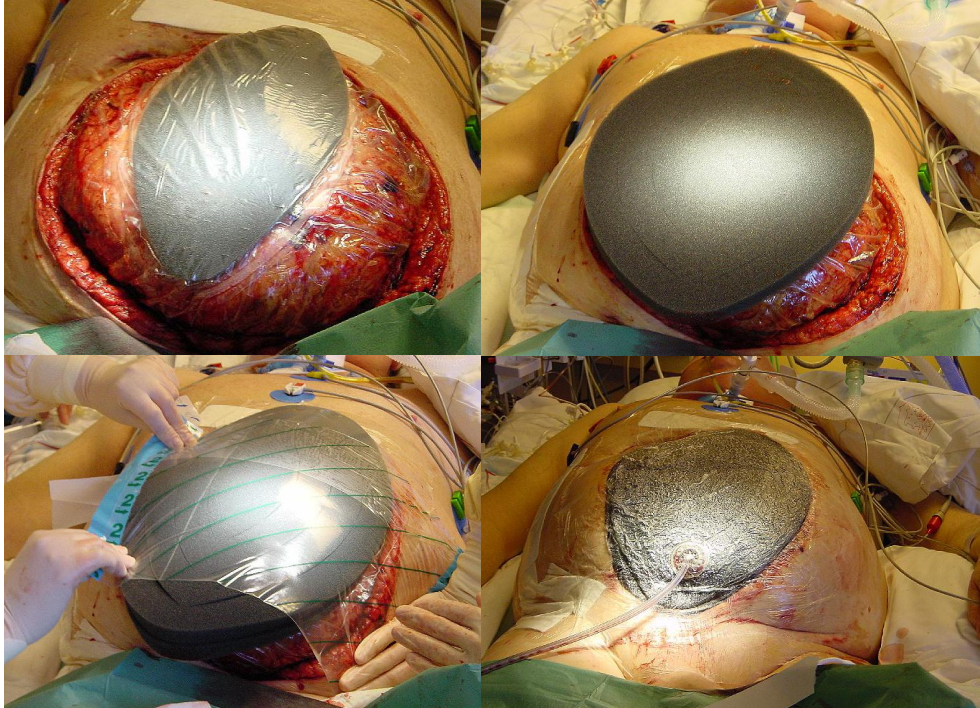


Figure 15. Abdominal V.A.C.®.

Recently, two new VAWC devices for the OA have been introduced: the ABThera™ system from KCI, and Renasys™ from Smith and Nephew.

Advantages of commercial VAWC systems compared to a home-made vacuum pack:

- Ease of use
- Large visceral protective layer, preventing adhesions
- Calibrated distribution of negative pressure
- Polyurethane sponges at suction/tissue interface

The disadvantage compared to the vacuum pack is the increased cost.

Fascial closure rates with existing techniques

In a systematic review by Boele van Hensbroek et al. in 2009, fascial closure rates for different TAC techniques were compared (weighted percentages with 95 % confidence intervals)⁶⁷:

- V.A.C.® 60 % (54–66)
- Vacuum pack 52 % (49–54)
- Artificial burr (Wittmann patch™) 90 % (86–95)
- Silo (Bogota bag) 29 % (20–37)
- Mesh/sheet 23 % (20–25)
- Skin only closure 43 % (34–53)
- Zipper 39 % (31–47)

There was presumed to be a large selection bias in the systematic review, since many of the studies lacked description of inclusion criteria. Another weakness was the lack of standardization of techniques.

A word of caution

At the same time surgeons appreciated the practical advantages of using vacuum therapy in OA situations, concerns were raised on possible damaging effect of negative pressure in this setting⁷⁹⁻⁸². It was argued that enteric fistulas in patients with open abdomens were increasing and that this coincided with increased use of vacuum therapy for OA management.

Regardless of this increase in prevalence, a prerequisite for VAWC to be a contributing factor to the development of intestinal fistulas, is that the negative pressure to some extent reaches the bowel surface and causes tissue damage. This was the motivation for the experimental study (paper IV) in this thesis⁸³. Another conceivable explanation to the apparent increase in fistula prevalence might be increased survival of severely ill patients – patients with increased risk of enteric fistula.

Vacuum therapy for fistula management

Paradoxically, at the same time there were concerns that VAWC might cause fistulas, it was used to treat fistulas. The “fistula VAC” was first described in 2006⁸⁴ and has since been reported in several studies (Figure 16)^{54,85-87}. With this method, it is possible to isolate the fistula output from the open abdomen. In most cases, the



Figure 16. Fistula VAC (© Kari Palo, reproduced with permission).

rest of the wound will become adherent (frozen abdomen) and will not be possible to apply the visceral protective layer. Instead, a non-adherent dressing is used to cover the intestines. The negative pressure does not appear to damage the surrounding bowel and cause new fistulas, despite the lack of an isolating barrier. Nevertheless, it would be preferable to apply some form of protection for the surrounding area. This hypothesis was the basis for part two of the experimental study (paper IV), studying the pressure isolating effect of paraffin gauzes⁸³.

Late incisional hernias

The use of OA therapy is increasing^{88,89} and its management is improving. In some of the earlier studies, more than half of patients ended up with a planned ventral hernia⁶⁷⁻⁶⁹, whereas almost all patients had successful closure in some recent studies⁹⁰⁻⁹³. It seems that it has become relevant to study the incidence of late incisional hernias after OA therapy with delayed primary fascial closure. Few studies briefly describe follow-up after OA therapy but no study exist with a primary

focus on long term results. This was the motivation for the follow-up study (paper II) of this thesis⁹⁴.

Classification of the open abdomen (OA)

In order for OA therapy to advance, it is mandatory to be able to describe clinical scenarios in a standardized fashion and compare different treatments and outcomes between studies. A classification system for the OA is a step in this direction.

Banwell and Téot classified dehisced abdominal wounds in 2003 as type I (superficial), type II (deep) and type III (complex)⁹⁵. A revised version was published by Swan and Banwell in 2005 (Table 1)⁹⁶:

Table 1. Classification of open abdominal wounds by Swan & Banwell⁹⁶

Classification	Wound type
I	Superficial – Skin defect only
II	Deep – Exposed bowel or omentum
III	Complex – Presence of intra-abdominal sepsis
IV	Complex – Presence of enterocutaneous fistulae
a	Prosthetic material absent
b	Prosthetic material present

(Swan & Banwell © MA Healthcare, reproduced with permission)

In 2009, an international consensus group proposed a classification system more directly aimed at describing the complexity of the OA and the ultimate goal of achieving abdominal closure as quickly as clinically appropriate (Table 2). OA grades, according to this system, has been reported in several clinical studies^{90,92,93,97-100}.

Table 2. Classification of the open abdomen (OA) by WSACS 2009¹⁰¹

Grade	Description
1A	Clean OA without adherence between bowel and abdominal wall or fixity (lateralization of the abdominal wall)
1B	Contaminated OA without adherence/fixity
2A	Clean OA developing adherence/fixity
2B	Contaminated OA developing adherence/fixity
3	OA complicated by fistula formation
4	Frozen OA with adherent/fixed bowel; unable to close surgically; with or without fistula

(Björck et al. © Springer, reproduced with permission)

An amended classification scheme was published by the World Society of the Abdominal Compartment Syndrome (WSACS) in 2013, together with updated consensus definitions and clinical practice guidelines for the treatment of intra-abdominal hypertension and abdominal compartment syndrome (Table 3)³⁴. No study has been published where any of the aforementioned classification systems are methodically evaluated.

Table 3. Amended classification of the open abdomen (OA) by WSACS 2013³⁴

1 No fixation

- 1A Clean, no fixation
- 1B Contaminated, no fixation
- 1C Enteric leak, no fixation

2 Developing fixation

- 2A Clean, developing fixation
- 2B Contaminated, developing fixation
- 2C Enteric leak, developing fixation

3 Frozen abdomen

- 3A Clean, frozen abdomen
- 3B Contaminated, frozen abdomen

4 Established enteroatmospheric fistula, frozen abdomen

(Kirkpatrick et al., © Springer, reproduced with permission)

Vacuum-assisted wound closure and mesh-mediated fascial traction

Background

Before the vacuum-assisted wound closure with mesh-mediated fascial traction (VAWCM) technique was developed, several patients with an OA at Skåne University Hospital were managed with VAWC. The patients were mostly elderly patients with underlying diseases such as peritonitis, ruptured AAA or mesenteric ischemia and required OA therapy for a long time. This was in contrast with many of the current studies which comprised mostly relatively young trauma patients needing OA therapy of relatively short duration.

We experienced an unsatisfactory fascial closure rate after OA therapy and too many of our patients ended up with a large planned ventral hernia. VAWC therapy alone was insufficient when prolonged OA therapy was necessary.

The combination of vacuum therapy with fascial traction had been described in the literature. In 2003, Navsaria et al. described a modification of the Sandwich

technique, combining it with a vacuum pack and loosely tied retention sutures in the fascia. Delayed primary fascial closure was achieved in 53 %¹⁰². In 2006, Fantus et al. described a combination of Wittmann patch with vacuum pack and in the same year, Cothren et al. described the use of VAWC combined with fascial retention sutures^{91,103}. These were small studies (11 and 14 patients, respectively), but resulted in 100 % fascial closure rates in trauma patients.

An improved technique was needed for OA management in our clientele, one which would combine the advantages of VAWC with adjustable tension of the fascia without compromising fluid permeability. The tension should be applied along the total length of the incised fascia and not involve repeated fascial manipulations. The result was the VAWCM technique.

Description of the VAWCM technique

A polypropylene mesh was divided into two halves and sutured to the fascial edges on each side. If an abbreviated laparotomy was indicated, the insertion of the mesh could be postponed, and instead applied at the first appropriate reoperation. A VAWC system was then applied (V.A.C.TM Abdominal Dressing System; KCI, San Antonio, Texas, USA). The visceral protective layer (perforated polyethylene sheet with a central polyurethane sponge) was cut to appropriate size and spread out under the abdominal wall as far as possible in all directions, covering the whole inside of the abdominal wall, to the paracolic gutters, over the liver and to the pelvis. The two mesh halves were then sutured together in the midline (Figure 17 and 18).

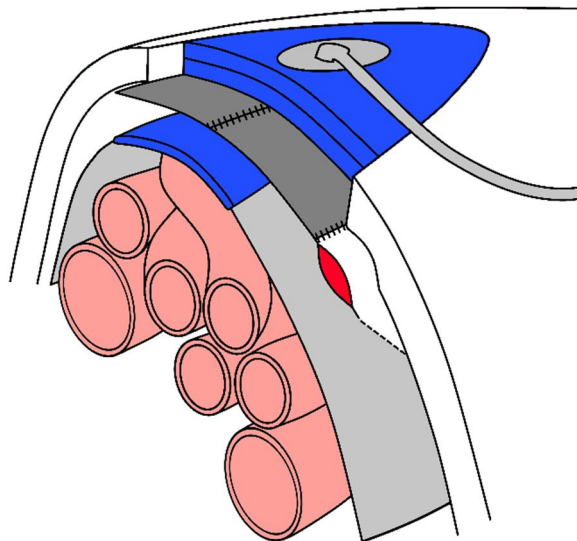


Figure 17. Schematic drawing of VAWCM (own picture © Wiley, reproduced with permission)

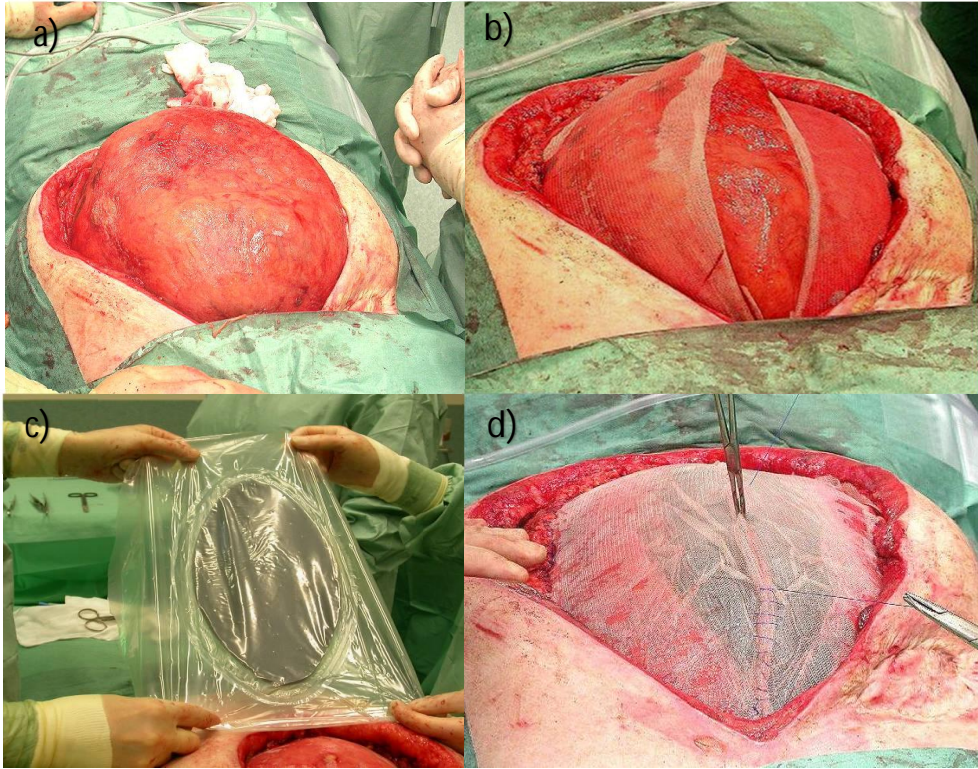


Figure 18. VAWCM technique: a) OA where VAWC alone is insufficient for abdominal closure; b) the mesh is sutured to the fascial edges; c) the visceral protective layer is placed intra-abdominally; d) the mesh is sutured in the midline (own picture © Springer, reproduced with permission).

Black polyurethane sponges were placed on top of the mesh, between the abdominal wall edges, the wound was covered with occlusive self-adhesive polyethylene sheets and then connected to the negative pressure unit (Figure 19).



Figure 19. VAWCM technique: sponges are placed above mesh and negative pressure applied.

Continuous negative pressure of -125 mmHg was the standard setting, but could be adjusted according to the surgeon's preference.

The dressing was changed under general anesthesia every 3 days, or earlier if indicated. At each dressing change, the mesh was opened in the midline and the visceral protective layer removed. Abdominal cavity was inspected, potential fluid collections were removed and any adhesions to the abdominal wall were released. Care was taken not to damage the bowel and no attempts were made to release adhesions between bowel loops. After applying a new visceral protective layer, the mesh was sutured together in the midline with moderate tension and the vacuum dressing applied. The level of tension was determined by the operating surgeon. In general, moderate tension was accomplished by pulling the mesh by hand or with surgical forceps to a level where the mesh halves could be sutured together comfortably. Intra-abdominal pressure was closely monitored postoperatively in the ICU in order to be able to release tension of the mesh, if necessary. Dressing changes were occasionally performed without mesh tightening.

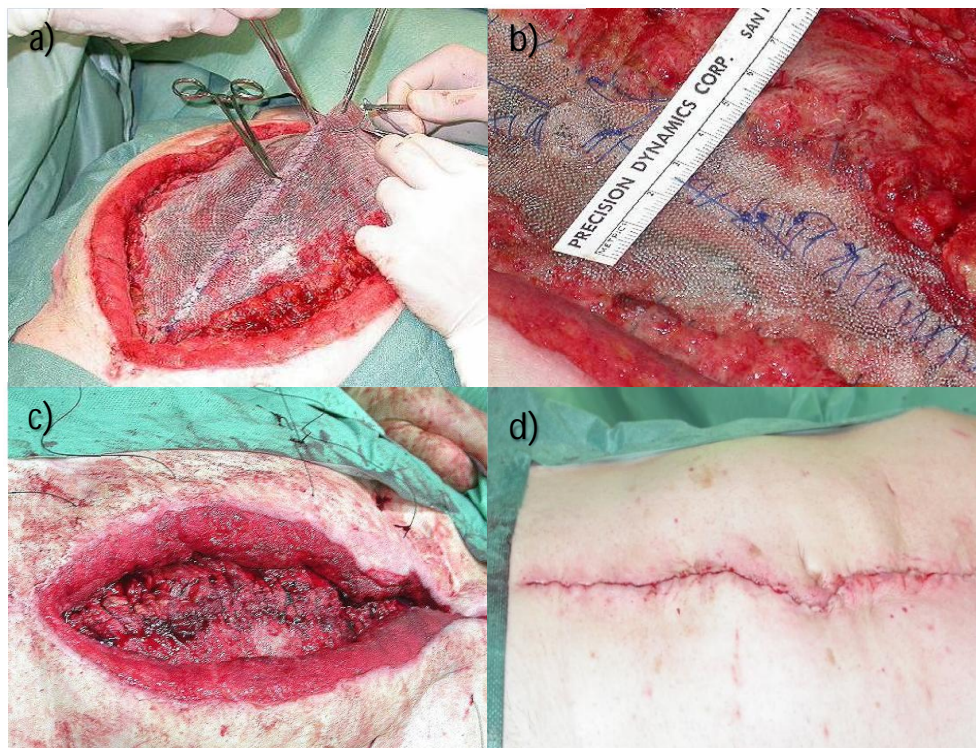


Figure 20. VAWCM technique: traction of the mesh during dressing changes until finally mesh is removed and the fascia and skin sutured (own picture © Springer, reproduced with permission).

As the intra-abdominal swelling decreased, the abdominal wall edges were brought closer together with each dressing change (Figure 20). Finally, the temporary mesh was removed and the fascia closed with a running PDS™ suture, using a standardized suturing technique with a suture length to wound length ratio of at least 4 to 1.

Pilot study

The VAWCM technique was initially evaluated in a pilot study on seven patients, published in 2007¹⁰⁴. Delayed primary fascial closure was achieved in all patients after a median of 32 days, without any technique related complication.

The abdomen must not alone contain its viscera, it must fit them, while an intra-abdominal viscus should not embarrass its host, nor its fellows.

Law of the Abdomen – Michael Gerard Baggot, an anesthesiologist who from 1951 and onwards recommended that surgeons avoided closing the abdomen under tension, leaving it temporarily open instead¹⁰⁵.

Aims of the thesis

OA therapy may be the best surgical option in certain life-threatening situations. Potential complications to OA therapy include damage to the exposed bowel leading to enteric fistulas, and inability to close the abdomen afterwards leading to large ventral hernias. VAWCM is a novel technique for temporary closure of the OA, intended to increase chances of subsequent delayed primary fascial closure without increasing the risk of complications.

A classification system for the open abdomen was recently proposed by WSACS, with the aims of improving open abdomen therapy and aiding clinical research. The system has not been evaluated.

The aims of this thesis were to study:

- Short-term clinical outcome of OA therapy with VAWCM, primarily fascial closure and factors associated with failure of fascial closure, mortality and morbidity and possible technique-related complications.
- One-year clinical outcome of OA therapy with VAWCM with regards to incisional- and parastomal hernias, abdominal wall discomfort and frequency of hernia repair operations after one year.
- Validity and reliability of the open abdomen classification system by WSACS from 2013 and to propose instructions for use with the classification.
- Physiological effects of VAWC in an open abdomen, more specifically: the extent of negative pressure reaching the bowel; the efficacy of the VAWC system in draining fluid from the abdominal cavity; and whether paraffin gauzes can be effectively used as pressure isolation when placed between the vacuum source and the bowel.

The destiny of lone prophets – however truthful they are – is to be ridiculed and ignored, and such was Baggot's fate.

– *Moshe Schein about Michael Gerard Baggot*¹⁰⁶.

Patients and methods

Ethics and clinical trial registration

The prospective, multicenter study (papers I–III) was approved by the ethics committee of Lund University and was registered at <http://www.clinicaltrials.gov> (registration number: NCT00494793).

The experimental animal study (paper IV) was approved by the ethical committee on animal experiments in Malmö/Lund, Sweden.

Overview – all studies

Overview of all studies included in this thesis is shown in Table 4.

Table 4. Overview of patients and subjects, all papers

Paper	Design	Subjects
Paper I	Prospective cohort study	111 consecutive OA patients
Paper II	Prospective cohort study, follow up	70 patients alive at 1 year
Paper III	Validity and reliability study	Same patients as in paper I
Paper IV	Experimental animal study	6 pigs

Patients – prospective cohort study (papers I–III)

All consecutive patients treated with VAWCM at four Swedish hospitals (Malmö, Uppsala, Falun and Gävle), between April 2006 and August 2009, were included. Out of 151 patients treated with OA, 111 fulfilled the inclusion criteria.

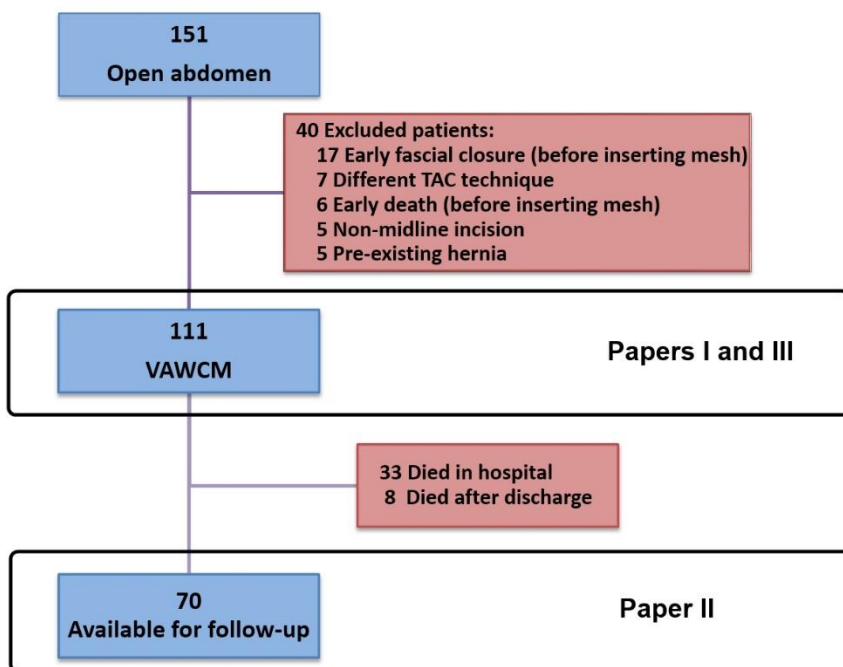


Figure 21. Overview of patients in the prospective cohort study

An overview of patient allocation is shown in Figure 21. Exclusion criteria are shown in Table 5. Exclusion due to early fascial closure or death was termed “anticipated OA treatment < 5 days” in paper I.

Table 5. Exclusion criteria, prospective cohort study

Exclusion criteria	No. of patients	Description
Age under 18 years	0	Did not occur during the study period
Not VAWCM		In an abbreviated laparotomy, the insertion of the temporary mesh was postponed, and in some patients never inserted due to early fascial closure or death. In the beginning of the study period, a few patients received other TAC method.
– Early fascial closure	17	
– Surgeons preference	6	
– Early death	7	
Prior abdominal wall hernia	5	In case of an existing ventral hernia, mesh closure was planned from start, and evaluation of primary fascial closure thus irrelevant.
Non-midline incision	5	Mainly patients with bilateral subcostal incisions after hepatic or pancreatic resections.

Methods, prospective cohort study (papers I and II)

Procedure

Data was prospectively registered according to the study protocol. Patients with necrosis, perforation or fistula of the intestines or other organs (e.g. pancreas) were reassessed individually to identify possible complications to the VAWCM treatment. OA grade was registered according to the WSACS classification published in 2009.

Follow-up was scheduled one year after abdominal closure. Data was retrieved from medical records, including information on events that had occurred after OA therapy was ended. All patients were offered a follow-up, consisting of clinical examination and a CT scan of the abdominal wall (Table 6).

Table 6. Follow-up protocol

• Clinical examination	–	Performed by a senior surgeon at the outpatient clinic
	–	Presence of midline or parastomal hernia were noted
	–	Discomfort from the midline and/or the stoma area were noted
• CT scan of the abdominal wall	–	Performed in supine position without a Valsalva maneuver
	–	Ventral and parastomal hernias definitions as shown below
	–	Assessed independently by one radiologist and three surgeons, consensus reached in case of discrepancy
	–	Fascial diastasis was measured in patients without incisional hernia
	–	No CT was performed in case a hernia was already diagnosed (clinically, on CT or at operation) or if no hernia had been diagnosed at a laparotomy

Definitions

Delayed primary fascial closure

The temporary mesh that was used for fascial traction is removed and the whole length of the incised fascia is closed with a running PDS suture

Mesh closure

The temporary mesh is removed and the abdominal wall is reconstructed with a new mesh. A mesh could be placed in an intra-peritoneal, sublay (behind the rectus muscle) or onlay (above the anterior rectus fascia) position. A reinforcing onlay mesh above a completely closed fascia was registered as mesh closure.

Permanent abdominal wall closure

Permanent, same-hospital-stay closure of the abdominal wall, using suture or mesh.

Intra-abdominal pressure (IAP)

IAP was indirectly measured as urinary bladder pressure (Figure 22). Through a catheter, the bladder was emptied and 20 ml of saline were infused. Using a transparent urinary catheter, end-expiratory urinary bladder pressure was measured by the height of the fluid column over the pubic symphysis, with the patient in supine position. When possible, IAP was measured before initiation of OA therapy. Repeated IAP measurements were made during the OA treatment.

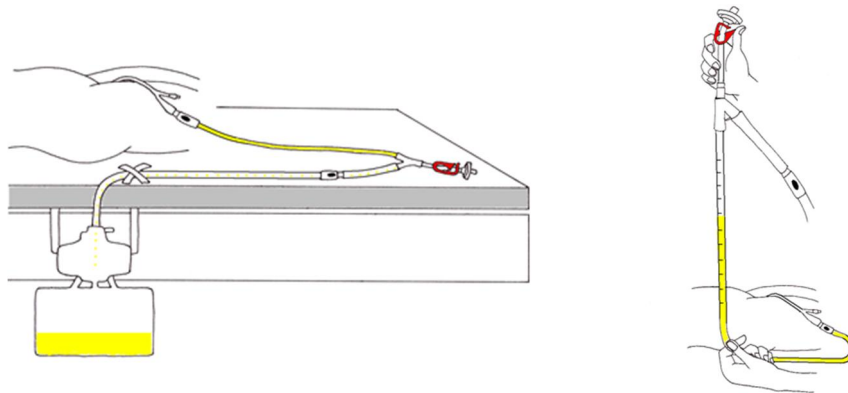


Figure 22. Measurement of intra-abdominal pressure (Foley Manometer © Holtech Medical, reproduced with permission)

Intra-abdominal hypertension (IAH)

Defined as proposed by WSACS: a sustained or repeated IAP ≥ 12 mmHg³⁴.

Abdominal compartment syndrome (ACS)

Defined as proposed by WSACS: a sustained IAP > 20 mmHg associated with a new organ dysfunction³⁴.

The Sequential Organ Failure Assessment (SOFA) score

SOFA score was designed to describe the severity of multiple organ dysfunction in critically ill patients (Table 7)¹⁰⁷. The total score is a sum of 6 subscores for the different organ systems, each generating 0-4 points.

Table 7. Sequential Organ Failure Assessment (SOFA) score

SOFA score	1	2	3	4
<i>Respiration</i>				
PaO ₂ /FiO ₂ , mmHg	<400	<300	<200 with respiratory support	<100
<i>Coagulation</i>				
Platelets × 10 ³ /mm ³	<150	<100	<50	<20
<i>Liver</i>				
Bilirubin, mg/dl (μmol/l)	1.2–1.9 (20–32)	2.0–5.9 (33–101)	6.0–11.9 (102–204)	>12.0 (>204)
<i>Cardiovascular</i>				
Hypotension	MAP < 70 mmHg	Dopamine ≤ 5 or dobutamine (any dose) ^a	Dopamine > 5 or epinephrine ≤ 0.1 or norepinephrine ≤ 0.1	Dopamine > 15 or epinephrine > 0.1 or norepinephrine > 0.1
<i>Central nervous system</i>				
Glasgow Coma Score	13–14	10–12	6–9	<6
<i>Renal</i>				
Creatinine, mg/dl (μmol/l) or urine output	1.2–1.9 (110–170)	2.0–3.4 (171–299)	3.5–4.9 (300–440) or < 500 ml/day	>5.0 (>440) or < 200 ml/day

^a Adrenergic agents administered for at least 1 h (doses given are in μg/kg·min)

(Vincent et al.¹⁰⁷ © Springer, reproduced with permission).

Analysis according to intention-to-treat or per protocol

According to the intention-to-treat (ITT) principle, results are analyzed according to the initial treatment assignment, whereas an analysis per protocol is based on the actual treatment a patient receives. In an analysis of fascial closure, patients who die before closure are regarded as failure of fascial closure according to ITT but are excluded from an analysis per protocol.

Incisional hernia

Incisional hernia was defined as proposed by the European Hernia Society (EHS) as: “Any abdominal wall gap with or without a bulge in the area of a postoperative scar, palpable or perceptible by clinical examination or imaging”¹⁰⁸. It was decided that defects less than 1 cm were unreliable on the CT scan, and these were excluded. Width and length of the incisional hernia defect(s) was defined according to EHS (Figure 23)¹⁰⁹.

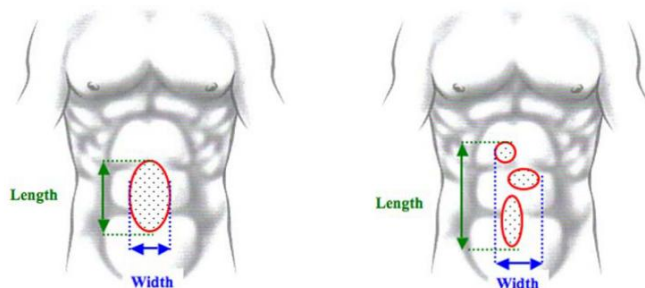


Figure 23. Width and length of the hernia area (Muysoms et al. © Springer, reproduced with permission).

Parastomal hernia

Parastomal hernia was classified as proposed by Moreno-Matias et al, using a CT scan¹¹⁰.

Table 8. Classification of parastomal hernia according to Moreno-Matias et al.

Type	Content of hernia sac
0	Peritoneum follows the wall of the bowel forming the stoma, with no formation of a sac
Ia	Bowel forming the colostomy with a sac < 5 cm
Ib	Bowel forming the colostomy with a sac > 5 cm
II	Sac containing omentum
III	Intestinal loop other than the bowel forming the stoma

(Moreno-Matias et al. © Blackwell 2009, reproduced with permission)

Methods – evaluation of the OA classification (paper III)

Procedure

Validity

All operative reports for all patients (n = 753) were evaluated and the OA grade registered for each operation. The results of the 2013 WSACS OA classification system, i.e. OA grades, were compared to clinical results, i.e.:

- Fascial closure
 - Delayed primary fascial closure (suture)
 - Permanent abdominal wall closure (suture or mesh)
- Mortality
 - Mortality with OA (i.e. before it was appropriate to end OA therapy and attempt fascial closure)
 - In-hospital mortality

Any floor or ceiling effects were assessed by calculating the percentage of patients receiving the lowest or highest possible score, respectively.

Recent amendments to the 2013 WSACS OA classification system were evaluated by comparing it with the former version from 2009.

Reliability

A sample of 108 operative reports were randomly selected and assessed separately by three raters for inter-rater analysis. The results of the original rater (who assessed all 753 operative reports) were not used for this analysis, in order to avoid potential bias. All raters were surgeons experienced in OA therapy. The “instructions for use” were presented to the raters beforehand. For test-retest analysis, the same operative reports were re-assessed by the same raters after a delay of 4–6 weeks.

Definitions

OA grade 4

Grade 4 is defined as “established enteroatmospheric fistula, frozen abdomen”, according to the main document in the original publication by WSACS in 2013 (Table 8)^{34,101}. In supplement 6, outlining the rationale for the amendments, there is no mention of a frozen abdomen. Since not all enteroatmospheric fistulas (EAFs) in our material were associated with a frozen abdomen, we decided to register all EAFs, with or without frozen abdomen, as grade 4.

Validity

The validity of a test is the degree to which the test measures what it claims to measure. In this case, the validity of the OA classification was defined as how well the results of the classification (OA grades) corresponded with clinical results (facial closure and mortality).

Floor and ceiling effects

Floor or ceiling effects are considered to be present when >15 % of patients receive the highest or lowest score, respectively¹¹¹. Large floor or ceiling effects may lead to difficulty in distinguishing patients from each other or to measure changes over time (e.g. effects of therapy).

Inter-rater reliability

Inter-rater reliability is defined as the degree of agreement among raters.

Test-retest reliability

Test-retest reliability, or repeatability, is defined as the variation in results by the same individual at different times.

Instructions for use

It was noticed during the grading process, that clear definitions of the terms used in the classification were needed in order to standardize the grading procedure and minimize discrepancies in interpretation between users. Consequently, detailed instructions for use were constructed and used in the grading process. The instructions contain detailed definition of terms and instructions applicable to diverse clinical scenarios, as well as a flow chart for use in the grading process (Figures 24–26).

Classification of the open abdomen

Instructions for use

Definition of open abdomen (OA)

An abdominal wound requiring temporary abdominal closure due to the skin and fascia not being closed after laparotomy (WSACS, 2013). Note that “skin-only closure” is not open abdomen according to this definition.

OA classification (WSACS 2013)

Grade 1. No fixation

1A: *clean*

1B: *contaminated*

1C: *enteric leak*

Grade 2. Developing fixation

2A: *clean*

2B: *contaminated*

2C: *enteric leak*

Grade 3. Frozen abdomen

3A: *clean*

3B: *contaminated*

Grade 4. Established enteroatmospheric fistula (EAF)

How to grade

At the end of every operation (both initial laparotomy and each dressing change), asses:

- Fixation according to 1 to 3 (no fixation, developing fixation, frozen abdomen).
- Contamination according to A to C (clean, contaminated, enteric leak).
- Presence of enteroatmospheric fistula, grade 4.

Definitions

Fixation

Adhesions between viscera and the abdominal wall and/or lateral retraction of the abdominal wall muscles, preventing fascial closure in the midline.

Grade 1: No fixation

- Abdominal cavity is free of adhesions all the way to the paracolic gutters laterally, over the liver cranially and to the pelvis caudally.
- It is expected to be possible to subsequently bring abdominal wall together in the midline.
- Limited adhesions around stomas (incl. gastrostomies, feeding jejunostomies etc.) are not fixation.
- Adhesion between bowel loops do not affect fascial closure and are not fixation.
- If all adhesions between viscera and abdominal wall are released at the end of the present operation, it should be registered as no fixation.

Grade 2: Developing fixation

- An intermediate state of adhesions or fixation.
- Adhesions between viscera and abdominal wall or abdominal wall stiffness that causes difficulties in approximating fascial edges.
- Adhesions that are released in the present operation are not developing fixation.

Grade 3: Frozen abdomen

- Extensive adhesions or a fixated abdominal wall that precludes fascial closure.
- Other methods of abdominal closure, such as mesh reconstruction or planned ventral hernia (e.g. with skin grafting), are necessary.

Contamination

Grade A: Clean

Absence of conditions defined as contamination or enteric leak. If contamination is removed, abdomen may be considered clean at the next dressing change operation, or when appropriate.

Grade B: Contaminated

The following states are to be considered as contaminated:

- Infections engaging the OA, such as purulent peritoneal inflammation, intra-abdominal abscess or laparotomy wound infection.
- Infections not engaging the abdominal cavity (e.g. pyelonephritis) are not contamination
- Necrotic tissue, such as bowel (regardless of perforation) or wound necrosis.
- Ischemia without necrosis is not contamination
- Other contamination, such as traumatic wounds penetrating abdomen, perforation of genito-urinary tract (including Bricker conduit), leakage from bile ducts or bile duct anastomoses, bowel contents from excluded rectal stump or from stoma bag

Grade C: Enteric leak

- Perforation of any part of the gastrointestinal tract with contact to the abdominal cavity.
- Includes leakage from gastrostomy or jejunostomy entrances.
- If a perforation is successfully surgically treated (e.g. by primary suture, resection of the perforated bowel segment, exteriorization into a stoma or a controlled enterocutaneous fistula) or ceases with conservative treatment (clean-up and drainage), then the grade is changed at next dressing change operation to clean or contaminated, as appropriate.

Enterocutaneous fistula

Grade 4: Enterocutaneous fistula (EAF)

- An enteric leak that becomes chronic with continuous leakage in the OA and at a later stage will be surrounded with granulation.
- Frozen abdomen will usually develop, unless fistula is treated actively (e.g. with VAWC).
- Enterocutaneous fistulas (ECF), per definition, do not have a connection to the open abdomen and are therefore not registered as grade 4.

Classification of the open abdomen

Flow chart

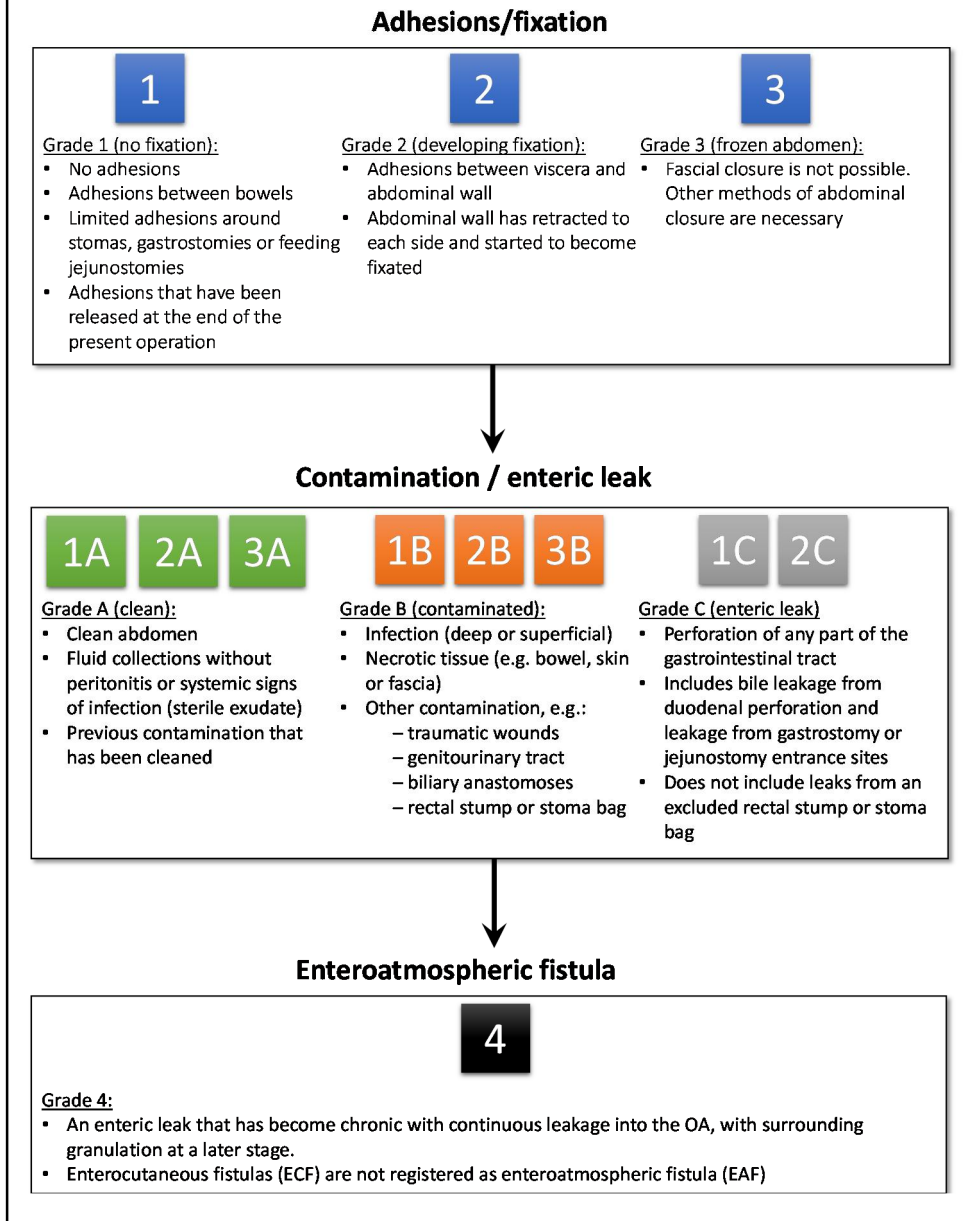


Figure 26. Instructions for use – flow chart for intraoperative use (page 3)

Methods and subjects – experimental study (paper IV)

Animal subjects

In order to best simulate OA therapy in humans, it was determined that pigs of a weight of approximately 60 kg were the most suitable option. For ethical reasons, it was decided to use as few animals as possible. After consulting a statistician, it was determined that 6 subjects were the minimum for reliable statistical calculations. Accordingly, six domestic pigs of both genders were used, with a median weight of 58 kg (range 52–62 kg).

Experimental procedure

The animals were operated under general anesthesia. OA therapy was prepared as in a human patient. ABThera™ open abdomen dressing and V.A.C.™ negative pressure unit (KCI, Inc., San Antonio, TX, USA) were used (Figures 27 and 28).



Figure 27. Experimental study on OA therapy in a swine model

Sensors for negative pressure measurement were placed in the dressing and in the abdominal cavity, as shown in figure 29. The pressure at each sensor position was measured at five different settings of the negative pressure unit: -50 , -75 , -100 , -125 , and -150 mmHg. Intra-abdominal pressure was allowed to return to zero before changing to the next pressure setting.

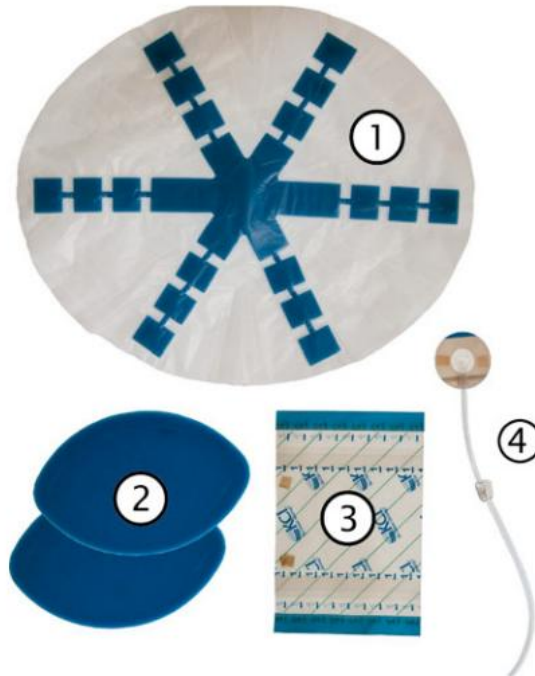


Figure 28. ABThera™ open abdomen negative pressure therapy system: 1) Visceral protective layer 2) Polyurethane foams 3) Self-adhesive polyethylene drapes 4) A tubing set with an interface pad 5) A vacuum source, not shown in picture (own picture © Springer, reproduced with permission).

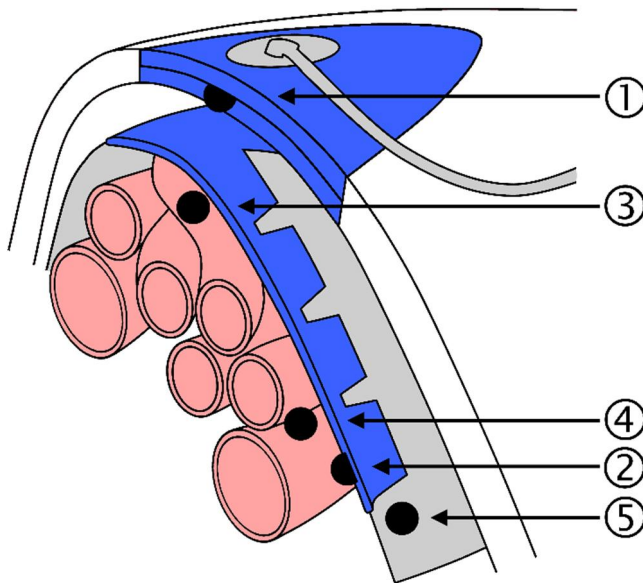


Figure 29. Positions of pressure sensors during the experimental study of OA therapy in a porcine model (own picture © Springer, reproduced with permission).

For the second part of the experiment, sheets of paraffin gauzes in eight layers were placed on top of the bowel with pressure sensors positioned directly underneath and above. Negative pressure measurements were then carried out at each of the five different pressure settings used previously and any reduction in pressure over the paraffin gauzes was noted.

In the last part of the experiment, 200 ml of saline were infused into the abdominal cavity through a catheter. After running the negative pressure unit on -75 mmHg for 10 minutes, the drained volume was registered. After neutralizing the pressure, the procedure was repeated at a pressure setting of -150 mmHg.

At the end of the experiment, the animals were euthanized with an IV infusion of potassium chloride.

Statistics

Data management and statistical analyses were performed using the SPSS software, versions 17 through 21 (SPSS Inc., Chicago, IL, USA and IBM Corp., Armonk, NY, USA).

Continuous variables were expressed as median and range or interquartile range. Group differences were analyzed with Mann–Whitney U (two independent samples), Kruskal-Wallis test ($>$ two independent samples) or Wilcoxon signed rank test (dependent samples), as appropriate. Discrete variables were expressed in proportions. Group differences were analyzed with χ^2 (Chi square) test or Fisher's exact test for differences in proportion; and Spearman's rank correlation coefficient or Kendall's τ -b test for correlations, as appropriate. A p-value of < 0.05 was considered statistically significant. In a multivariate analysis, significant associations were expressed in terms of odds ratio (OR) with a 95 % confidence interval (CI).

Fascial closure was initially analyzed on the basis of intention to treat. Since failure of fascial closure was predominantly due to death, fascial closure was analyzed per protocol (excluding patients who died with OA), in order to separate factors associated with failure of fascial closure from factors causing death.

In a binary classification test, sensitivity (true positive rate) is defined as the proportion of actual positives which were correctly identified as such. Specificity (true negative rate) is defined as the proportion of actual negatives which were correctly identified as such.

For validity analysis, OA grades were converted into ordinal numbers (1–9) according to internal order (1A, 1B, 1C, 2A, 2B, 2C, 3A, 3B, 4). Randomization was performed using a random number generator function in SPSS. Inter-rater reliability and test-retest reliability were expressed as proportional agreement and intraclass correlation coefficient (ICC), both with 95 % confidence intervals. A floor

or ceiling effect was considered to be present when > 15 % of participants received the lowest or highest score, respectively¹¹¹.

Strength of agreement was interpreted based on ICC¹¹²: Poor agreement (< 0.20), Fair agreement (0.21–0.40), Moderate agreement (0.41–0.60), Good agreement (0.61–0.80) and very good agreement (0.81–1.0).

It is a most unhappy calamity that a patient, whose life one is endeavoring to save, should die before an operation is completed, but it is a risk that has occasionally to be faced.

– *James Hogarth Pringle, 1908⁶*.

Results

OA therapy with vacuum-assisted wound closure and mesh-mediated fascial traction (papers I and II)

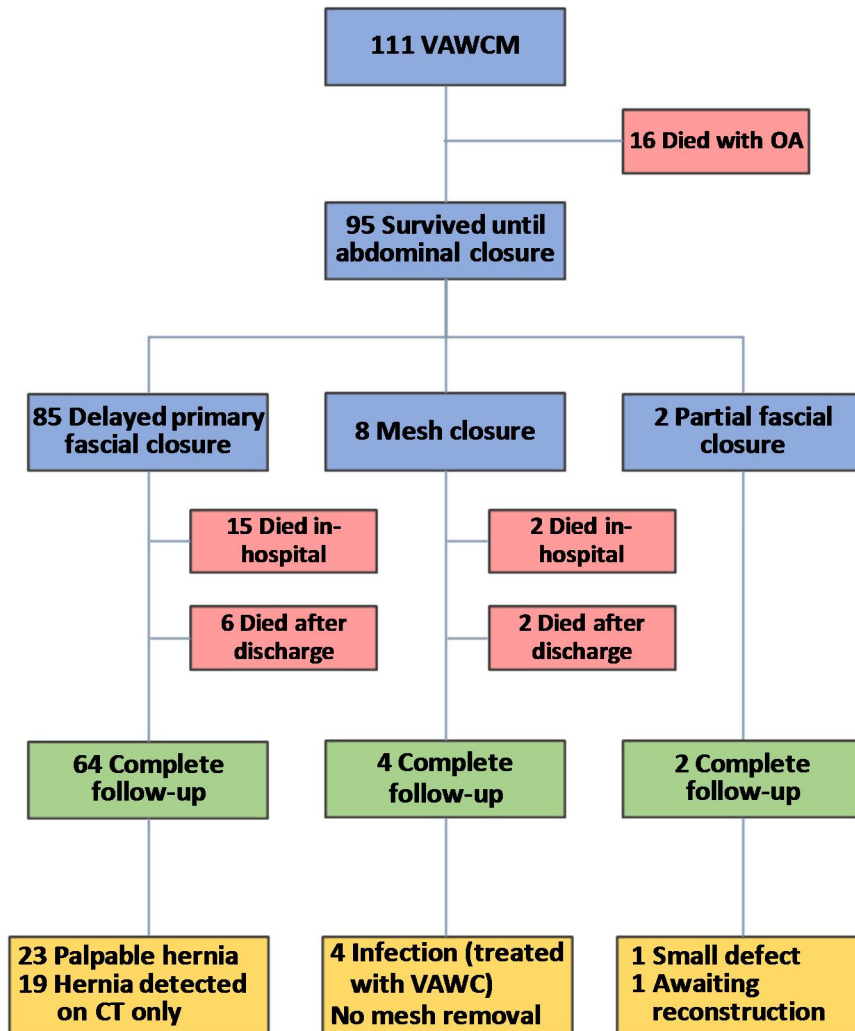


Figure 30. Overview mortality, fascial closure and abdominal status at one year.

Patient characteristics

Table 9. Patients treated with OA and VAWCM

Number of patients	111
Male	81 (73 %)
Female	31 (27 %)
Age	68 years (20–91)
Age, trauma patients (n=9)	48 years (21-75)
Body mass index, male	25.1 (19.4–41.5) kg/m ²
Body mass index, female	23.6 (16.1–38.9) kg/m ²

Patients with stomas or anastomoses

Enteric anastomoses or stomas created at the initial OA laparotomy or at an immediately preceding operation are shown in Table 10. The choice of anastomoses or stomas was made on a clinical indication regardless of planned OA therapy. All stomas were created in the standard location through the rectus abdominis muscle. Patients with a new anastomosis or stoma had similar fascial closure rates and mortality. Patients with new anastomosis had higher risk of enteric leak ($p<0.001$) or fistula ($p<0.001$).

Table 10. Patients with a new enteric anastomosis or stoma

Anastomosis (≥ 1)	33
Ileostomy	18
Colostomy	32

Indications for OA therapy

Indications for not closing the laparotomy wound (irrespective of underlying disease) are shown in Table 11. Each patient could have one or more indications.

Table 11. Indication for OA therapy (could be ≥ 1 for each patient)

Not possible to close abdomen without excessive tension	77 (69 %)
Increased abdominal pressure preoperatively (measured in 46 patients)	
– Intra-abdominal hypertension (IAH)	22 (20 %)
– Abdominal compartment syndrome (ACS)	22 (20 %)
Need for drainage of severe intra-abdominal infection	29 (26 %)
Abbreviated laparotomy with planned re-laparotomy (damage control)	
– Trauma	9 (8 %)
– Re-assessment of bowel necrosis (regardless of sepsis)	14 (13 %)
– Wound dehiscence	18 (16 %)

Underlying disease contributing to OA therapy was categorized in three groups according to disease etiology (Table 12). Patients with intestinal ischemia due to arterial thrombo-embolism were classified as having vascular disease, while other causes of bowel ischemia, such as strangulation, were classified as visceral disease.

Table 12. Underlying disease categories

Visceral surgical disease	57 (51 %)
Vascular disease	45 (41 %)
Trauma	9 (8 %)

Vacuum-assisted wound closure and mesh-mediated fascial traction

Technical results of the vacuum-assisted wound closure and mesh-mediated fascial traction (VAWCM) technique are shown in Table 13.

Table 13. General results of VAWCM therapy

Duration	14 (4–87) days
Number of dressing changes	5 (2–22)
Number of mesh tightening procedures	4 (0–10)
Fascial diastasis at initial laparotomy	17 (5–40) cm

Negative pressure level was set according to the surgeon’s discretion and was not stated in the study protocol. Standard setting as recommended by the manufacturer was –125 mmHg continuous pressure. Pressure settings are shown in Table 14. One patient with hemophilia and a severe risk of re-bleeding was treated with 0 mmHg during most of the treatment time.

Table 14. Negative pressure setting during OA therapy with VAWCM

Continuous	102 (92 %)
0 mmHg	1
50 mmHg	12
75 mmHg	17
100 mmHg	15
125 mmHg	47
150 mmHg	10
Intermittent	9 (8 %)
50 mmHg	6
75 mmHg	2
125 mmHg	1

Pressure setting used during the majority of the OA period

Effect of OA therapy on intra-abdominal hypertension or abdominal compartment syndrome

It was not possible to measure IAP before initiation of OA therapy in all patients, due to the acute nature of illness and initiation of therapy, but was measured in 46 patients (Table 15). Postoperatively, IAP was repeatedly measured in all patients for monitoring of the effects of OA therapy and mesh traction.

Table 15. Intra-abdominal pressure and effects of initiation of OA therapy

Registration of IAP before initiation of OA	46
Intra-abdominal hypertension (IAP 12–20 mmHg)	22 (20 % of all 111 patients)
Abdominal compartment syndrome (IAP>20 mmHg)	22 (20 % of all 111 patients)
IAP before initiation of OA (median, range; n=46)	20 (9–43) mmHg
IAP immediately after initiation of OA (median, range; n=46)	11 (5–19) mmHg

Raised IAP was seen in 96 % (44/46) of measurements or 40 % (44/111) of all patients. ACS was present more often in patients with vascular disease than visceral surgical disease (13 vs. 6 patients; $p = 0.050$). Ten of 13 vascular patients with ACS had undergone surgery for an AAA. IAP decreased significantly with initiation of OA treatment ($p < 0.001$)

In summary

IAH or ACS was present in at least 40 % of patients. IAP decreased with initiation of OA treatment.

Effects of mesh tightenings on intra-abdominal pressure

It was not necessary at any time during the study period to release mesh tension due to increasing IAP caused by excessive traction. In one patient, the mesh was released temporarily, due to raised IAP following severe *Clostridium difficile* colitis.

In summary

Fascial traction during dressing changes did not cause postoperative increase in IAP.

Effect of OA therapy on organ failure

SOFA scores from immediately before and from the morning after initiation of OA therapy are compared in Table 16.

Table 16. Changes in SOFA score on initiation of OA therapy	Before	After	p
SOFA score, all patients (n = 46)	8 (0–16)	8 (0–16)	0.854
SOFA score, patients with IAH (n = 44)	10 (2–16)	10 (2–16)	0.097
Respiratory (P _a O ₂ /F _i O ₂ ratio), all patients		Improved	0.003
Respiratory (P _a O ₂ /F _i O ₂ ratio), patients with IAH		Improved	0.008
Coagulatory (platelet count)		Unchanged	0.543
Circulatory		Unchanged	0.917
Renal		Unchanged	0.361
Hepatic (bilirubin level)		Worsened	<0.001

All values are median and range

In summary

SOFA score had not improved the day after initiation of OA therapy.

Fascial closure

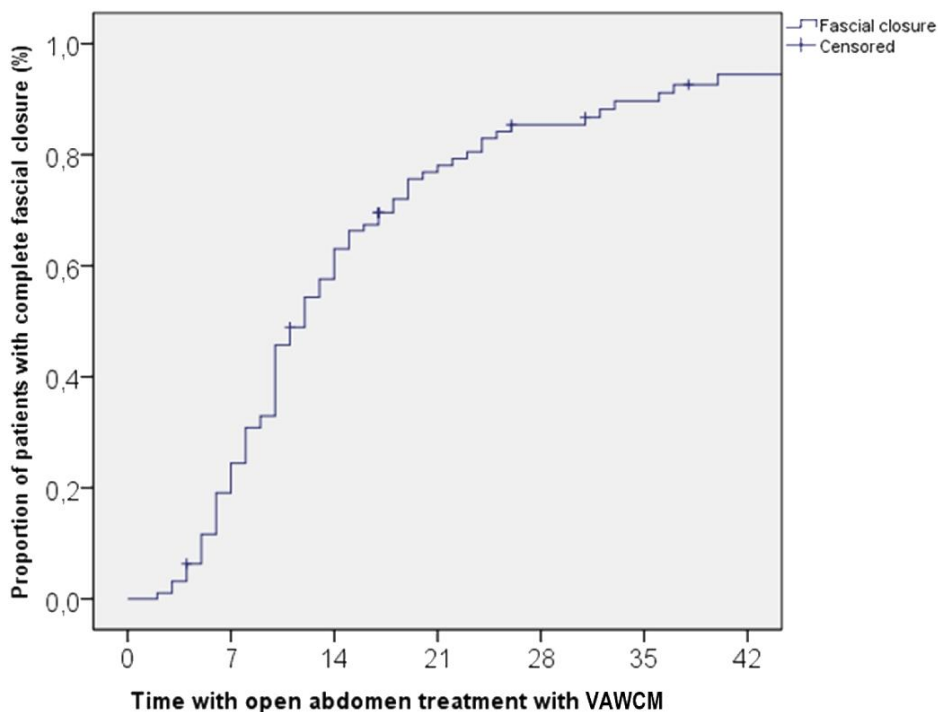
Overview of fascial closure is shown in Figure 30 and Table 17. In an intention-to-treat analysis of fascial closure, patients who died before fascial closure are regarded as failure of fascial closure. In the analysis per protocol, only surviving patients are included in the calculation, compensating for the fact that failure of delayed primary fascial closure was seen in 26 patients, of whom 16 (62 %) died before it was clinically appropriate to end OA therapy and attempt fascial closure.

Table 17. Fascial closure rate

Number of patients	Fascial closure	Intention-to-treat	Per protocol (survivors only)
85	Delayed primary fascial closure	77 %	} 98 %
8	Permanent closure with mesh	7 %	
2	Partial closure	2 %	
16	Not closed (died with OA)	14 %	
111		100 %	

Delayed primary fascial closure

The ultimate goal of VAWCM therapy, to remove the temporary mesh and suture the fascia when an OA was no longer necessary, was achieved in 85 patients (Table 23). Suture length to wound length ratio, measured in 63 patients, was in median 5.5 (range 3.2–17.1). Cumulative fascial closure is shown in Figure 31.



Patients at risk: 95 76 39 19 11 7 3

Figure 31. Cumulative delayed primary fascial closure in 95 patients who survived until abdominal closure (per protocol analysis). The number of patients at risk (alive) at each time is shown below the time axis.

Mesh closure

Abdominal wall closure with mesh reconstruction or reinforcement was performed in eight patients (Table 18). In four patients, the fascia was completely closed in the midline but a mesh was used due to previous wound dehiscence. The standard method for mesh reconstruction at our department (except in grossly contaminated fields) is with a synthetic mesh in a sublay position. The reason for deviating from the standard method of mesh reconstruction, was previous surgery in the retromuscular space (n=3) or surgeon's preference (n=3). In one patient, a collagen mesh (Permacol™) was used by a plastic surgeon, while the other patients were operated by visceral/hernia surgeons using a polypropylene mesh. Component separation was not performed in any of these patients.

Table 18. Mesh closure in 8 patients at the end of VAWCM therapy

Patient	Fascial diastasis	Indication for mesh	Mesh placement	Mesh type
1	0	Wound dehiscence	Onlay	Polypropylene
2	0	Wound dehiscence	Sublay	Polypropylene
3	0	Wound dehiscence	Sublay	Polypropylene
4	0	Wound dehiscence	Onlay	Polypropylene
5	10 cm	Frozen abdomen	Onlay	Polypropylene†
6	2 cm	Frozen abdomen	Onlay	Collagen
7	3 cm	Frozen abdomen	IPOM	Polypropylene‡
8	7 cm	Frozen abdomen	Onlay	Polypropylene‡

† Fascial defect closed with soft tissue underneath regular polypropylene mesh.

‡ Composite polypropylene mesh with cellulose cover (Proceed™).

Partial fascial closure

Complete fascial closure was not possible in two patients, both due to ossification in the wound. One had minimal remaining fascial diastasis and the other a diastasis of 10 cm. Both had complete skin closure. In essence, these were small, planned ventral hernias.

Permanent abdominal closure

Same-hospital-stay permanent closure of the abdomen (suture or mesh), was achieved in 93 patients or 98 % of patients surviving the OA period.

Frozen abdomen

Five patients developed a frozen abdomen. With continuous VAWCM therapy, fascial diastasis in these patients had been reduced to 3–10 cm. None required a planned ventral hernia. Four patients were closed with a mesh reconstruction while one patient died of a myocardial infarction before attempted closure.

In summary

Delayed primary fascial closure was achieved in 89 % and same-hospital-stay permanent abdominal closure (suture or mesh) in 98 % of patients surviving the OA period. No patient received a large planned ventral hernia.

Risk factors for failure of fascial closure

Intention-to-treat analysis

Possible risk factors for failure of fascial closure were analyzed in a univariate analysis and variables with possible association ($p < 0.10$) were entered into a multivariable binary logistic regression analysis (Table 19).

Table 19. Factors associated with failure of delayed primary fascial closure (intention-to-treat analysis)

Variable	No. of patients	Univariate analysis	Multivariate analysis
OA duration > 14 days	59	p = 0.020	
OA duration > 21 days	37	p = 0.011	Not significant
ICU stay > 21 days	48	p = 0.049	Not significant
Renal replacement therapy	38	p = 0.058	Not significant
Intestinal fistula	8	p = 0.001	OR 8.55 (1.47– 49.7); p = 0.017

Only intestinal fistula remained as an independent factor associated with failure of fascial closure in the multivariate analysis.

Per-protocol analysis

By excluding the 16 patients who died during OA therapy, factors causing death were separated from factors causing failure of delayed primary fascial closure. The same variables were used as in the ITT analysis, and in a similar fashion, factors with $p < 0.10$ were entered into a multivariate analysis (Table 20).

Table 20. Factors associated with failure of delayed primary fascial closure (per protocol analysis)

Variable	No. of patients	Univariate analysis	Multivariate analysis
OA duration > 14 days	59		OR 5.47 (1.01–29.6; p = 0.048)
ICU stay > 21 days	48		Not significant
Renal replacement therapy	38		Not significant
Intestinal fistula	8		Not significant
Duration of OA therapy	(all)	p = 0.022	

In the multivariate analysis, OA duration > 14 days was found to be independently associated with failure of fascial closure (OR 5.47 (1.01–29.6); $p = 0.048$). Compared with the ITT analysis, intestinal fistula was no longer associated with failure of delayed primary fascial closure. In other words, association with these variables in the ITT analysis was due to their association with mortality.

In summary

In the ITT analysis, only intestinal fistula was found to be an independent factor associated with failure of fascial closure. When patients who died before fascial closure were excluded from the analysis, only long duration of OA was associated with failure of delayed primary fascial closure.

Intestinal fistulas

Ten enteric perforations (9 %) appeared during OA therapy, of whom six (5 %) became permanent enteroatmospheric fistulas (Table 21). In paper I, eight possibly VAWCM related enteric fistulas are mentioned. Since then, the definition of fistula has been clarified³⁴ and after re-assessment of all operative reports (performed in connection with paper III), non-permanent enteric perforations and enterocutaneous fistulas have been excluded from the list. Seven patients had intestinal ischemia. All ten patients had a new enteric anastomosis. One patient had a colostomy but none had a jejunostomy or ileostomy.

Table 21. Treatment and outcome for enteric perforations and enteroatmospheric fistulas

Initial treatment	Outcome	Underlying disease	Clinical course
Passive drainage	Stopped	Iatrogenic small bowel perforation	Delayed primary fascial closure → discharged from hospital
Passive drainage	EAF	Bowel ischemia	Died with OA
Passive drainage	EAF	Bowel ischemia	Died with OA
Passive drainage	EAF	ACS due to ileus	Died with OA
Attempt to divert to ECF	EAF	Bowel ischemia	Died in hospital with closed abdomen but continued intra-abdominal leakage
Bowel resection → clean abdomen → perforation at different location → passive drainage	EAF	Bowel ischemia	Died with OA
Passive drainage, then diverted to ECF	EAF → clean abdomen	Bowel ischemia	Died 5 months later with closed abdomen, still in hospital
Diverted to ECF	Clean abdomen	Bowel ischemia	Died in hospital with clean OA and stable ECF
Primary suture	Clean abdomen	Perforated diverticulitis	Died 5 days later without new leak
Perforated segment taken out as stoma	Clean abdomen	Bowel ischemia	Discharged from hospital after delayed primary fascial closure

In summary

Ten patients developed an enteric perforation during OA therapy, of whom six became established EAFs. Most (7/10) had bowel ischemia. All had enteric anastomoses and none had a proximal stoma. Two patients survived, where development into an EAF was avoided.

Re-exploration

Three patients needed re-exploration and repeated OA therapy, due to aorta graft infection (n=1), enteric fistula (n=1) and rising IAP (16 mmHg) after previous ACS (n=1). One patient needed re-suture of wound dehiscence. All four patients had ACS from start.

Other complications

Overview of complications, other than the previously mentioned enteric perforations and fistulas, appearing during OA therapy with VAWCM are shown in Table 22.

Table 22. Other complications during/after OA therapy with VAWCM

Perforation of rectal stump	4
Leakage of bowel contents into VAWC system	
– From loose stoma bag	3
– From disrupted colostomy	1
Ossification in the wound	3
Hemorrhage	
– From rectus muscle	2
– From liver	1
Re-suture for wound dehiscence	1
Intra-abdominal abscess after abdominal closure	4

Leakage from a rectal stump

Contamination during OA therapy due to perforation in a necrotic staple line in an excluded rectal stump, was seen in 4 patients. All were successfully treated by re-suture and VAWCM therapy was continued.

Heterotopic ossification

Ossification in the wound interfered with fascial closure in three patients. In one patient, primary suture of the fascia was achieved after resection of the bone formation, whereas in two patients, resection was not performed and the fascia was partially closed (minimal remaining diastasis in one patient and 10 cm in the other).

Hemorrhage

There were three instances of bleeding, shown in Table 22. After hemostasis, VAWC therapy was continued as before in two patients, but one patient, who had hemophilia and was considered to have a severe risk of re-bleeding, was treated with passive drainage (0 mmHg) during most of the OA treatment time.

Intra-abdominal abscess after abdominal closure

An intra-abdominal abscess after closure of the abdomen was seen in four patients. Three were successfully treated with percutaneous drainage, while one needed re-operation with a short repeated OA therapy due to aortic graft infection.

Skin complications after abdominal closure with a mesh

Seven out of the eight patients who underwent mesh closure, had some form of skin complication. Four required subcutaneous VAWC therapy and wound revisions. None required mesh removal.

Mortality

Mortality for the OA study, from initiation of OA therapy to one year follow-up is shown in Figure 29 and table 24.

Table 24. Mortality rate (all 111 patients)

14.5 % in hospital with OA:	} 30 % in-hospital mortality	} 37 % total mortality at 1 year
15.5 % in hospital with closed abdomen		
7 % after hospital discharge < 1 year		

Sixteen patients died before it was clinically appropriate to end OA therapy and attempt abdominal closure. Another 17 patients died in hospital after abdominal closure. In other words, life-threatening conditions, such as sepsis and multiple organ dysfunction, persisted even after the disease of the abdomen had been treated. Of the 78 patients that were discharged from hospital, 8 (10 %) died in the first year.

In-hospital mortality

Possible risk factors for in-hospital mortality were analyzed in a univariate analysis and factors with a possible association ($p < 0.10$) were entered into a multivariate analysis (Table 25).

Table 25. Factors associated with in-hospital mortality ($p < 0.10$). Intention-to-treat analysis

Variable	No. of patients	Univariate analysis	Multivariate analysis
Age ≥ 75 years	25	$p = 0.080$	OR 1.21 (1.02–1.43); $p = 0.027$
Intestinal ischemia	26	$p = 0.012$	Not significant
Failure of fascial closure †	26	$p < 0.001$	OR 44.5 (1.13–1748); $p = 0.043$
Ventilator ≥ 14 days	43	$p = 0.006$	
Renal replacement therapy	38	$p = 0.005$	
ICU stay > 21 days	48	$p = 0.031$	
Intestinal fistula ‡	8	$p = 0.006$	Not significant
Any Stoma	44	$p = 0.087$	Not significant
Duration of ventilator-assisted respiration	All	$p = 0.001$	Not significant
Duration of renal replacement therapy	All	$p = 0.006$	Not significant
Duration of ICU stay	All	$p = 0.006$	Not significant
Fluid overload (weight increase ≥ 10 kg)	All	$p = 0.013$	Not significant
SOFA score before OA treatment	All	$p = 0.082$	Not significant

† 16 out of 26 were due to mortality. ‡ Intestinal fistulas according to original definition ($n=8$).

Causes of death

Causes of death from initiation of OA therapy until one year follow-up are summarized in Table 26.

Table 26. Causes of death

During OA therapy ($n = 16$)	8 Multiple organ dysfunction and/or sepsis
	6 Cardiac event
	1 Pneumonia
	1 Cerebrovascular insult
In-hospital, closed abdomen ($n = 17$)	10 Multiple organ dysfunction and/or sepsis
	4 Pneumonia
	2 Cardiac event
	1 Cerebrovascular insult
After hospital discharge ($n = 8$)	3 Generalized malignancy
	3 Cardiac event
	2 Chronic sepsis

In summary

Age > 75 years and failure of fascial closure were found to be independently associated with in-hospital mortality according to ITT analysis.

Incisional hernia

Incidence

Incisional hernia incidence is shown in Table 27. In all, 14 (22 %) patients had a symptomatic hernia.

Table 27. Incisional hernia one year after OA therapy

Any modality (clinical examination, CT or operation)	42 / 64 (66 %)
Clinically detectable	23 / 64 (36 %)
Symptomatic and clinically detectable	12 / 64 (19 %)
Operated for a hernia (in the first year)	7 / 64 (11 %)

Size

The width of the hernia area according to the CT scan was 5.0 cm (1.0–20) cm and the size 61 (0.50–520) cm² (median, range). Both width ($p = 0.031$) and area ($p = 0.025$) were significantly larger for symptomatic than for asymptomatic patients. In the 35 patients with a CT-verified hernia, 66 % had multiple fascial defects.

In summary

The incidence of incisional hernias was high, but most hernias were small and asymptomatic.

Risk factors for incisional hernia development

Potential risk factors for development of an incisional hernia were assessed in a univariate analysis, shown in table 28. Factors showing a trend towards association ($p < 0.10$), i.e. parastomal hernia at 1 year, obesity, and renal replacement therapy, were entered into a multivariate analysis.

Table 28. Factors associated with incisional hernia 1 year after OA therapy with VAWCM ($p < 0.10$)

Variable	No. of patients	Univariate analysis	Multivariate analysis
Patients alive at 1 year	70		
Obesity (BMI ≥ 30 kg/m ²)	10	$p = 0.076$	Not significant
Maximum weight ≥ 100 kg	19	$p = 0.086$	
Renal replacement therapy	15	$p = 0.060$	Not significant
Parastomal hernia (of 31 stoma patients)	18	$p = 0.018$	OR 8.9 (1.2–68.8); $p = 0.035$

In summary

Only the presence of a parastomal hernia at 1 year was independently associated with the presence of a midline incisional hernia.

Parastomal hernia

Thirty-one out of the 64 patients (48 %) with previous delayed primary fascial closure who were alive one year after OA therapy had a stoma: ileostomy (n = 6), colostomy (n = 20), or both (n = 5). Among them, 18 (58 %) were found to have a parastomal hernia, 15 of whom were clinically detectable and nine were symptomatic. Concomitant incisional hernia was present in 15 (83 %) of the 18 patients with a parastomal hernia. Of the 15 patients with available CT examination, eight were class I b, two were class II and five were class III.

Other findings

Operations during the follow-up interval

Ten patients were operated with a laparotomy before the one year follow-up, of whom seven had a repair of incisional hernia (Table 29). Three patients had parastomal hernia, of whom two were repaired with a stoma takedown and one was left unrepaired due to peritoneal carcinomatosis.

Table 29. Operations within the first year after OA therapy

Primary indication for operation	Number of operations	Repair of incisional hernia
Repair of incisional hernia	2	2
Bowel resection	2	2
Stoma takedown	6	3
Total	10	7 (11 %)

Fascial diastasis in non-hernia patients

Median fascial diastasis in the patients who did not have a hernia was 4.8 (1.0–7.9). All but one had a diastasis > 25 mm.

Heterotopic ossification

Ossification in the midline postoperative scar was found in 19 patients (30 %). In 15 of the 19 cases, ossification was present in the vicinity of the xiphoid process. None had ossification near the pubic symphysis while 13 patients had ossification in multiple parts of the wound.

Sensitivity and specificity of a clinical investigation compared to any modality

Although CT was considered gold standard, it was found that in three patients a hernia was diagnosed clinically but not on a CT scan, where a thin but uninterrupted fascial cover led to the diagnosis of fascial diastasis. The sensitivity and specificity of clinical examination compared to all modalities (CT and clinical examination, i.e. the final diagnosis) is shown in Figure 32.

		Any modality	
		Hernia	No hernia
Clinical examination	Hernia	17	0
	No hernia	21	18

Sensitivity: $17/38 = 45\%$ (29–62%)
Specificity: $18/18 = 100\%$ (81–100%)

Figure 32. Sensitivity and specificity of clinical investigation, with 95 % confidence interval.

Follow-up of patients with previous mesh closure

In all four surviving patients who had abdominal wall closure with permanent mesh reinforcement, CT scans showed an intact abdominal wall with no signs of a hernia or mesh displacement. In two patients, the wound was not completely healed at the time of follow-up despite skin grafting in one. Both of these patients had smaller parts of the mesh excised during wound revisions, but no patient required total mesh removal. The other two patients were asymptomatic. One patient had a colostomy with no sign of a parastomal hernia.

Follow-up of patients with previous partial fascial closure

In two patients, complete fascial closure was not possible because of ossification in the wound. Both patients were alive at the time of follow-up. One patient had a 10 cm large defect that was later repaired with a sublay polypropylene mesh reconstruction (Figures 33–34). The other patient had a small defect that was not clinically detectable, and surgical repair was not scheduled. Neither patient had a stoma.



Figure 33. Large defect during ongoing OA therapy and subsequent hernia in a patient who developed ossification in the wound.

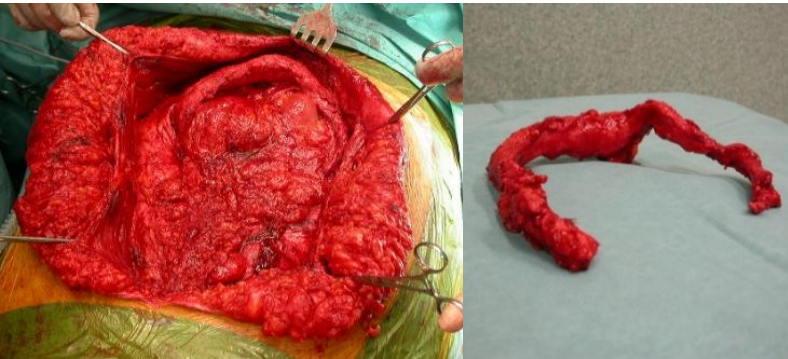


Figure 34. Hernia repair operation in the same patient one year after OA therapy with removal of horse-shoe shaped bone formation and mesh reconstruction of the abdominal wall.

Validity and reliability of the OA classification system (paper III)

Validity

For assessment of validity, it was evaluated whether the outcome of the classification system (OA grades) were associated with clinical outcome variables (fascial closure and mortality).

Initial OA grade

No correlations were found between the OA grade at initial OA laparotomy and clinical outcome. Eight patients were registered as grade 2 from start, since they had

adherences from previous operations which were not released completely during the initial laparotomy.

Most complex OA grade for each patient

Correlation was found between the most complex grade registered for each patient during the OA period, and failure of delayed primary fascial closure as well as mortality during OA therapy (Table 30). Ninety-one percent of patients had OA grades 1 or 2 throughout the entire OA period, and 20 % had only grade 1A.

Worsening OA grade

Association was seen between worsening of OA grade (ascending to a more complex OA grade without a later improvement) and higher mortality during OA therapy (Table 30).

Patients with grade 1A only

Patients, who had grade 1A during the entire OA period had similar outcome as patients who at some point received a more complex OA grade (Table 30).

Table 30. Association between most complex OA grade and clinical outcome

Most complex OA grade	No. of patients	Delayed primary fascial closure (suture)	Permanent abdominal wall closure (suture or mesh)	Mortality during OA	In-hospital mortality
All patients	111	89 % r = -0.20 p = 0.050	98 % r = -0.080 p = 0.44	14 % r = 0.20 p = 0.033	31 % r = -0.034 p = 0.72
Worsening grade (vs. others)	38 vs 73	79 % p = 0.063	97 % p = 0.52	24 % p = 0.045	32 % p = 0.88
1A (vs others)	22 vs 89	90 % p = 1.0	100 % p = 1.0	9 % p = 0.74	41 % p = 0.24

OA grade at abdominal closure or death

Among patients who received delayed primary fascial closure, 67 % had grade 1A and 32 % grade 2A. One patient had grade 1B at fascial closure, due to contamination from a urine bladder perforation, repaired simultaneously. Patients who died during OA therapy did not have more complex final OA grade than those who survived until abdominal closure (p = 0.10).

Contamination

Contamination (grades 1B or 2B) compared with similar clean grades (1A or 2A) did not affect outcome. Patients with contamination at the index operation had

similar outcome as patients with clean abdomen from start. Likewise, patients with grades 1B or 2B as the most complex grade had similar outcome as patients with corresponding clean grades (1A and 2A) as the most complex grade ($p = 0.12$, $p = 1.0$, $p = 0.73$ and $p = 0.74$ for delayed primary fascial closure, permanent abdominal wall closure, mortality during OA therapy and in-hospital mortality, respectively).

Fixation

Patients with developing fixation (grades 2A and 2B) as the most complex grade had similar fascial closure rates as patients with corresponding non-fixed grades (1A and 1B) as the most complex grade ($p = 0.63$ and $p = 0.37$ for delayed primary fascial closure, respectively). Mortality during OA therapy was similar ($p = 0.73$), but in-hospital mortality was lower in the group with fixation ($p = 0.042$).

Frozen abdomen

Delayed primary fascial closure rate was lower in patients with frozen abdomen (since the definition of a frozen abdomen is that primary closure is not possible). Permanent abdominal wall closure, using a mesh, was achieved in all four surviving patients. Mortality was similar to that in patients without frozen abdomen ($p = 0.55$ and $p = 1.0$ for mortality during OA therapy and in-hospital mortality, respectively).

Enteric leaks

Ten enteric leaks developed during OA therapy (Table 21). Four were successfully treated and two of them survived to be discharged from hospital, while the other six developed an EAF. In these patients, fascial closure rate was similar but mortality was higher ($p = 1.0$, $p = 1.0$, $p = 0.001$ and $p = 0.001$ for delayed primary fascial closure, permanent abdominal wall closure, mortality during OA therapy and in-hospital mortality, respectively).

Enteriatmospheric fistulas

Out of the ten enteric leaks that developed during OA therapy, six became established EAFs, three after an unsuccessful attempt of surgical treatment and three after conservative treatment from start (Table 21). Four established EAFs were treated with passive drainage and eventually became frozen abdomens while two were actively treated and remained non-frozen, one of which was ultimately turned into a controlled ECF. All of the EAF patients, including the one with successful fistula treatment, died in hospital. Mortality was higher for patients with EAFs but fascial closure rate did not differ ($p = 1.0$, $p = 1.0$, $p = 0.004$ and $p = 0.001$ for delayed primary fascial closure, permanent abdominal wall closure, mortality during OA therapy and in-hospital mortality, respectively).

Floor and ceiling effects

A floor effect was observed with 20 % of patients having the lowest grade (1A) as the most complex grade registered throughout the OA period. Out of all 753 operative reports, 459 (61 %) were grade 1A. Six patients (5 %) received the highest possible grade (grade 4) and thus there was no ceiling effect.

Changes in the 2013 version

Thirteen percent of patients received one or more different grade when changing from the 2009 to the amended 2013 classification system.

Fistulas, according to the 2009 classification included enterocutaneous (ECF) or enteroatmospheric fistulas (EAF). With the 2013 classification, these patients were converted to enteric leaks or EAFs and a few were converted to an ECF with a clean abdomen.

Frozen abdomen according to the 2009 classification included both clean, frozen abdomens and EAF in a frozen abdomen. With the 2013 classification, these patients had either clean, frozen abdomen or EAF. These patient groups were seen to have very different outcomes with 100 % in-hospital mortality in the EAF group and 20 % for frozen abdomen.

In summary

Most complex grade and worsening of OA grade had association with clinical outcome, as did development of grade C (enteric leak) and grade 4 (EAF). Contamination, fixation and frozen abdomen were not associated with worse clinical outcome. Floor effect was observed.

Reliability

Inter-rater reliability

Inter-rater agreement between each two raters was 76–82 % and intra-class correlation coefficient (ICC) was 0.68–0.80. Agreement was lower (although not significant) when the least complex grade (1A) or the four least complex grades (1A, 1B, 2A and 2B) were excluded from the calculation. Agreement between all three raters simultaneously was seen in 70 %.

Test-retest reliability (repeatability)

Test-retest agreement for the three raters respectively was 70–96 % and ICC was 0.55–0.97. Agreement was lower (although not significant) when the least complex grade (1A) or the four least complex grades (1A, 1B, 2A and 2B) were excluded from the calculation.

In summary

Inter-rater reliability was classified as good and test-retest reliability as moderate to good. Agreement was lower for the more complex grades.

Physiological effects of vacuum therapy in an open abdomen (paper IV)

Negative pressure in the abdominal cavity during VAWC therapy

Negative pressure measurements at five different sensor positions (Figure 29) and at five different levels of applied negative pressure are summarized in Figure 35.

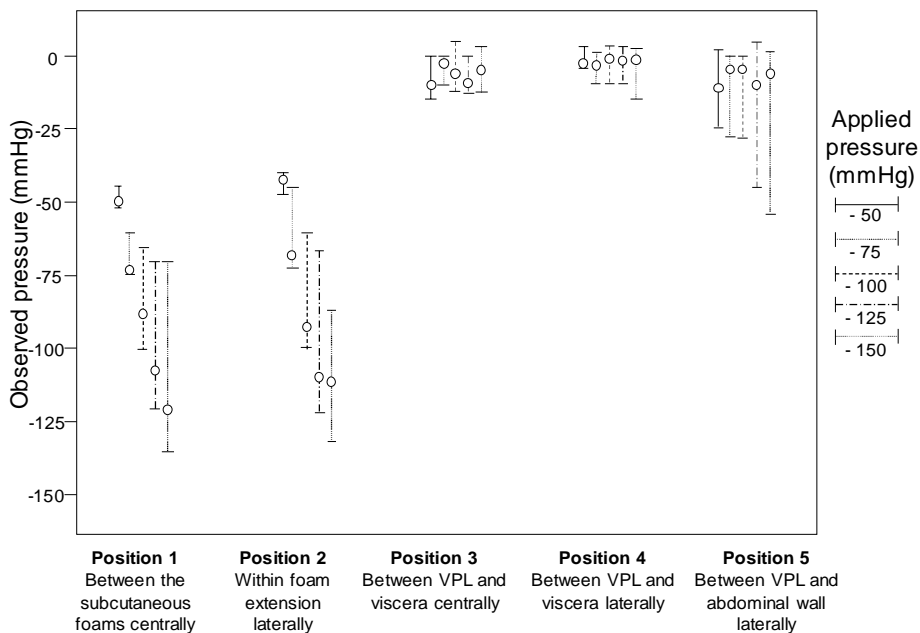


Figure 35. Observed pressure (median and range for the 6 animals) for all sensor positions and negative pressure settings. VPL visceral protective layer (own picture © Springer, reproduced with permission).

Pressure reaching the outer surface of the bowel is shown in positions 3 and 4. Median pressure (for the six animals) was between -2 and -10 for the different pressure settings. The lowest single measurement was -15 mmHg (animal 4 at -50 mmHg and animal 4 at -150 mmHg).

In summary

Negative pressure reaching the bowel was limited, regardless of negative pressure setting. Maximal single measurement was – 15 mmHg.

Pressure isolation with paraffin gauzes

The pressure isolation of paraffin gauzes in eight layers, placed on the bowel surface intra-abdominally (without visceral protective layer in between), is shown in figure 36. Median reduction in pressure was 13 % and the maximal single measurement showed a pressure reduction of 28 %.

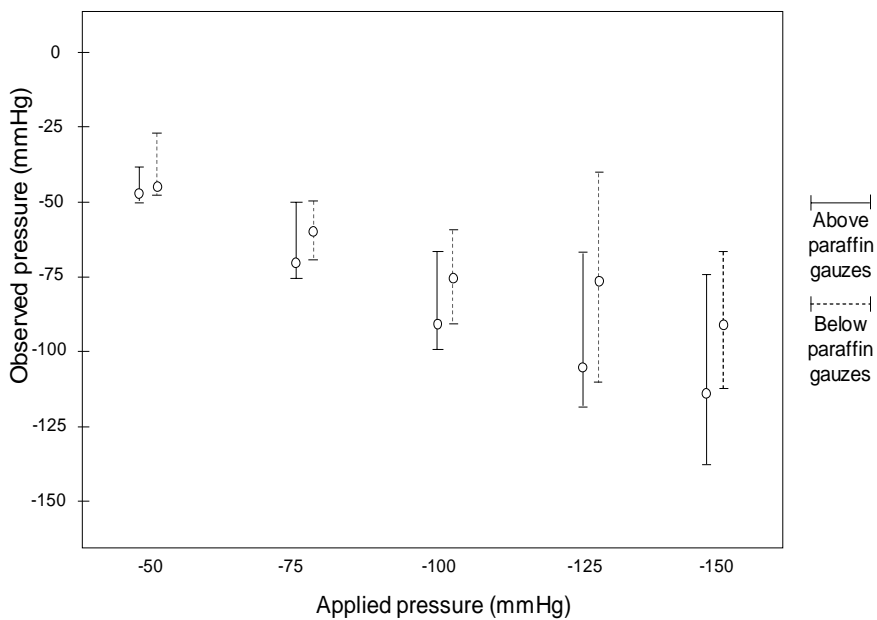


Figure 36. Pressure isolation of paraffin gauze in eight layers. Median pressure and range is shown for each pressure setting (own picture © Springer, reproduced with permission).

In summary

Paraffin gauzes are not useful as isolation against negative pressure.

Fluid drainage

The efficacy of the VAWC system in draining fluid from the abdominal cavity is shown in Figure 37. At a setting of -75 mmHg, 95 % (88–152 %) of the infused volume had been drained after 10 minutes, and 124 % (105–167 %) at a setting of -150 mmHg (median, range).

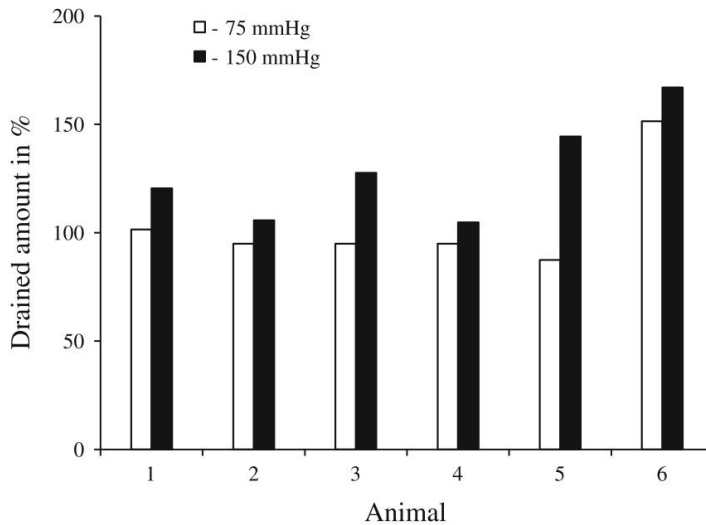


Figure 37. Fluid drainage from the abdominal cavity, shown individually for each animal. Drained amount is expressed as a percentage of the volume previously infused (own picture © Springer, reproduced with permission).

In summary

VAWC using the ABThera™ system drains the abdominal cavity thoroughly of fluid.

The judicious surgeon who chooses this method should in no way fear the whispered loss of his surgical manhood.

– *Dr. Alexander J. Walt in 1978, withdrawing his 1969 statement that there was “virtually no place in modern surgery for gauze packing of the liver”* ^{113,114}.

General discussions

Evidence for open abdomen therapy

OA therapy evolved as a result of surgeons' efforts to handle abdominal emergencies. Although the practical benefits may seem obvious to the practicing surgeon, it has been difficult to obtain concrete scientific proof of its advantages since controlled studies are extremely difficult to carry out in these critically ill patients.

When abdominal closure is impossible, the use of OA therapy follows by necessity. Such situations include major tissue losses of the abdominal wall or severe intra-abdominal or retroperitoneal swelling. Relative indications, also based on common sense, include planned re-laparotomy, where OA is a practical alternative to suturing the fascia and re-opening it the next day²⁹.

The benefits of the damage control concept with a quick, life-saving operation in a trauma situation have been known for some time³⁰. OA therapy is an integral part in damage control, enabling rapid closure as well as easy access at the next operation. However, long-term benefits of OA therapy in these situations have not been proven, with many patients suffering from wound complications, fistulas and subsequent hernias⁸⁸.

Evidence for the use of OA therapy in severe peritonitis or acute pancreatitis, compared to planned or on-demand re-laparotomies, have been conflicting as well and OA therapy might not be warranted in all instances⁸⁸. In one of the rare examples of a randomized controlled study in the setting of OA treatment, Robledo et al. compared open versus closed management of severe peritonitis and found higher mortality in patients receiving OA therapy¹¹⁵.

Although decompressive laparotomy saves lives in patients with abdominal compartment syndrome (ACS), there is no clear evidence of beneficial effects in situations with intra-abdominal hypertension (IAH) without ACS^{34,88,116}. However, a retrospective study by Cheatham, on 478 patients with IAH or ACS, showed that survival improved during the study period of 5 years, parallel to increased use of OA therapy⁵¹.

Studies comparing different temporary abdominal closure (TAC) techniques have proven difficult to perform properly. One problem is the heterogeneity of OA patients, ranging from short-term OA therapy in a young trauma patient awaiting a

second look re-laparotomy, to an unstable septic patient with multiple organ dysfunction, needing weeks of OA therapy. In the current VAWCM study, most patients were elderly, non-trauma patients with multiple illnesses, receiving long-term OA therapy, whereas many other large-sample studies describe OA therapy in relatively young trauma patients, treated for a relatively short period^{67-69,73,117}. Another complicating factor in this context is the paucity of critically ill patients receiving OA therapy (except possibly in large trauma centers), which necessitates multicenter participation.

One of few existing OA-related randomized controlled trials found in the literature is a study by Bee et al. from 2008, comparing absorbable mesh (Vicryl™) with vacuum dressing⁸². This frequently cited study showed higher intestinal fistula incidence in the group treated with vacuum therapy, although not statistically different, with most fistulas being related to the use of enteral feeding tubes. The risk for leakage at enteral feeding tube sites during OA therapy was noted more than two decades ago by Schein, who recommended total parenteral nutrition or nutrition via nasogastric tube during OA therapy¹¹⁸. Other controversies include that the vacuum treated group was a combination of 26 patients with vacuum pack and 5 with V.A.C.® and that only 51 out of 248 patients treated with OA were included. Delayed fascial closure rates were low with 26 % in the mesh group and 31 % in the vacuum group.

In a British study from 2013 by Carlson et al., information on 578 OA patients was collected online after a nationwide invitation to acute care hospitals for participation. Most patients had peritonitis (69 %). The study showed that the use of VAWC was not associated with higher mortality or intestinal fistula rate than other techniques (mostly Bogota bag)¹¹⁹. An inclusion bias was probably present, with 105 out of 269 invited hospitals registering patients. Primary fascial closure rate was low, especially in the VAWC group (41 %) and reported incidence of intestinal fistulas was 14 % in the VAWC group and 8.5 % in the non-VAWC group.

An American multicenter study from 2013 by Cheatham et al. compared VAWC (ABThera™) and vacuum pack in 280 patients, mostly trauma patients (71 %). The study showed that VAWC was superior to vacuum pack with regards to fascial closure and mortality⁵². Delayed primary fascial closure rate was 69 % using VAWC and 51 % with vacuum pack. Fistula incidence in both groups was 4 %.

One randomized controlled study is ongoing, with results anticipated in late 2013. Again, ABThera™ and vacuum pack are compared, with a focus on systemic inflammatory response¹²⁰.

Physiological effects

Beneficial effect of decompressive laparotomy has been observed in many studies and systematic reviews^{34,45,48,116,120-123}. In the VAWCM study (paper I), intra-abdominal pressure (IAP) was measured preoperatively whenever possible, especially when raised IAP was suspected. Due to the acute nature of illness, however, it was not possible to measure preoperative IAP in all patients. With initiation of OA therapy, median IAP decreased from 20 to 11 mmHg. During subsequent VAWCM dressing change operations, fascial traction, applied according to the surgeon's discretion, did not cause increased IAP.

The SOFA score was developed in order to follow daily physiological changes in ICU patients to evaluate the severity of multiple organ dysfunction¹⁰⁷ and is proposed as an option for monitoring OA therapy³⁴. The results of paper I showed no change in SOFA score the day after initiation of OA, compared with prior to decompressive laparotomy. Similar results were seen in a study by Batacchi et al. on 66 patients, showing no significant change in SOFA score after 24 hours¹²⁴. It seems that SOFA score is not responsive to early physiological changes after decompressive laparotomy and that more sensitive methods are needed. For example, Cystatin C and Cystatin C-based glomerular filtration rate may be more sensitive than creatinine and urinary output (included in the SOFA score) to measure changes in renal function¹²⁵.

Fascial closure

When comparing fascial closure rates between studies, it must be kept in mind that definitions of abdominal closure may differ. The Open Abdomen Advisory Panel (USA) defines primary fascial closure as complete closure with or without mesh; partial fascial closure as remaining fascial diastasis bridged by mesh; and planned ventral hernia as an open wound allowed to granulate and then covered with a skin graft¹²⁶. In the VAWCM study (paper I), delayed primary fascial closure was defined as complete suture of the fascia without the use of a prosthetic mesh; any form of fascial closure involving a mesh, including complete fascial closure with an onlay mesh reinforcement, was defined as mesh closure; and subtotal fascial closure with skin closure over the remaining defect was registered as partial fascial closure. These definitions were chosen in order to best represent the end result with regards to abdominal wall reconstruction.

In the early days of OA therapy, all attention was on the main goal to save the patient's life and closure of the abdomen was a secondary concern. Typically, if the abdomen could not be closed within a week, it became a frozen abdomen which

could not be closed at all¹²⁷. In some studies, majority of patients ended up with non-closable abdomen and the end result was a giant planned ventral hernia^{67,68}.

As OA management has evolved, fascial closure rates have improved. In a systematic review, weighted percentages of fascial closure were 23–43 % with early non-vacuum TAC techniques and 52–60 % with vacuum dressing⁶⁷. Wittmann patch generated 90 % closure rate, but was based mainly on one report of pooled retrospective data¹²⁸. With VAWCM (paper I), delayed primary fascial closure was achieved in 89 % of surviving patients and permanent, same-hospital-stay closure of the abdominal wall in 98 %. This is a high fascial closure rate, especially considering that most patients were elderly non-trauma patients undergoing long-term OA therapy. Importantly, no patient received a planned ventral hernia with skin grafting. In the two patients with incomplete fascial closure (due to ossification in the wound), skin closure was possible without difficulty.

Component separation technique¹²⁹⁻¹³¹ was not performed in any of the patients in the study. Perhaps primary fascial closure would have been possible in some of the eight patients, who were closed with a mesh, using this technique. However, incisional hernia repair with the components separation technique has been shown to result in a high incidence of recurrent hernias^{132,133}. The technique is used only in selected cases at our institution, in combination with a synthetic mesh.

A biological mesh was used in one patient at another institution in this multicenter study. Biological meshes are not used for abdominal wall closure at our institution, due to non-proven durability and extremely high costs. Opinions differ on whether synthetic meshes can be used in non-sterile fields such as open abdomens. In American guidelines biological meshes are recommended instead^{126,134}. Others, including WSACS, point out that evidence supporting the use of biological meshes, is lacking^{34,135}. Many of the patients in paper I who were closed with a synthetic mesh, had postoperative skin complications, but all were treatable without mesh extirpation. These were obviously the most complex patients with regards to abdominal closure, having the highest risk of complications. In other situations, abdominal wall closure using a synthetic polypropylene or polyvinyl (PVDF) mesh has worked well in our hands and has been used numerous times in non-sterile fields. In a recent study by Berrevoet et al. on 724 consecutive ventral hernia repairs, an infected mesh could almost always be salvaged (51 out of 54) using superficial VAWC therapy, indicating that the fear of using a synthetic mesh in other than clean operative fields may be unnecessary¹³⁶.

Complications

Intestinal fistulas

Similar to facial closure rates, the definition of intestinal fistulas may vary between studies, resulting in different fistula incidences in similar cohorts. In the VAWCM study (paper I), both permanent and non-permanent perforations as well as a few non-enteric fistulas (such as pancreas fistulas) were reported in the study protocol and all possible complications to VAWCM therapy were reported in the paper. During the preparation of paper III, all operative reports were re-assessed using a clear definition. Non-permanent enteric perforations and enterocutaneous fistulas were removed from the list, leaving only permanent enteroatmospheric fistulas.

The incidence of intestinal fistulas in paper I, excluding non-permanent enteric perforations and enterocutaneous fistulas, was 5 % (6 out of 111), which is lower than in many other studies, especially considering that most of our patients were non-trauma patients^{52,67,69,119}.

There have been ongoing discussions among surgeons whether the use of vacuum therapy in the setting of an OA was safe in terms of potential damage to the bowel by the negative pressure^{80-82,137}. However, OA therapy in itself, inevitably carries an inherent risk of bowel injury and fistula formation, with the bowel exposed to an unnatural environment and manipulated during dressing changes. Underlying diseases, such as bowel ischemia, sometimes requiring multiple resections, and multiple organ dysfunction syndrome increase the risks even further. Due to heterogeneity of existing studies with regards to e.g. underlying pathology, age, and co-morbidities as well as criteria for OA therapy and VAWC management, it was difficult to interpret whether the development of fistula was caused by or coincided with increased use of VAWC. However, recent data does not support a causal relationship between VAWC and fistula development:

- The experimental study in this thesis (paper IV) showed that the actual negative pressure reaching the surface of the bowel, during VAWC therapy in pigs, was only a few mmHg. It seems unlikely that this level of negative pressure should cause pressure damage, although long term effect on vulnerable bowel has not been studied.
- The use of VAWC in fistula treatment, where negative pressure is applied on the bowel surrounding the fistula without a interposing pressure barrier, does not seem to cause new fistulas^{84,86,87,138}.
- Systematic reviews do not show higher fistula rates in connection with vacuum therapy⁶⁷⁻⁶⁹.

- A study from 2013 by Carlson et al. on 578 patients receiving OA therapy, predominantly patients with peritonitis (69 %), did not show an increased risk for intestinal fistulas or mortality in patients receiving VAWC¹¹⁹.
- A study from 2013 by Cheatham et al. on 280 patients, comparing VAWC with vacuum pack, in predominantly trauma patients (71 %) shows low incidence of intestinal fistulas (4 %) in both groups⁵².

Intraabdominal infections

One important aspect of OA therapy is the removal of fluid collections which may evolve into an abscess. The experimental study (paper IV) showed that VAWC effectively drains fluid from the abdomen. At each dressing change, the abdominal cavity should be inspected for possible remaining fluid collections, but with the greatest care to avoid damaging the bowel and thereby risking fistula formation. It is important that the visceral protective layer is tucked all the way to the paracolic gutters, not only to prevent adhesions to the abdominal wall, but also to facilitate drainage of fluid. In the VAWCM study (paper I), four intra-abdominal abscesses were diagnosed after delayed primary fascial closure, indicating effective fluid drainage in a clinical situation as well.

Ossification of the wound

Heterotopic ossification in the laparotomy wound interfered with fascial closure in three patients (paper I) and was frequently seen on CT scans at one year (paper II). This is a known complication in situations such as hip replacement surgery, spinal cord injuries, traumatic amputations, and burn injuries and has recently been shown to occur in up to 25 % of non-OA laparotomies^{139,140}. Seeding of bone and cartilage forming cells due to surgical incisions into the xiphoid process or pubic symphysis has been suggested as a possible cause. However, ossification in other locations as well as the absence of ossification in most sternotomy patients indicates that other mechanisms must be involved as well¹⁴⁰. It is plausible that VAWC therapy is involved in the ossification process, i.e. that the same mechanisms that induce granulation tissue formation also affect bone and cartilage⁷⁵. Dispersion of fluid through the VAWC system could help spread bone and cartilage forming cells in the wound bed. However, no other studies could be found in the literature describing heterotopic ossification in connection with OA therapy.

Hemorrhage

Risk for bleeding is a contraindication for the use of VAWC therapy¹⁴¹. In the VAWCM study (paper I), there were few bleeding complications despite negative pressure coming in direct contact with the rectus muscle in all patients and a few patients having liver trauma. In cases of bleeding, vacuum therapy was discontinued in one patient with hemophilia, but in the other two patients, therapy was continued as before after hemostasis was achieved.

Mortality

In-hospital mortality in the VAWCM study (papers I-II) was similar to that seen in other studies and demonstrates the severity of the underlying conditions as well as co-morbidities in these elderly patients^{67,119}.

Several in-hospital deaths occurred after abdominal closure due to non-OA related reasons. In other words, life-threatening conditions, such as sepsis and multiple organ dysfunction in patients with limited physiological reserve, persisted after the abdominal condition had been treated. Mortality risk persisted after hospital discharge, with 10 % of those who were discharged from the hospital dying within the first year.

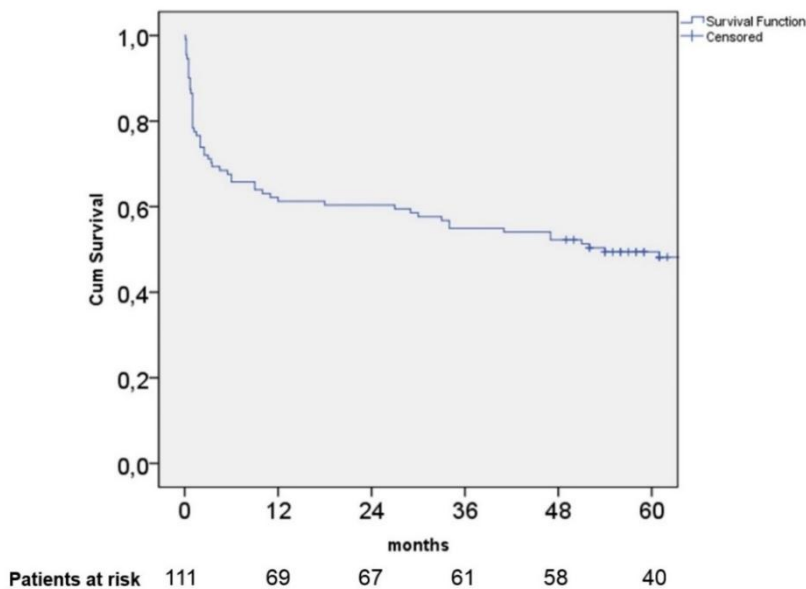


Figure 38. Five-year cumulative survival curve for patients with OA treated with VAWCM. The number of patients at risk (alive) at each time is shown below the time axis. Tick marks indicate censored data.

Association was seen between mortality and failure of fascial closure according to ITT analysis. However, this was not due to causal relationship but can be explained by the fact that failure of fascial closure was often caused by death (16 out of 26 cases). The association was not seen in the analysis per protocol.

An assessment of cumulative survival showed that approximately 50 % of the study patients are predicted to be alive at 5 year. (Figure 38).

Incisional hernias

Long-term results after OA therapy are sparsely described in the literature. We found no other study that described methodical follow-up with assessment of hernia incidence, although follow-up is mentioned briefly in several publications^{36,42,93,98,102,142-149}.

In many earlier OA studies, a majority of the patients developed a frozen abdomen, resulting in a planned ventral hernia^{127, 67,68}. With those premises, concerns for subsequent development of an incisional hernia in the patients who received primary closure were obviously irrelevant. With the majority of patients receiving delayed primary fascial closure in contemporary OA studies, late incisional hernias have become clinically relevant.

It was suspected that the incidence of incisional hernia after OA therapy and delayed primary fascial closure would be higher than after an elective laparotomy. An incidence of 66 % was surprising, since this is considerably higher than the 0–21 %, reported after acute or elective laparotomies¹⁵⁰. In reality, the difference in hernia incidence between OA and non-OA situations might be less extreme than the incidence figures above indicate. Firstly, the prospective design of the VAWCM study, including both clinical and CT scan examinations, allows detection of the smallest of hernias, in all surviving patients, which undoubtedly results in a higher hernia incidence. If based on clinical examination, the hernia incidence in the VAWCM would have been 36 % instead of 66 %. Had symptomatic patients been identified through a telephone interview and summoned to a follow-up for a clinical examination only, as is reported in some studies, the incidence would have been 19 %. A retrospective review of medical records would have revealed an incidence of hernia repair operations of 11 %. Secondly, hernia incidence after non-OA laparotomies might be considerably higher than reported. Large variations in reported incidences is an indication of differences in hernia definitions and methodology of the follow-up procedure¹⁵⁰. Hernia incidences close to zero are probably not realistic. Three studies on incisional hernias could be identified where patients were followed-up using a CT for diagnosis. One study showed an incidence

of 60 % after open AAA surgery¹⁵¹ and another one showed 51 % after colon resection¹⁵². One study showed an incidence of 23 % after AAA surgery, but in this study, protrusion of abdominal contents through the fascial gap was a criterion for diagnosis. A recent study by Bloemen et al. where 456 laparotomy patients were examined with ultrasound showed 23 % hernia incidence¹⁵³.

It can be debated whether small, asymptomatic hernias, not detectable on clinical examination are of any clinical significance. In fact, only a small fraction of the symptomatic, palpable hernias were repaired, and by that definition most of the hernias diagnosed in this study were insignificant. A 5-year follow-up is pending, which may reveal further information on the clinical course in these patients.

It is possible that the manipulation of the abdominal fascia during mesh suture and traction in the VAWCM method, increases the incidence of incisional hernia. Further studies are required to evaluate whether other TAC methods result in lower hernia incidences. Delayed primary fascial closure rate would have to be taken into consideration, as well as skin complications, where traction is applied to abdominal wall instead of fascia.

A radical solution would be to close all open abdomens with a mesh. In fact, even conventional (non-OA) laparotomies, at least in high-risk patients, might benefit from routine mesh closure, considering the high incidence of incisional hernias found with ultrasound or CT^{154,155}.

Parastomal hernias

In paper II, parastomal hernia was defined as proposed by Moreno-Matias¹¹⁰. These criteria include hernias found only on CT, allowing for more hernias to be diagnosed than with clinical examination only. On the other hand, clinical investigation was not performed during Valsalva maneuver, nor was the CT performed in a prone position, as suggested by Jänes^{156,157}, maneuvers that perhaps had resulted in even higher incidence of parastomal hernia.

The incidence of parastomal hernia one year after OA therapy was almost as high as that of incisional hernia (58 %). Unlike the ventral hernias, however, most were clinically detectable (15 of 18) and half (9 of 18) were symptomatic.

No other study could be found where parastomal hernia after OA therapy was investigated. Recent studies on parastomal hernias after non-OA surgery indicate that the incidence might be higher than previously reported. In a study by Moreno-Matias et al.¹¹⁰, where patients were examined clinically and with a CT scan, the incidence was 60 %. In another study by the same authors, the incidence was 41 % on clinical examination and 52 % according to CT scans¹⁵⁸. Jänes et al. found an incidence of 50 % after 1 year and 81 % after 5 years, using clinical examination

during a Valsalva maneuver¹⁵⁶. A small study by Cingi et al. showed an incidence of 52 % with clinical examination and 78 % with CT¹⁵⁹.

Concomitant incisional hernia was present in most of the patients with a parastomal hernia (15 of 18). A literature search revealed no reports on such association. One possible explanation is that there is a common risk factor, affecting both parastomal and incisional hernias. However, the parastomal hernia incidence in the VAWCM study is comparable to that seen in other studies, suggesting that OA therapy does not increase the risk of parastomal hernias, only incisional hernias.

Other techniques combining vacuum and traction

Other methods have been described, utilizing the same principles as VAWCM, i.e. combining vacuum therapy and fascial traction, showing high fascial closure rates as well.

In 2006, Cothren et al described 100 % fascial closure rate in 14 trauma patients⁹¹. Multiple white V.A.C.® sponges were placed intra-abdominally instead of the visceral protective layer (Figure 39). Despite the absence of a pressure isolating barrier, no enteric fistulas were reported in this small study.

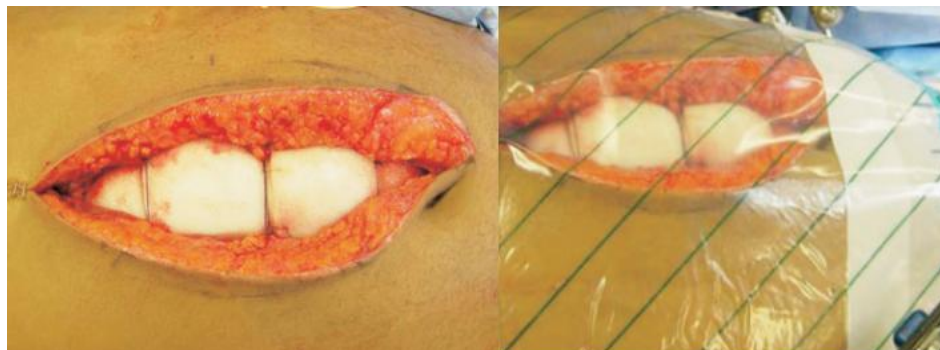


Figure 39. Modified V.A.C.® with retention sutures and white sponges instead of visceral protective layer (Cothren et al. ⁹¹ © Elsevier, reproduced with permission).

In 2009, Koss et al described 100 % fascial closure rate in 17 trauma patients using “ties and VAC”(Figure 40)¹⁶⁰. Fascial traction was achieved with interrupted retention sutures.

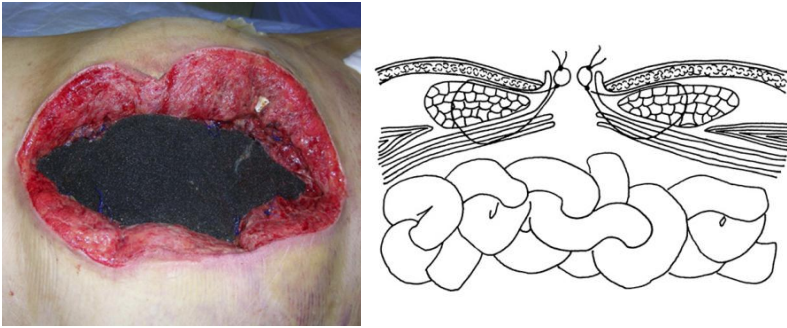


Figure 40. V.A.C.® with retention sutures (Koss et al.¹⁶⁰ © Elsevier, reproduced with permission)

In 2012, Kafka-Ritsch described 87 % fascial closure rate in 160 patients, mostly peritonitis, using VAWC and interrupted, dynamic retention sutures (Figure 41)⁹⁷.

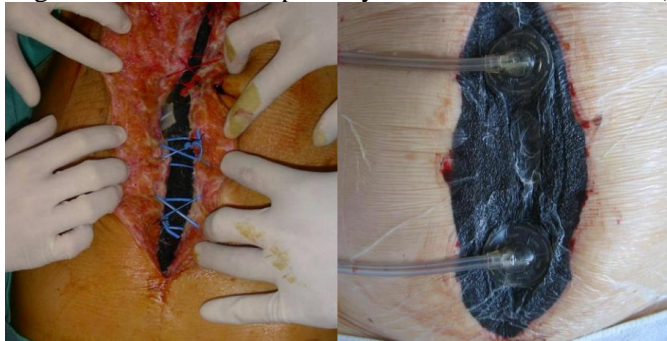


Figure 41. V.A.C.® with retention sutures (Kafka-Ritsch et al.⁹⁷ © Springer, reproduced with permission).

Abdominal Re-approximation Anchor System (ABRA™) is a commercially available device based on dynamic retention sutures through the abdominal wall (Figure 42). In 2011, Verdam described 88 % closure rate in 16 surviving patients with peritonitis⁹⁸ and in 2013, Haddock described 83 % closure rate in 36 patients with mixed abdominal pathology¹⁴⁴. Both studies combined ABRA™ with V.A.C.®

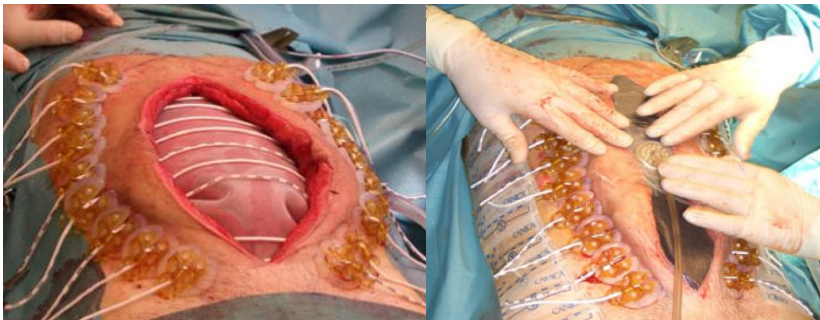


Figure 42. ABRA™ in combination with V.A.C.® (Verdam et al.⁹⁸ © Springer, reproduced with permission).

One problem with ABRA™ is the risk of pressure sores in the skin and/or fascia, which occurred in 66 % in the study by Verdam (Figure 43). All healed eventually, but with remaining scars. Another issue is the high cost of the device, in addition to the cost of VAWC.



Figure 43. Pressure sores after ABRA™ therapy (Verdam et al.⁹⁸ © Springer, reproduced with permission).

Trans-abdominal wall traction (TAWT™) is another commercially available device which is designed as a modification of the Wittmann Patch™ (Figure 44). In 2013, Dennis et al. achieved fascial closure in 32 trauma patients using the device (with mesh reinforcement in all patients). Potential drawbacks include risk of skin complications, as well as increased cost.

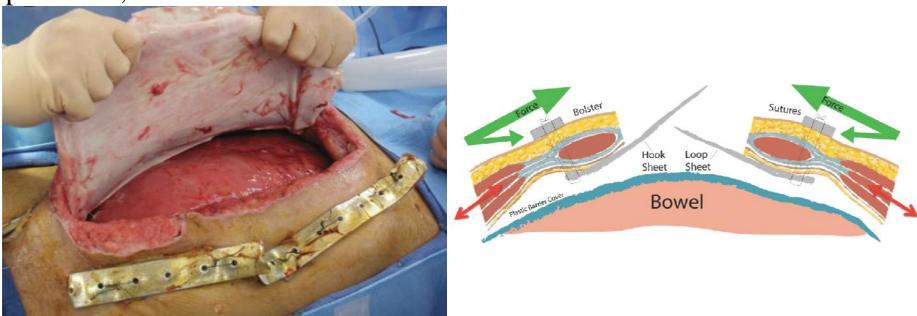


Figure 44. TAWT™ (Dennis et al. © Lippincott, Williams & Wilkins, reproduced with permission)

Increasing use of VAWCM

We decided to use a commercial VAWC kit instead of a home-made vacuum pack despite higher cost, due to the safety of calibrated negative pressure, beneficial effects on wound granulation and ease of use. By using a mesh for fascial traction, forces are evenly distributed throughout the whole length of the fascia, avoiding the need for coarse retention sutures and the risk of damage from individual sutures. A generic polypropylene mesh has the advantage of being fully permeable for fluid

and is less expensive than commercially available traction devices. Applying traction through the abdominal wall has the advantage of not manipulating the fascia, but with a high risk of pressure sores and poor cosmetic results. Long-term follow-up is needed to reveal whether the devices cause fascial damage resulting in incisional hernias in the long run.

Five clinical studies on VAWCM therapy have been published, including the previously described pilot study and prospective multicenter study (Table 31). To date, only Scandinavian studies have been published.

Table 31. Studies on OA therapy using VAWCM

Author	Year	Study period	Number of patients	Median age	Non-trauma patients (%)	OA duration (days)	Fascial closure (survivors)	In-hospital mortality
Petersson ¹⁰⁴	2007	2005	7	65	86	32	100	14
Seternes ⁹³	2010	2006-09	9	70	100	10	100	33
Acosta ⁹⁰	2011	2006-09	111	68	92	14	89	30
Rasilainen ⁹²	2012	2008-11	50	60	100	9	93	38
Kleif ¹⁶¹	2012	2009-11	16	66	100	9	50	19

In the last study¹⁶¹, VAWCM was initiated if fascial closure with VAWC alone was unsuccessful, whereas in the other studies VAWCM was used from start.

Open abdomen classification

The OA classification is based on very large combined clinical experience of the members of the WSACS consensus group. Nonetheless, a methodological evaluation is necessary for a new classification to reach full scientific credibility.

The results from paper III support the continued use of the OA classification system by WSACS. We hope that our instructions for use will be of benefit for the application of the classification in clinical practice in the future and that these will lead to a more uniform interpretation of the classification and higher inter- and intra-rater reliability.

We also suggest that the definition of grade 4 includes enteroatmospheric fistulas in a non-frozen abdomen, since with modern OA management, such as VAWCM, fistulas may be treated without the development of a frozen abdomen in all cases.

The severity of OA grades in a patient cohort should not be confused with the severity of underlying disease. The classification system is designed to monitor the progress of OA management and the complexity of the OA state, not the medical precondition of the patients treated. If patients remain in low OA grades, it represents successful OA management. On the other hand, in referral hospitals, complex initial OA grades may indicate that difficult OA management is at hand.

Methodological issues

A double blind, randomized controlled study is the highpoint of clinical research, irresistible to any editor of a scientific journal. Unfortunately, controlled studies in the life-threatening, emergency settings of OA therapy are extremely complicated to perform.

Absence of control group

After seeing the results of the pilot study, it was considered important to evaluate the safety and efficacy of the VAWCM method in a larger cohort. A controlled study, comparing it with previously used TAC methods, was not considered feasible due to long inclusion period to reach adequate number of patients in each group. It was decided to perform a prospective cohort study instead with four hospitals participating. A controlled study would add methodological strength and was considered. During the early stages of planning, a control group was selected, consisting of patients undergoing elective midline laparotomy for aortic aneurysm repair or colorectal surgery. However, this study design was abandoned when it became apparent that a large control group would be needed, and that the comparison would only be applicable for the evaluation of late incisional hernias while other comparisons would be clinically irrelevant.

Retrospective analysis

The OA classification by WSACS had not been published when the VAWCM study was initiated in 2006. Consequently, OA classification was not present in the study protocol, nor were the operating surgeons aware of which information relevant to the future OA classification system, should be included in the operative report. To avoid this weakness in future studies, prospective registration is recommended, with OA grade registered in connection with each surgical procedure.

Type II statistical error

Falsely accepting a null-hypothesis (i.e. $p\text{-value} > 0.05$) when there in reality exists a difference between groups, is called a type II statistical error (or that the study is underpowered). This may occur when results of a clinical study involve few individuals in one or more groups, for example with rare disorders or rare complications and/or when too few patients are included in the study.

Even though the VAWCM study is one of the largest existing studies on OA therapy, relatively few individuals developed adverse outcome, such as failure of fascial closure and intestinal fistulas. When these subgroups were compared with possible risk factors, some of the groups consisted of only a few patients. This resulted in lack of statistical significance regardless of possible associations. It might very well be that additional risk factors had been identified, if more patients had been included in the study or if complications had been more common. As an example, obesity, a well-known risk factor for incisional hernia¹³⁴, was not found significantly associated with incisional hernia in paper II ($p=0.076$).

Intention-to-treat analysis

In an intention-to-treat (ITT) analysis, results are analyzed according to the initial treatment assignment instead of the actual received treatment. It is considered the most appropriate methodology in randomized clinical studies, and is designed to avoid the effects of problems such as patient drop-out or cross-over.

There are potential weaknesses with the application of ITT analysis, such as the interpretation of missing data – in this case, death before fascial closure. According to an ITT analysis, patients who died before fascial closure are regarded as failure of fascial closure. Unless there is a causal relationship between mortality and non-closable abdomen (i.e. those patients who died would have had failure of fascial closure), this does not correctly represent fascial closure rate and the interpretation of risk factors would be misinterpreted. In the ITT analysis, 16 out of 26 (62 %) failures of fascial closure were due to non-OA-related death (Table 26). Consequently, failure of fascial closure was erroneously found to be a risk factor for mortality. In paper I, this was compensated for by also performing a per-protocol analysis of fascial closure (including only surviving patients).

Lessons learned from experience in open abdomen therapy

Fascial traction

Initially, we were concerned about excessive fascial traction which would lead to raised intra-abdominal pressure (IAP). IAP was monitored closely, even intra-operatively. It was found that moderate traction, i.e. up to a level where the mesh halves could be sutured together comfortably, did not lead to increased IAP. Intra-operative IAP monitoring was cumbersome and was later abandoned.

Tearing of the mesh from the fascia occurred occasionally and was then re-sutured. Perhaps this was due to excessive traction or to patient factors, such as coughing or infection. Whether such fascial tearing inflicts fascial damage increasing the risk of subsequent incisional hernia, remains to be determined.

Fascial closure

In practice, fascial closure after OA therapy is no longer an issue of great concern at our institution. All patients in need of OA therapy are treated without hesitation and when an open abdomen is no longer necessary, it can almost always be closed.

It is crucial that VAWCM is applied in an optimal way from the start, preparing for fascial closure at the end of OA therapy. The visceral protective layer must be carefully applied at each dressing change, tucked underneath the abdominal wall as far as possible in all directions, adjusting for stomas and the falciform ligament. Otherwise, adhesions may have formed already at the next dressing change operation, which may be impossible to release.

A learning curve was observed, with OA duration becoming shorter in the latter part of the study period as experience increased among surgeons involved in OA management.

Mesh closure

If no progress is made towards fascial closure at two or three dressing change operations, a frozen abdomen is developing and further attempts for fascial traction will probably be unsuccessful. At this point, it is necessary to find another way of abdominal closure. We prefer to use the same technique as we use for elective hernia repair, i.e. a polypropylene or polyvinyl mesh in a sublay (retro-muscular) position. If the retro-rectus space is inaccessible, intra-peritoneal (IPOM) or onlay mesh may be used. In case of fascial- or skin necrosis, subcutaneous VAWC therapy may be continued after the mesh reconstruction and the skin closed at a later time.

Skin closure

It is important to prepare for skin closure, as well as fascial closure. The skin and subcutaneous tissue should not be allowed to retract laterally or be pulled down towards the fascia. As the fascial edges are brought closer together, the polyurethane sponges should gradually be made smaller, pulling the skin together. Surgical release of retracted skin or revision of necrotic areas should be performed in good time before closure.

Stomas in the open abdomen

It has been suggested that stomas should be avoided in the OA if possible, or at least placed far laterally, away from the OA¹²⁶. In our experience, this was not a major problem. Stomas were created on a clinical indication and placed in a standard position through the rectus muscle, without consideration for the upcoming OA therapy. It is essential to cover the skin bridge between the stoma and the wound edge with a strip of adhesive gel (V.A.C.® gel) to prevent loosening of the stoma bag and stools contaminating the wound.

Bowel ischemia

Patients with bowel ischemia were at the highest risk of developing enteroatmospheric fistulas. Perhaps fistula incidence might have been reduced if more extensive bowel resection had been performed or if diverting stomas had been used more frequently. The mortality rate might not have decreased though, owing to short bowel syndrome associated with high output stomas¹⁶².

Ossification of the wound

If grown large enough, ossification will interfere with fascial closure. In two patients, we closed the fascia below the ossified area and planned for abdominal wall reconstruction at a later time. In retrospect, it is possible that this could have been avoided. If ossification is detected early, simple resection is probably possible in most cases, and if necessary, the abdomen can be closed with an immediate mesh reconstruction.

Open abdomen classification

We found that retrospective registration of OA grades from operative reports was time-consuming as well as unreliable. If the classification system is to be used, it is essential that OA grade is prospectively registered at each dressing change operation. We propose the use of a flow chart (see under methods) which we found helpful.

If the soldier had to confine himself to one chemical product, it might well be vaseline which can lubricate his rifle, soften his boots, smarten his hair on parade, cure his constipation, and, if need be, heal his wounds.

– *Sir William Heneage Ogilvie in an article from 1940 on abdominal war wounds, containing the first modern description of open abdomen therapy (using vaseline gauzes)*⁷.

Conclusions

- The VAWCM method provided a high fascial closure rate after long-term OA treatment in mostly elderly, non-trauma patients. Most patients remained in a low OA grade. Technique-related complications were few. Incidence of intestinal fistulas was comparable to other studies.
- Incisional hernia incidence 1 year after OA therapy with VAWCM was high. Most hernias were small and asymptomatic, with few requiring surgical repair during the first year, unlike the giant planned ventral hernias of the past.
- The validity and reliability analysis of the OA classification system by WSACS showed that each patient's most complex OA grade, worsening of OA grade without later improvement, as well as development of grade C (enteric leak) or grade 4 (EAF) were found to be associated with worse clinical outcome (failure of fascial closure and mortality). Every effort should be made to prevent patients from ascending to a more complex OA grade, to try to repair enteric leaks and to avoid enteroatmospheric fistulas.
- Negative pressure reaching the bowel during VAWC therapy with the ABThera™ system was limited, regardless of negative pressure setting. Reduced therapy pressure does not lead to reduced pressure at the bowel surface. The system drains the abdominal cavity completely of fluid. Paraffin gauzes are of limited value as a means of pressure isolation at the bowel surface.

The abdominal wound is but partially closed by sutures. The edges are not closely approximated but are generally partially drawn together by two or three silkworm-gut sutures between which and the intestines is placed a compress of gauze. A wound which gaps somewhat affords freer exit for the escape of the peritoneal secretions.

– *Andrew J. McCosh in an article from 1897 on the treatment of general septic peritonitis*¹⁶³.

Future perspectives

With improved temporary abdominal closure techniques such as VAWCM, abdominal closure is now possible in most patients when OA therapy is ended. This does not mean that OA therapy should not be taken seriously. On the other hand, when OA therapy is indicated, the decision can be taken without hesitation and without concerns for having to spend the weeks or months trying to heal a frozen abdomen. Perhaps the decision to initiate OA therapy based on relative indications, such as planned reoperation and wound dehiscence will be easier to make.

Most studies show that both vacuum and traction is needed for optimum OA management. VAWCM is simple to use with a short learning curve and is relatively inexpensive compared to other methods, especially compared to a frozen abdomen. For complicated open abdomens needing more than one second look operation, VAWCM is an ideal method. More and more surgeons are now using this method to manage open abdomens.

Further studies, comparing different TAC methods, are needed to reveal whether fascial manipulation and traction is the cause of the high incidence of incisional hernias. It might well be the OA therapy in itself, combined with underlying disease that is causing the increased risk. Additional studies on hernia incidence after conventional laparotomies, using CT diagnosis, are also needed for fair comparison.

A five-year follow up of our patients is pending, where the long term hernia incidence will be determined based on clinical examination. The study will also show how many of the hernias currently seen only on CT will become symptomatic and palpable over time.

Perhaps the high incisional hernia rate should be considered unacceptable. One possible solution is to close all open abdomens with a permanent mesh. A variation of this strategy has been applied in several patients (not included in the studies in this thesis) with promising early results. Early in the OA period, a permanent mesh is placed in the retro-muscular space on each side, as would have been done in an elective repair. This mesh is then used for fascial traction during OA therapy. Excess mesh is excised as the fascial edges are brought closer together. When appropriate, the mesh edges and preferably the fascial edges as well, are sutured together in the midline using a non-absorbable suture. An evaluation of the outcome in these patients is pending.

The medical attendant is reduced to the choice of either abandoning his patient to certain death, or of resorting to laparotomy for the possibility, faint though it may be, which it alone holds out for relief and recovery.

– *Lewis S. Pilcher in an article from 1886 on the indications on laparotomy in cases of intestinal obstruction*¹⁶⁴.

Populärvetenskaplig sammanfattning

År 2005 opererades en 65-årig man i Malmö för ett bråck på stora kroppspulsådern. Det var en lång och komplicerad operation med stor blodförlust. Massiv blodöverföring och stora mängder vätska samt blodtryckshöjande mediciner måste tillföras under och efter operationen. Under det efterföljande dygnet steg trycket i bukhålan till en nivå då blodcirkulationen till njurarna och bukorganen påverkades med risk för bestående skador. I en sådan situation måste man åstadkomma en minskning av buktrycket och detta görs effektivast genom en ny operation där den ihop sydda bukväggen öppnas igen, vätska och blod avlägsnas ur bukhålan som sedan lämnas öppen, d.v.s. att bukväggen och såret inte sys ihop efter avslutad operation. På detta sätt åstadkommer man en maximal sänkning av trycket på organen. Detta gjordes i vår patients fall med syfte att, så snart svullnaden efter blödningen lagt sig, operera honom igen för att sy ihop bukväggen. Förutom blödning och svullnad kan det finnas andra orsaker som gör att man väljer att behandla med öppen buk (ÖB) under en viss tid. En kraftig infektion i bukhålan som behöver rensas upp eller blodcirkulationsstörning i tarmarna, som ofta kräver ytterligare operation inom något dygn, är andra exempel på orsaker till ÖB-behandling. Behandlingen kan vara livräddande men innebär också många svårigheter och risk för komplikationer.

Under tiden buken är öppen måste de blottade tarmarna skyddas för att förhindra skador, som i värsta fall kan leda till att det går hål på tarmen och en s.k. tarmfistel, en fruktad och i dessa situationer inte sällan dödlig komplikation, uppstår. En annan svårighet är att det ofta rinner stora mängder vävnadsvätska från det öppna buksåret, som leder till vätskeförluster och behov av täta förbandsbyten, vilket är krävande för både patient och personal. Bukmuskulerna drar isär sårkanterna och detta, tillsammans med bildning av sammanväxningar mellan bukväggens insida och tarmarna, gör att det i många fall inte är möjligt att sy ihop bukväggen igen trots att det akuta tillståndet är över. Resultatet blir då till slut ett stort invalidiserande bukväggsbråck, d.v.s. ett område med hudbeklädda tarmar utan täckande bukvägg, något som kräver en omfattande operation för att reparera i ett senare skede.

De senaste åren har behandling med ÖB blivit allt vanligare. Överlevnad hos svårt sjuka patienter har ökat men samtidigt har problemen som följer med behandlingen blivit synligare. Genom att bandagera såret med ett tarmskyddande lufttätt plastförband kopplat till en pump för skapande av ett reglerbart undertryck, minskar risken för tarmskador och chansen att kunna sy ihop buken igen ökar, samtidigt som sårvärden förenklas. I tidigare mestadels nordamerikanska studier med denna metod, ingick till

överbäggande delen unga och för övrigt friska patienter som utsatts för skador och bara behövde en kortare tids behandling med ÖB. I Sverige är patienterna istället oftast äldre, med flera andra försvärande sjukdomar, som därmed ofta drabbas av ett komplicerat sjukdomsförlopp som kräver lång tids behandling. Vi upplevde tidigare att många av våra patienter inte gick att stänga buken på, trots användande av undertrycksbehandlingen som varit framgångsrik i de amerikanska rapporterna.

Just på detta sätt var det i vår patients fall. För att förbättra möjligheten till bukstängning arbetade vi fram en omläggningsteknik som kombinerar behandling med ett speciellt avpassat undertrycksförband med måttligt drag i bukväggskanterna genom ett insytt nät. Nätet är genomsläppligt för vätska som fortsatt kan dräneras genom förbandet, samtidigt som det motverkar att bukväggskanterna dras åt sidorna. När svullnaden i buken lagt sig kan kanterna successivt dras samman för att slutligen sys ihop, efter att nätet tagits bort. Vår patient ovan var den förste som detta prövades på, med stor framgång då bukväggen kunde sys ihop efter 14 dagars behandling. Det lyckade resultatet blev startskottet för de studier som ingår i denna avhandling.

Studie I och II i avhandlingen gick ut på att bedöma behandlingsresultaten och möjliga komplikationer till metoden. På fyra sjukhus i Sverige behandlades 111 patienter med metoden under åren 2006 till 2009. Patienterna var gamla (median ålder 68 år) och svårt sjuka (nästan en tredjedel avled på sjukhuset) och behövde lång tids behandling med öppen buk (mediantid 2 veckor). Fem procent av patienterna utvecklade hål på tarmen, s.k. tarmfistel, vilket är jämförbart med andra studier. Komplikationer som direkt bedöms bero på tekniken var få. Bukväggen kunde sys ihop i en större andel av patienterna än vad som tidigare rapporterats. Av de som överlevde kunde bukväggen sys ihop hos 89 % och stängas med hjälp av förstärkande nät hos ytterligare 9 %. Hos två patienter kunde bukväggen enbart delvis förslutas pga. brosk-bildning i såret och en av dessa patienter behövde opereras senare för ett bukväggsbräck. Efter ett år undersöktes patienterna på mottagningen samt med en datortomografi-undersökning (DT) av buken och bukväggen för bedömning av hur många bukväggs-bräck som uppkommit hos de 70 patienter som då fortfarande var i livet. Totalt kunde, i de flesta fallen små och symtomlösa bräck, påvisas hos 66 % av patienterna. Hade uppföljningen istället inskränkt sig till en fråga till patienterna om förekomst av en symptomgivande svullnad i snittet hade bräckfrekvensen fallit till 19 %. Resultaten visar: att tekniken är användbar även i situationer med äldre, svårt sjuka patienter; att risken för att skada tarmen är låg; att chansen är god att kunna sy ihop bukväggen; att det är vanligt med mindre men oftast symtomlösa bukväggsbräck efter ett år; och att det går att helt undvika de stora invalidiserande bukväggsbräcken vi tidigare hade sett.

I studie III utvärderades ett klassificeringssystem för ÖB, vars användande är av vikt för att kunna analysera och jämföra resultat av olika behandlingsmetoder. Klassificeringssystemet introducerades för några år sedan men har inte tidigare utvärderats vetenskapligt. Resultaten visade att systemets klassificeringsgrader, som avser att beskriva hur komplicerat tillståndet i den ÖB är, svarade väl mot behandlingsresultaten, den s.k. validiteten var hög. I vilken

utsträckning olika användare gjorde liknande gradering enligt systemet samt hur samma användare graderade vid två olika tillfällen, den s.k. reliabiliteten för klassifikationssystemet testades också och befanns vara god.

Studie IV var en djurexperimentell studie där sex nedsövda grisar opererades och ÖB-förband anlades på samma sätt som vid behandling av våra patienter. Studiens syfte var att besvara tre frågor av vikt för säkerheten med användande av undertryck vid ÖB-behandling. En misstanke om att antalet tarmfistlar hade ökat med ökat användande av undertryck i samband med ÖB-behandling hade rapporterats i litteraturer. En förutsättning för att undertrycket skulle kunna vara förklaringen är att detta sprider sig genom förbandet till tarmen och där åstadkommer en sugorsakad skada. Den första delen av studien var att mäta undertrycket på olika lokaler i bukhålan under pågående undertrycksbehandling. Den andra delen av försöket gick ut på att mäta hur väl undertrycksförbandet avlägsnade vätska från bukhålan, en fråga som var viktig eftersom kvarvarande vätskerester kan bli infekterade och leda till varansamlingar och blodförgiftning. Den tredje frågan vi önskade besvara var om det fanns någon annan möjlighet att skydda tarmar och annan känslig vävnad från undertrycket än användande av det skyddande plastförband som vanligtvis läggs mellan tryckkällan och bukhålan. I vissa situationer, t.ex. om sammanväxningar mellan tarmar och bukväggens insida gjort att bukhålan inte längre är tillgänglig, så är det inte möjligt att applicera detta förband, men undertrycksbehandling kan ändå vara önskvärd att fortsätta. Det har föreslagits att vaselinindränkta kompresser, placerade mellan tryckkällan och den vävnad man önskar skydda, möjligen skulle kunna fungera genom att reducera undertrycket som verkar direkt på vävnaden. Resultaten av studiens olika delar visar: att undertrycket vid tarmytan var lågt och risken för sugskador på tarmen bedöms, som en följd av detta, vara liten; all vätska som finns i bukhålan sugs ut genom förbandet, vilket rimligen minskar risken för infektioner i bukhålan; att vaselinkompresser i flera lager inte förmår minska undertrycket från förbandet till underliggande vävnader, och den skyddande effekt av vaselinkompresser, som vi har noterat kliniskt, uppnås genom annan mekanism än minskat undertryck.

Sammanfattningsvis har vi i denna avhandling: undersökt behandlingsresultaten på kort och längre sikt av en ny behandlingsmetod för ÖB-behandling, som kombinerar undertrycksbehandling med nät-förmedlat drag i bukväggskanterna; utvärderat ett klassificeringssystem av vikt för framtida forskning om ÖB; samt klarlagt ett antal frågor rörande säkerheten vid användande av undertrycksbehandling vid ÖB.

Som nästa steg i vår forskning rörande ÖB-behandling väntar 5-årsuppföljning av våra studiepatienter, för utvärdering av bukväggsfunktion och livskvalitet. En förändring från användande av ett tillfälligt nät för drag i bukväggskanterna till förmån för ett permanent nät, som kan användas som förstärkning när buken sys ihop vid avslutningen av ÖB-behandlingen, är en spännande vidareutvecklingsmöjlighet. Detta skulle sannolikt undanröja problemen med de sena bukväggsbräcken men behöver studeras noga ur säkerhetssynpunkt.

There will always be connected with laparotomy the inherited dread of opening that ominous peritoneal cavity.

– *Christian Fenger in an article from 1885 on the treatment of chronic peri-uterine abscesses by means of laparotomy*¹⁶⁵.

Acknowledgements

I would like to express my sincere gratitude and appreciation to all who have supported me during the years it has taken to complete this thesis. In particular I would like to thank:

- My supervisors, Agneta Montgomery, Ulf Petersson and Stefan Acosta.
- My co-authors Martin Björck, Birger Pålsson, Anders Wanhainen, Mats Svensson, Khatereh Djavani, Olle Ekberg, Sandra Lindstedt and Joanna Hlebowicz, as well as statistician Jan-Åke Nilsson.
- Professors Bengt Jeppsson and Henrik Thorlacius at Skåne University Hospital.
- My colleagues at Skåne University Hospital.
- My friends and family.
- My beloved Annah and Isak.

Without financial support, this thesis would not exist. I would like to express my gratitude for received grants from the following institutions:

- Region of Skåne research grant received from the Medical Faculty, Lund University (ALF).
- The Einar and Inga Nilsson foundation for surgical research at the Department of Surgery in Malmö.
- Skåne county council's research and development foundation (FoU).
- Anders Borgströms fellowship, Skåne University Hospital, Malmö.
- KCI Inc. for an unrestricted (unconditional) research grant received in 2008.
- The Maggie Stephens foundation for medical research.

An open abdomen is a double-edged sword.

– *Thordur Bjarnason, this thesis.*

References

1. Richardson JD. Changes in the management of injuries to the liver and spleen. *J Am Coll Surg* 2005;200:648-69.
2. Halsted W. Ligature and suture material. The employment of fine silk in preference to catgut and the advantages of transfixing tissues and vessels in controlling hemorrhage. Also an account of the introduction of gloves, gutta-percha tissue and silver foil. *Journal of the American Medical Association* 1913;60:1119-26.
3. Kusnetzoff K, Pensky J. Etudes cliniques et experimentales sur la chirurgie du foie. *Revue Chirurgia* 1896;16:954-92.
4. Kusnetzoff K, Pensky J. Sur la resection partielle du foie. *Revue Chirurgia* 1896;16:501-21.
5. Schroeder W. The process of liver hemostasis: reports of cases. *Surgery, Gynecology & Obstetrics* 1906;2:52.
6. Pringle JH. V. Notes on the Arrest of Hepatic Hemorrhage Due to Trauma. *Ann Surg* 1908;48:541-9.
7. Ogilvie WH. The late complications of abdominal war wounds. *The Lancet* 1940;2:253-6.
8. Lucas CE, Ledgerwood AM. Prospective evaluation of hemostatic techniques for liver injuries. *J Trauma* 1976;16:442-51.
9. Calne RY, McMaster P, Pentlow BD. The treatment of major liver trauma by primary packing with transfer of the patient for definitive treatment. *Br J Surg* 1979;66:338-9.
10. Feliciano DV, Mattox KL, Jordan GL, Jr. Intra-abdominal packing for control of hepatic hemorrhage: a reappraisal. *J Trauma* 1981;21:285-90.
11. Stone HH, Strom PR, Mullins RJ. Management of the major coagulopathy with onset during laparotomy. *Ann Surg* 1983;197:532-5.
12. Rotondo MF, Schwab CW, McGonigal MD, et al. 'Damage control': an approach for improved survival in exsanguinating penetrating abdominal injury. *J Trauma* 1993;35:375-82; discussion 82-3.
13. Anderson ED, Mandelbaum DM, Ellison EC, Carey LC, Cooperman M. Open packing of the peritoneal cavity in generalized bacterial peritonitis. *Am J Surg* 1983;145:131-5.
14. Duff. Abdominal sepsis managed by leaving abdomen open. *Surgery* 1981.
15. Steinberg D. On leaving the peritoneal cavity open in acute generalized suppurative peritonitis. *Am J Surg* 1979;137:216-20.

16. Pujol JP. La non fermeture des incisions abdominales d'urgence. Techniques et résultats. Doctoral dissertation. . Paris: University of Pierre and Marie Curie, Sorbonne University; 1975.
17. Lundgren F, Broomé A. [Severe Peritonitis - Open Abdomen]. Swedish. Svensk Kirurgi [Journal of the Swedish Surgical Society] 1977;35:143.
18. Broome A, Hansson L, Lundgren F, Smedberg S. Open treatment of abdominal septic catastrophies. World J Surg 1983;7:792-6.
19. Hudspeth AS. Radical surgical debridement in the treatment of advanced generalised peritonitis. Archives of surgery 1974;110:1233-36.
20. Wendt E. Über den Einfluß des intraabdominalen Druckes auf die Absonderungsgeschwindigkeit des Harnes. Archiv der Physiologische Heilkunde 1876;17:527-46.
21. Emerson H. Intra-abdominal pressures. Archives of internal medicine 1911;7:754-84.
22. Schein M. Abdominal Compartment Syndrome: Historical Background. . In: Ivatury R, ed. Abdominal Compartment Syndrome. Georgetown, Texas: Landes Biosciences; 2006:1-7.
23. Baggot MG. Abdominal blow-out: a concept. Current researches in anesthesia & analgesia 1951;30:295-9.
24. Baggot MG. Herniation as exemplified by abdominal wound dehiscence; varieties, etiology, and management: a personal account. Irish medical journal 1978;71:54-7.
25. Kron IL, Harman PK, Nolan SP. The measurement of intra-abdominal pressure as a criterion for abdominal re-exploration. Ann Surg 1984;199:28-30.
26. Fietsam R, Jr., Villalba M, Glover JL, Clark K. Intra-abdominal compartment syndrome as a complication of ruptured abdominal aortic aneurysm repair. Am Surg 1989;55:396-402.
27. Gross RE. A new method for surgical treatment of large omphaloceles. Surgery 1948;24:277-92.
28. Ledbetter DJ. Congenital abdominal wall defects and reconstruction in pediatric surgery: gastroschisis and omphalocele. The Surgical clinics of North America 2012;92:713-27, x.
29. Schein M. Surgical management of intra-abdominal infection: is there any evidence? Langenbecks Arch Surg 2002;387:1-7.
30. Johnson JW, Gracias VH, Schwab CW, et al. Evolution in damage control for exsanguinating penetrating abdominal injury. J Trauma 2001;51:261-9; discussion 9-71.
31. Hoey BA, Schwab CW. Damage control surgery. Scandinavian journal of surgery : SJS : official organ for the Finnish Surgical Society and the Scandinavian Surgical Society 2002;91:92-103.
32. Mattox KL. Introduction, background, and future projections of damage control surgery. The Surgical clinics of North America 1997;77:753-9.
33. Cheatham ML, Malbrain ML, Kirkpatrick A, et al. Results from the International Conference of Experts on Intra-abdominal Hypertension and Abdominal Compartment Syndrome. II. Recommendations. Intensive Care Med 2007;33:951-62.

34. Kirkpatrick AW, Roberts DJ, De Waele J, et al. Intra-abdominal hypertension and the abdominal compartment syndrome: updated consensus definitions and clinical practice guidelines from the World Society of the Abdominal Compartment Syndrome. *Intensive Care Med* 2013;39:1190-206.
35. Malbrain ML, Cheatham ML, Kirkpatrick A, et al. Results from the International Conference of Experts on Intra-abdominal Hypertension and Abdominal Compartment Syndrome. I. Definitions. *Intensive Care Med* 2006;32:1722-32.
36. Miller PR, Thompson JT, Faler BJ, Meredith JW, Chang MC. Late fascial closure in lieu of ventral hernia: the next step in open abdomen management. *J Trauma* 2002;53:843-9.
37. Ortega-Deballon P, Radais F, Facy O. Aeroportia and acute abdominal pain: ischemic bowel necrosis. *Clinical Journal of Gastroenterology* 2008;1:157-9.
38. Wittmann DH, Schein M, Condon RE. Management of secondary peritonitis. *Ann Surg* 1996;224:10-8.
39. Bjorck M. Management of the tense abdomen or difficult abdominal closure after operation for ruptured abdominal aortic aneurysms. *Seminars in vascular surgery* 2012;25:35-8.
40. Bjorck M, Wanhainen A, Djavani K, Acosta S. The clinical importance of monitoring intra-abdominal pressure after ruptured abdominal aortic aneurysm repair. *Scandinavian journal of surgery : SJS : official organ for the Finnish Surgical Society and the Scandinavian Surgical Society* 2008;97:183-90.
41. Acosta S, Bjorck M. Modern treatment of acute mesenteric ischaemia. *Br J Surg* 2013; Nov 20. DOI 10.1002/bjs.9330.
42. Subramonia S, Pankhurst S, Rowlands BJ, Lobo DN. Vacuum-assisted closure of postoperative abdominal wounds: a prospective study. *World J Surg* 2009;33:931-7.
43. Malbrain ML, De laet IE, De Waele JJ. IAH/ACS: the rationale for surveillance. *World J Surg* 2009;33:1110-5.
44. Markell KW, Renz EM, White CE, et al. Abdominal complications after severe burns. *J Am Coll Surg* 2009;208:940-7; discussion 7-9.
45. Cheatham ML. Abdominal compartment syndrome: pathophysiology and definitions. *Scand J Trauma Resusc Emerg Med* 2009;17:10.
46. Cheatham ML. Abdominal compartment syndrome. *Curr Opin Crit Care* 2009;15:154-62.
47. Cheatham ML. Nonoperative management of intraabdominal hypertension and abdominal compartment syndrome. *World J Surg* 2009;33:1116-22.
48. De Waele JJ, De Laet I, Kirkpatrick AW, Hoste E. Intra-abdominal Hypertension and Abdominal Compartment Syndrome. *Am J Kidney Dis* 2011;57:159-69.
49. Dambrauskas. Interventional and surgical management of abdominal compartment syndrome in severe acute pancreatitis. *Lokal litauisk tidskrift* 2010.
50. Leppaniemi A, Hienonen P, Mentula P, Kempainen E. Subcutaneous linea alba fasciotomy, does it really work? *Am Surg* 2011;77:99-102.

51. Cheatham ML, Safcsak K. Is the evolving management of intra-abdominal hypertension and abdominal compartment syndrome improving survival?*. *Crit Care Med* 2010;38:402-7.
52. Cheatham ML, Demetriades D, Fabian TC, et al. Prospective study examining clinical outcomes associated with a negative pressure wound therapy system and Barker's vacuum packing technique. *World J Surg* 2013;37:2018-30.
53. Orgill DP, Manders EK, Sumpio BE, et al. The mechanisms of action of vacuum assisted closure: more to learn. *Surgery* 2009;146:40-51.
54. Tottrup A. Foley catheter enterostomy for postoperative bowel perforation: an effective source control. *World J Surg* 2010;34:2752-4.
55. Ivatury RR. Update on open abdomen management: achievements and challenges. *World J Surg* 2009;33:1150-3.
56. De Waele JJ, Leppaniemi AK. Temporary abdominal closure techniques. *Am Surg* 2011;77 Suppl 1:S46-50.
57. Sugrue M, D'Amours SK, Joshipura M. Damage control surgery and the abdomen. *Injury* 2004;35:642-8.
58. Feliciano DV, Burch JM. Towel clips, silos, and heroic forms of wound closure. In: Maull KI, ed. *Advances in Trauma and Critical Care*. Chicago: Year Book Medical Publishers; 1991:231-50.
59. Borráz OA. Manejo del Abdomen Séptico. Utilización del Polivinilo. Presented at the 15th congress of Avances en Cirugía e Infección, Bogotá. 1989.
60. Borráz OA. Abdomen abierto: la herida más desafiante. *Revista Colombiana de Cirugía* 2008;23:204-9.
61. Tremblay LN, Feliciano DV, Schmidt J, et al. Skin only or silo closure in the critically ill patient with an open abdomen. *Am J Surg* 2001;182:670-5.
62. Mayberry JC, Goldman RK, Mullins RJ, Brand DM, Crass RA, Trunkey DD. Surveyed opinion of American trauma surgeons on the prevention of the abdominal compartment syndrome. *J Trauma* 1999;47:509-13; discussion 13-4.
63. Steenvorde. Combining topical negative pressure and a Bogota bag for managing a difficult laparostomy. *Journal of wound care* 2004.
64. Mayer D, Rancic Z, Meier C, Pfammatter T, Veith FJ, Lachat M. Open abdomen treatment following endovascular repair of ruptured abdominal aortic aneurysms. *J Vasc Surg* 2009;50:1-7.
65. Wittmann DH, Aprahamian C, Bergstein JM. Etappenlavage: advanced diffuse peritonitis managed by planned multiple laparotomies utilizing zippers, slide fastener, and Velcro analogue for temporary abdominal closure. *World J Surg* 1990;14:218-26.
66. Schein M, Saadia R, Jamieson JR, Decker GA. The 'sandwich technique' in the management of the open abdomen. *Br J Surg* 1986;73:369-70.
67. Boele van Hensbroek P, Wind J, Dijkgraaf MG, Busch OR, Goslings JC. Temporary closure of the open abdomen: a systematic review on delayed primary fascial closure in patients with an open abdomen. *World J Surg* 2009;33:199-207.

68. Regner JL, Kobayashi L, Coimbra R. Surgical strategies for management of the open abdomen. *World J Surg* 2012;36:497-510.
69. Roberts DJ, Zygun DA, Grendar J, et al. Negative-pressure wound therapy for critically ill adults with open abdominal wounds: a systematic review. *The journal of trauma and acute care surgery* 2012;73:629-39.
70. Wittman DH. Staged Abdominal Repair: Development and Current Practice of an Advanced Operative Technique for Diffuse Suppurative Peritonitis. *Acta Chirurgica Austriaca* 2000;32:171-8.
71. Häggmark T, Linnander E. En enkel metod för successiv slutning av öppen buk [Swedish: A simple method for successive closure of the open abdomen]. *Svensk Kirurgi (Journal of the Swedish Surgical Society)* 2005;63:130-1.
72. Brock WB, Barker DE, Burns RP. Temporary closure of open abdominal wounds: the vacuum pack. *Am Surg* 1995;61:30-5.
73. Barker DE, Kaufman HJ, Smith LA, Ciraulo DL, Richart CL, Burns RP. Vacuum pack technique of temporary abdominal closure: a 7-year experience with 112 patients. *J Trauma* 2000;48:201-6; discussion 6-7.
74. Argenta LC, Morykwas MJ. Vacuum-assisted closure: a new method for wound control and treatment: clinical experience. *Ann Plast Surg* 1997;38:563-76; discussion 77.
75. Morykwas MJ, Argenta LC, Shelton-Brown EI, McGuirt W. Vacuum-assisted closure: a new method for wound control and treatment: animal studies and basic foundation. *Ann Plast Surg* 1997;38:553-62.
76. Garner M. Vacuum-assisted wound closure provides early fascial reapproximation in Trauma Patients with Open Abdomens. *Am J Surg* 2001.
77. Suliburk JW, Ware DN, Balogh Z, et al. Vacuum-assisted wound closure achieves early fascial closure of open abdomens after severe trauma. *J Trauma* 2003;55:1155-60; discussion 60-1.
78. Stonerock. Use of a Vacuum-Assisted Device to Facilitate Abdominal Closure. *Am Surg* 2003.
79. Fischer JE. A cautionary note: the use of vacuum-assisted closure systems in the treatment of gastrointestinal cutaneous fistula may be associated with higher mortality from subsequent fistula development. *Am J Surg* 2008;196:1-2.
80. Rao M, Burke D, Finan PJ, Sagar PM. The use of vacuum-assisted closure of abdominal wounds: a word of caution. *Colorectal Dis* 2007;9:266-8.
81. Trevelyan, Carlson GL. Is TNP in the open abdomen safe and effective. *Journal of wound care* 2009.
82. Bee TK, Croce MA, Magnotti LJ, et al. Temporary abdominal closure techniques: a prospective randomized trial comparing polyglactin 910 mesh and vacuum-assisted closure. *J Trauma* 2008;65:337-42; discussion 42-4.
83. Bjarnason T, Montgomery A, Hlebowicz J, Lindstedt S, Petersson U. Pressure at the bowel surface during topical negative pressure therapy of the open abdomen: an experimental study in a porcine model. *World J Surg* 2011;35:917-23.

84. Goverman J, Yelon JA, Platz JJ, Singson RC, Turcinovic M. The "Fistula VAC," a technique for management of enterocutaneous fistulae arising within the open abdomen: report of 5 cases. *J Trauma* 2006;60:428-31; discussion 31.
85. Woodfield JC, Parry BR, Bissett IP, McKee M. Experience with the use of vacuum dressings in the management of acute enterocutaneous fistulas. *ANZ J Surg* 2006;76:1085-7.
86. D'Hondt M, Devriendt D, Van Rooy F, et al. Treatment of small-bowel fistulae in the open abdomen with topical negative-pressure therapy. *Am J Surg* 2011;202:e20-4.
87. Marinis A, Gkiokas G, Argyra E, Fragulidis G, Polymeneas G, Voros D. "Enteroatmospheric fistulae"--gastrointestinal openings in the open abdomen: a review and recent proposal of a surgical technique. *Scandinavian journal of surgery : SJS : official organ for the Finnish Surgical Society and the Scandinavian Surgical Society* 2013;102:61-8.
88. Leppaniemi A. Leppäniemi. Laparostomy. Why and When? *Crit Care* 2010;14:216.
89. MacLean AA, O'Keefe T, Augenstein J. Management strategies for the open abdomen: survey of the American Association for the Surgery of Trauma membership. *Acta chirurgica Belgica* 2008;108:212-8.
90. Acosta S, Bjarnason T, Petersson U, et al. Multicentre prospective study of fascial closure rate after open abdomen with vacuum and mesh-mediated fascial traction. *Br J Surg* 2011;98:735-43.
91. Cothren CC, Moore EE, Johnson JL, Moore JB, Burch JM. One hundred percent fascial approximation with sequential abdominal closure of the open abdomen. *Am J Surg* 2006;192:238-42.
92. Rasilainen SK, Mentula PJ, Leppaniemi AK. Vacuum and mesh-mediated fascial traction for primary closure of the open abdomen in critically ill surgical patients. *Br J Surg* 2012;99:1725-32.
93. Seternes A, Myhre HO, Dahl T. Early results after treatment of open abdomen after aortic surgery with mesh traction and vacuum-assisted wound closure. *Eur J Vasc Endovasc Surg* 2010;40:60-4.
94. Bjarnason T, Montgomery A, Ekberg O, et al. One-Year Follow-up After Open Abdomen Therapy With Vacuum-Assisted Wound Closure and Mesh-Mediated Fascial Traction. *World J Surg* 2013;37:2031-8.
95. Banwell PE, Teot L. Topical negative pressure (TNP): the evolution of a novel wound therapy. *Journal of wound care* 2003;12:22-8.
96. Swan MC, Banwell PE. The open abdomen: aetiology, classification and current management strategies. *Journal of wound care* 2005;14:7-11.
97. Kafka-Ritsch R, Zitt M, Schorn N, et al. Open abdomen treatment with dynamic sutures and topical negative pressure resulting in a high primary fascia closure rate. *World J Surg* 2012;36:1765-71.
98. Verdam FJ, Dolmans DE, Loos MJ, et al. Delayed primary closure of the septic open abdomen with a dynamic closure system. *World J Surg* 2011;35:2348-55.

99. Navsaria P, Nicol A, Hudson D, Cockwill J, Smith J. Negative pressure wound therapy management of the "open abdomen" following trauma: a prospective study and systematic review. *World J Emerg Surg* 2013;8:4.
100. Padalino P, Dionigi G, Minoja G, et al. Fascia-to-fascia closure with abdominal topical negative pressure for severe abdominal infections: preliminary results in a department of general surgery and intensive care unit. *Surg Infect (Larchmt)* 2010;11:523-8.
101. Bjorck M, Bruhin A, Cheatham M, et al. Classification--important step to improve management of patients with an open abdomen. *World J Surg* 2009;33:1154-7.
102. Navsaria PH, Bunting M, Omshoro-Jones J, Nicol AJ, Kahn D. Temporary closure of open abdominal wounds by the modified sandwich-vacuum pack technique. *Br J Surg* 2003;90:718-22.
103. Fantus RJ, Mellett MM, Kirby JP. Use of controlled fascial tension and an adhesion preventing barrier to achieve delayed primary fascial closure in patients managed with an open abdomen. *Am J Surg* 2006;192:243-7.
104. Petersson U, Acosta S, Bjorck M. Vacuum-assisted wound closure and mesh-mediated fascial traction--a novel technique for late closure of the open abdomen. *World J Surg* 2007;31:2133-7.
105. Baggot MG. Common and inter-related complications of anesthesia in operations and obstetrics. *Current researches in anesthesia & analgesia* 1954;33:1-17.
106. Schein M. Historical background. In: Ivatury R, ed. *Abdominal compartment syndrome*: Landes Bioscience; 2006:1-7.
107. Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med* 1996;22:707-10.
108. Korenkov M, Paul A, Sauerland S, et al. Classification and surgical treatment of incisional hernia. *Langenbeck's Archives of Surgery* 2001;386:65-73.
109. Muysoms FE, Miserez M, Berrevoet F, et al. Classification of primary and incisional abdominal wall hernias. *Hernia* 2009;13:407-14.
110. Moreno-Matias J, Serra-Aracil X, Darnell-Martin A, et al. The prevalence of parastomal hernia after formation of an end colostomy. A new clinico-radiological classification. *Colorectal Dis* 2009;11:173-7.
111. McHorney CA, Tarlov AR. Individual-patient monitoring in clinical practice: are available health status surveys adequate? *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation* 1995;4:293-307.
112. Brennan P, Silman A. Statistical methods for assessing observer variability in clinical measures. *Bmj* 1992;304:1491-4.
113. Walt AJ. Founder's lecture: The mythology of hepatic trauma--or Babel revisited. *Am J Surg* 1978;135:12-8.
114. Walt AJ. The surgical management of hepatic trauma and its complications. *Ann R Coll Surg Engl* 1969;45:319-39.

115. Robledo FA, Luque-de-Leon E, Suarez R, et al. Open versus closed management of the abdomen in the surgical treatment of severe secondary peritonitis: a randomized clinical trial. *Surg Infect (Larchmt)* 2007;8:63-72.
116. De Waele JJ, Hoste EA, Malbrain ML. Decompressive laparotomy for abdominal compartment syndrome--a critical analysis. *Crit Care* 2006;10:R51.
117. Miller RS, Morris JA, Diaz JJ, Herring MB, May AK. Complications after 344 Damage-Control Open Celiotomies. *The Journal of Trauma: Injury, Infection, and Critical Care* 2005;59:1365-74.
118. Schein M. Planned reoperations and open management in critical intra-abdominal infections: prospective experience in 52 cases. *World J Surg* 1991;15:537-45.
119. Carlson GL, Patrick H, Amin AI, et al. Management of the open abdomen: a national study of clinical outcome and safety of negative pressure wound therapy. *Ann Surg* 2013;257:1154-9.
120. Roberts DJ, Jenne CN, Ball CG, et al. Efficacy and safety of active negative pressure peritoneal therapy for reducing the systemic inflammatory response after damage control laparotomy (the Intra-peritoneal Vacuum Trial): study protocol for a randomized controlled trial. *Trials* 2013;14:141.
121. Sugrue M, Buhkari Y. Intra-abdominal pressure and abdominal compartment syndrome in acute general surgery. *World J Surg* 2009;33:1123-7.
122. Balogh ZJ, Butcher NE. Compartment syndromes from head to toe. *Crit Care Med* 2010;38:S445-51.
123. Leppäniemi AK. Surgical management of abdominal compartment syndrome; indications and techniques. *Scand J Trauma Resusc Emerg Med* 2009.
124. Batacchi S, Matano S, Nella A, et al. Vacuum-assisted closure device enhances recovery of critically ill patients following emergency surgical procedures. *Crit Care* 2009;13:R194.
125. Grubb A, Nyman U, Bjork J. Improved estimation of glomerular filtration rate (GFR) by comparison of eGFRcystatin C and eGFRcreatinine. *Scandinavian journal of clinical and laboratory investigation* 2012;72:73-7.
126. Open Abdomen Advisory P, Campbell A, Chang M, et al. Management of the open abdomen: from initial operation to definitive closure. *Am Surg* 2009;75:S1-22.
127. Kreis BE, de Mol van Otterloo AJ, Kreis RW. Open abdomen management: a review of its history and a proposed management algorithm. *Medical science monitor : international medical journal of experimental and clinical research* 2013;19:524-33.
128. Wittmann DH. Staged Abdominal Repair: Development and Current Practice of an Advanced Operative Technique for Diffuse Suppurative Peritonitis *Acta Chirurgica Austriaca* 2000;32:171-8.
129. Leppaniemi A, Tukiainen E. Reconstruction of complex abdominal wall defects. *Scandinavian journal of surgery : SJS : official organ for the Finnish Surgical Society and the Scandinavian Surgical Society* 2013;102:14-9.
130. Rutherford EJ, Skeete DA, Brasel KJ. Management of the patient with an open abdomen: techniques in temporary and definitive closure. *Curr Probl Surg* 2004;41:815-76.

131. Ramirez OM, Ruas E, Dellon AL. "Components separation" method for closure of abdominal-wall defects: an anatomic and clinical study. *Plast Reconstr Surg* 1990;86:519-26.
132. de Vries Reilingh TS, van Goor H, Rosman C, et al. "Components separation technique" for the repair of large abdominal wall hernias. *J Am Coll Surg* 2003;196:32-7.
133. Ko JH, Wang EC, Salvay DM, Paul BC, Dumanian GA. Abdominal wall reconstruction: lessons learned from 200 "components separation" procedures. *Archives of surgery* 2009;144:1047-55.
134. Ventral Hernia Working G, Breuing K, Butler CE, et al. Incisional ventral hernias: review of the literature and recommendations regarding the grading and technique of repair. *Surgery* 2010;148:544-58.
135. Montgomery A. The battle between biological and synthetic meshes in ventral hernia repair. *Hernia* 2013;17:3-11.
136. Berrevoet F, Vanlander A, Sainz-Barriga M, Rogiers X, Troisi R. Infected large pore meshes may be salvaged by topical negative pressure therapy. *Hernia* 2013;17:67-73.
137. Fischer JE. A cautionary note: the use of vacuum-assisted closure systems in the treatment of gastrointestinal cutaneous fistula may be associated with higher mortality from subsequent fistula development. *Am J Surg* 2008;196:1-2.
138. Becker HP, Willms A, Schwab R. Small bowel fistulas and the open abdomen. *Scandinavian journal of surgery : SJS : official organ for the Finnish Surgical Society and the Scandinavian Surgical Society* 2007;96:263-71.
139. Kim J, Kim Y, Jeong WK, Song SY, Cho OK. Heterotopic ossification developing in surgical incisions of the abdomen: analysis of its incidence and possible factors associated with its development. *J Comput Assist Tomogr* 2008;32:872-6.
140. Koolen PG, Schreinemacher MH, Peppelenbosch AG. Heterotopic ossifications in midline abdominal scars: a critical review of the literature. *Eur J Vasc Endovasc Surg* 2010;40:155-9.
141. ABThera. Instructions for Use, KCI Inc. 2010.
142. Gäddnäs. Continuous retention suture for the management of open abdomen. A high rate of delayed fascial closure. *Scandinavian journal of surgery : SJS : official organ for the Finnish Surgical Society and the Scandinavian Surgical Society* 2007.
143. Goodman MD, Pritts TA, Tsuei BJ. Development of a novel method of progressive temporary abdominal closure. *Surgery* 2010;148:799-805; discussion -6.
144. Haddock C, Konkin DE, Blair NP. Management of the open abdomen with the Abdominal Reapproximation Anchor dynamic fascial closure system. *Am J Surg* 2013;205:528-33; discussion 33.
145. Howdieshell TR, Proctor CD, Sternberg E, Cue JI, Mondy JS, Hawkins ML. Temporary abdominal closure followed by definitive abdominal wall reconstruction of the open abdomen. *Am J Surg* 2004;188:301-6.
146. Miller PR, Meredith JW, Johnson JC, Chang MC. Prospective Evaluation of Vacuum-Assisted Fascial Closure After Open Abdomen. *Annals of Surgery* 2004;239:608-16.

147. Vertrees A, Greer L, Pickett C, et al. Modern management of complex open abdominal wounds of war: a 5-year experience. *J Am Coll Surg* 2008;207:801-9.
148. Wondberg D, Larusson HJ, Metzger U, Platz A, Zingg U. Treatment of the open abdomen with the commercially available vacuum-assisted closure system in patients with abdominal sepsis: low primary closure rate. *World J Surg* 2008;32:2724-9.
149. Horwood J, Akbar F, Maw A. Initial experience of laparostomy with immediate vacuum therapy in patients with severe peritonitis. *Ann R Coll Surg Engl* 2009;91:681-7.
150. Diener MK, Voss S, Jensen K, Buchler MW, Seiler CM. Elective midline laparotomy closure: the INLINE systematic review and meta-analysis. *Ann Surg* 2010;251:843-56.
151. Hartog D, Dur AHM, Kamphuis AGA, Tuinebreijer WE, Kreis RW. Comparison of ultrasonography with computed tomography in the diagnosis of incisional hernias. *Hernia* 2008;13:45-8.
152. Timmermanns L, Deerenberg E, Lamme B, Jeekel J, Lange J. Parastomal hernia is an independent risk factor incisional hernia in patients with end colostomy (with additional information from the oral presentation). *Hernia* 2013;17:S11.
153. Bloemen A, van Dooren P, B FH, Hoofwijk AG. Comparison of ultrasonography and physical examination in the diagnosis of incisional hernia in a prospective study. *Hernia* 2012;16:53-7.
154. Bevis PM, Windhaber RA, Lear PA, Poskitt KR, Earnshaw JJ, Mitchell DC. Randomized clinical trial of mesh versus sutured wound closure after open abdominal aortic aneurysm surgery. *Br J Surg* 2010;97:1497-502.
155. Hidalgo MP, Ferrero EH, Ortiz MA, Castillo JM, Hidalgo AG. Incisional hernia in patients at risk: can it be prevented? *Hernia* 2011;15:371-5.
156. Janes A, Cengiz Y, Israelsson LA. Preventing parastomal hernia with a prosthetic mesh: a 5-year follow-up of a randomized study. *World J Surg* 2009;33:118-21; discussion 22-3.
157. Janes A, Weisby L, Israelsson LA. Parastomal hernia: clinical and radiological definitions. *Hernia* 2011;15:189-92.
158. Serra-Aracil X, Bombardo-Junca J, Moreno-Matias J, et al. Randomized, controlled, prospective trial of the use of a mesh to prevent parastomal hernia. *Ann Surg* 2009;249:583-7.
159. Cingi A, Cakir T, Sever A, Aktan AO. Enterostomy site hernias: a clinical and computerized tomographic evaluation. *Dis Colon Rectum* 2006;49:1559-63.
160. Koss W, Ho HC, Yu M, et al. Preventing loss of domain: a management strategy for closure of the "open abdomen" during the initial hospitalization. *J Surg Educ* 2009;66:89-95.
161. Kleif. Promising results after vacuum-assisted wound closure and mesh-mediated fascial traction. *Danska läkartidningen* 2012.
162. Block TA, Acosta S, Bjorck M. Endovascular and open surgery for acute occlusion of the superior mesenteric artery. *J Vasc Surg* 2010;52:959-66.

163. McCosh AJ. II. The Treatment of General Septic Peritonitis. *Ann Surg* 1897;25:687-97.
164. Pilcher LS. I. Laparotomy for Intestinal Obstruction. *Ann Surg* 1886;3:214-21.
165. Fenger C. I. Chronic Peri-uterine Abscess, and its Treatment by Laparotomy. *Ann Surg* 1885;1:393-423.

Medicinae doctores in chirurgia, Malmö, Lund University

1951	Arne Malm	1971	Erik G Ohlsson
1953	Erik Åkerlund	1971	Sune Isacson
1953	Nils P Berg	1972	Jörgen Gundersen
1953	Nils Carstam	1973	Bo Phil
1955	Anders Wenckert	1973	Bo Husberg
1955	Las G Hallen	1974	Lars Janzon
1957	Lawe Svanberg	1974	Sigvard Olsson
1958	Torsten Widén	1974	Jerzy Senyk
1959	Ivar Borg	1974	Göran Ekelund
1959	Arne Weiber	1975	Bengt Pallin
1959	Knut Haeger	1975	Sven Kristersson
1960	Stig Borgström	1976	Rabbe Takolander
1961	Karl-Fredrik Aronsen	1976	Nils T Johansson
1961	Oddvar Eiken	1976	Sverker Hellsten
1961	Carl-Fredrik Liedberg	1977	Pål Svedman
1962	Bertil Olow	1977	Anders Henricsson
1963	Claes-Göran Backström	1977	Sune Wetterlin
1963	Thorsten Stenberg	1977	Sven Genell
1967	Sten Jacobsson	1977	Bo Lindell
1970	Bengt Lindskog	1978	Olof Lannerstad
1971	Bertil Robertsson	1978	Magnus Åberg
1971	Björn F Ericsson	1978	Allan Eddeland

1978	Hasse Jiborn	1985	Måns Bohe
1979	Anders Borgström	1986	Henry Svensson
1980	Ingrid Tengrup	1987	Heitti Teder
1980	Göran Balldin	1987	Hans Högstrom
1981	Stephan Brandstedt	1988	Per Uden
1982	Tomas Lindhagen	1988	Erik Svartholm
1982	Harald Ljungner	1988	Per-Anders Abrahamsson
1982	Carlos Esquivel	1989	Toste Länne
1982	Igor Niechajev	1990	Bengt Hjelmqvist
1982	Einar Vernersson	1990	Nils H Persson
1983	Svend Borup Christensen	1990	Henrik Åkesson
1983	Afzal Vazeery	1990	Thomas Mätzsch
1983	Johan Sällström	1990	Magnus Delshammar
1983	Jan-Bertil Wieslander	1990	Anders Törnqvist
1983	Bill Marks	1990	Magnus Erlansson
1983	Bengt Lindblad	1990	Jan Brunkwall
1984	Anders Larsson	1991	Johan Ottosson
1984	Peter Blomquist	1991	Ragnar Källén
1984	Åke Lasson	1991	Lars Salemark
1984	Claes-Göran Björck	1991	Claes Forssell
1984	Staffan Källero	1991	Agneta Montgomery
1984	Per Almquist	1991	Jan Berglund
1984	Anne-Greth Bondeson	1991	Hans Olof Håkansson
1984	Peter Konrad	1992	Henrik Bengtsson
1984	Magnus Grabe	1992	Thomas Troeng
1985	Anders Lindhagen	1992	Michael Hartmann
1985	Stefan Arvidsson	1992	Peter Björk
1985	Kent Jönsson	1992	Anita Ringberg
1985	Hans Hedlund	1992	Henrik Weibull

1992	Erney Mattsson	1999	Håkan Weiber
1992	Thorvaldur Jonsson	2000	Ingvar Syk
1992	Magnus Bergenfeldt	2001	Xiao Wei Zhang
1993	Anders Lundell	2001	Christer Svedman
1993	Baimeng Zhang	2001	Ulf Petersson
1994	Stefan Matthiasson	2001	Mats Bläckberg
1994	Staffan Weiber	2001	Peter Månsson
1994	Björn Sonesson	2001	Tor Svensjö
1995	Jan Stewenius	2001	Ursula Mirastschijski
1995	Björn Arnljots	2001	Torbjörn Söderstrom
1995	Jan Holst	2002	Thomas Sandgren
1995	Leif Israelsson	2002	Max Nyström
1995	Per Jönsson	2002	Rene Schramm
1996	Norman Jensen	2002	Ervin Tóth
1996	Jens Peter Garne	2002	Daniel Klintman
1996	Hans Bohe	2002	Åke Mellström
1997	Wayne Hawthorne	2002	Amjid Riaz
1997	Öyvind Östraat	2002	Matthias Corbascio
1997	Yilei Mao	2003	Nina Kvorning
1998	Diya Adawi	2003	Gudmundur Danielsson
1998	Liselotte Frost-Arner	2003	Fritz Berndsen
1998	Martin Malina	2003	Salathiel Mzezewa
1998	Thomas Björk	2004	Marianne Starck
1998	Mats Hedberg	2004	Li Xiang
1998	Håkan Brorson	2004	Karl Malm
1998	Magnus Becker	2004	Claes Jansen
1999	Zhonquan Qi	2004	Peter Danielsson
1999	Stefan Appelros	2004	Lisa Rydén
1999	Göran Ahlgren	2005	Ann-Cathrin Moberg

2005	Anders Holmström	2012	Milladur Rahman
2005	Helene Malm	2012	Su Zhang
2005	Carolin Freccero	2012	Jan Erik Slotta
2005	Nishtman Dizeyi	2012	Åsa Olsson
2005	Cecilia Österholm Corbascio	2012	Martin Öberg
2005	Saad Elzanaty	2012	Songen Zhang
2005	Björn Lindkvist	2013	Zirak Hasan
2006	Louis Banka Johnson	2013	Karzan Hamad Palani
2006	Henrik Dyhre	2014	Thordur Bjarnason
2006	Erik Almqvist		
2006	Yusheng Wang		
2007	Peter Mangell		
2007	Martin Persson		
2008	Sara Regnér		
2008	Stefan Santén		
2008	Asaduzzaman Muhammad		
2008	Mattias Laschkse		
2009	Martin Almquist		
2009	Farokh Collander Farzaneh		
2010	Dorthe Johansen		
2010	Björn Schönmeyr		
2010	Fredrik Jörgren		
2010	Patrik Velander		
2010	Andrada Mihăescu		
2011	Salma Butt		
2011	Emma Hansson		
2011	Aree Omer Abdulla		
2011	Darbaz Awla		
2012	Martin Rehn		