OPEN ABDOMINAL TREATMENT: HOW MUCH EVIDENCE DO WE HAVE?

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Table of Contents

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EDITORIAL
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Editorial: Open Abdominal Treatment: How Much Evidence Do We Have?

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Keywords: open abdomen, peritonitis, abdominal trauma, abdominal compartment syndrome, vacuum therapy

Editorial on the Research Topic

Open Abdominal Treatment: How Much Evidence Do We Have?

Open abdominal treatment (OAT) is a surgical therapy strategy for critically ill patients with serious intra-abdominal pathologies. Since its introduction about 30 years ago, it has had a permanent place in trauma and damage control surgery, but also in treatment of visceral surgical emergencies. Applied to the right patient, the OAT strategy has been shown to reduce morbidity and mortality in patients whose systemic compensation mechanisms and physiological reserves (circulation, blood coagulation, etc.) are almost exhausted due to the serious intra-abdominal pathology.

This procedure and core topic of this issue is the result of a paradigm shift in emergency abdominal surgery. The aim of the OAT is to minimize the initial, surgical-related secondary damage through a shortened initial operation and a temporary abdominal wall closure. However, these patients then necessarily need one or more further surgical interventions. Thus, the initiation of the OAT represents a decisive course and the subsequent management an enormous logistical and medical challenge: Patients with OAT need a structured therapy concept with close coordination of surgery and intensive care medicine in order to benefit from the advantages of the procedure. Advantages include the shortened operating time for index surgery, the easy re-evaluation (second look), the possibility of repeated decontamination (lavage), a better ventilation situation, as well as an improvement in renal and intestinal perfusion.

Nevertheless, the OAT course is associated with serious potential disadvantages. The most elementary possible negative consequences are: the formation of entero-atmospheric fistulas, the lateral retraction of the abdominal wall fascia, which makes a later fascia closure much more difficult, and fluid losses through exposure of the viscera.

The present edition spans a wide range and reflects not only current knowledge but also new strategies and approaches. The attempt is made to map all important therapy goals, such as fascia traction and fistula prevention as well as hernia prophylaxis. This issue includes reports of many years of experience of a center with vacuum therapy as one of the most important and established therapy elements with a large patient population as well as new technologies for prophylactic mesh implantation with the aim of hernia prophylaxis on only a few patients. There are excellent descriptions of patient subgroups such as pancreatitis or experiences with abdominal compartment syndrome in ECMO patients. There are very interesting experimental works on the suction effect as well as review articles on important topics such as fistula prevention and dynamic fascia traction

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and, last but not least, on the important parameter, the outcome after treatment.

We wish you a lot of fun and knowledge while reading and would like to thank all authors for the successful cooperation.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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ORIGINAL RESEARCH
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The Need for Emergency Laparotomy With Open Abdomen Therapy in the Course of ECMO—A Retrospective Analysis of Course and Outcome

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Background: Abdominal compartment syndrome (ACS) can occur in patients placed on extra corporeal membrane oxygenation (ECMO). This implies the necessity of decompressive laparotomy followed by an open abdomen (OA) to prevent complications such as multi-organ-failure or death.

Methods: We searched for ECMO patients in our hospital database between July 2015 and April 2020 and selected those with an emergency laparotomy and OA therapy. Of these, we analyzed only patients who were treated with an OA after establishing the ECMO regarding patient-related parameters like sex, age, height, weight, and indications for ECMO as well as outcome parameters like complete fascial closure rate, mortality, length of stay in intensive care unit (ICU), length and kind of OA therapy, number of surgical procedures, dressing changes concerning negative pressure wound therapy (NPWT), and number of surgical revisions.

Results: In eight out of 421 patients (1.9%), a laparostoma had to be created during ECMO support. For temporary closure, either NPWT, abdominal packing, or both were used. The median length of OA therapy was 17 days, and the median length of stay in ICU was 42 days in total. The median number of surgical procedures and NPWT dressing changes was seven. In three of the eight patients, a surgical revision was necessary. The total mortality rate was 50%. In 75%, the fascia could be closed. Two patients died before final closure. In all deceased patients, an abdominal packing was necessary during the course of treatment; in the survivors, only once. No enteroatmospheric fistula or abscesses occurred.

Conclusions: ACS in patients placed on ECMO is a very rare condition with a considerable mortality rate but high secondary closure rate of the fascia. A necessary abdominal packing due to a severe bleeding seems to be a risk factor with a potentially fatal outcome.

Keywords: open abdomen, laparostoma, ECMO, abdominal compartment syndrome, NPWT

INTRODUCTION

A laparostoma is a non-closure of the fascia in cases of laparotomy, which is commonly an emergency procedure. Concerning this, there are a myriad of reasons for a laparostoma, and consequently, in many cases, a tension-free closure is impossible. Laparostoma is used to restore an adequate hemodynamic status, preventing an abdominal compartment syndrome (ACS) and deferring definitive intervention and anastomosis, until the patient is hemodynamically stable and appropriately resuscitated. Early identification and draining of a residual infection are of particular importance regarding the removal of infected or cytokine-loaded fluid, and thereby the control of any persistent source of infection is facilitated by a laparostoma (1–3). Despite all of those positive aspects improving many patients' outcomes, it is also important to face the risks and complications associated with an open abdomen (OA). While some patients require further surgical procedures during their inpatient stay, others are mainly affected by long-term complications such as a remaining fascial defect, which may require further treatment (1, 4, 5). Enteroatmospheric fistulas are an example of a long-term complication in patients during or after laparostoma, as are abscesses and the loss of abdominal wall domain. These can result in an increase in morbidity and mortality (1, 5, 6).

One possible reason for an emergency laparotomy without immediate primary closure is the development of ACS. Several risk factors for developing intraabdominal hypertension (IAH) as well as ACS, like large-volume fluid resuscitation and the presence of shock, hypotension, sepsis, massive intestinal swelling, or severe trauma, are described in literature (1, 2, 6–9). In addition, patients who have had ECMO created can develop ACS without having previously suffered trauma or abdominal sepsis following abdominal surgery (10, 11).

Due to the rarity of such cases, there is very little literature describing the course and the outcome of patients who develop an ACS after the establishment of an ECMO and require an OA. Our aim was to analyze the outcome, number of days with the OA, number of days in intensive care unit (ICU), number of surgical procedures, dressing changes concerning the negative pressure wound therapy (NPWT), and number of surgical revisions in such patients admitted to our ARDS and ECMO center in Cologne-Merheim Medical Center (CMMC) comparing our results with data about laparostoma patients on ECMO described in the literature.

MATERIALS AND METHODS

Patients

We performed a retrospective, single-center, observational cohort study of patients at the CMMC, Witten/Herdecke University teaching hospital, treated with laparostoma after the beginning of ECMO support from July 2015 to April 2020. Data were gathered from electronic medical records by searching our hospital's patient database for the ICD codes for "ECMO" and "laparostoma" / "laparotomy." The methods for inclusion of patients and patient-related data were specified a priori.

The patients included were placed on ECMO as well as treated with laparostoma. We only included patients with laparotomy leading to an OA after the initiation of ECMO to analyze a more homogeneous group.

The patient files were screened using the parameters mentioned below.

Definition of IAH and ACS

Intraabdominal pressure is defined as the steady-state pressure concealed within the abdominal cavity. In critically ill adults, it is ∼5–7 mmHg. IAH is defined as an intraabdominal pressure of more than 12 mmHg and is classified in four grades (grade I: 12–15 mmHg, grade II: 16–20 mmHg, grade III: 21–25 mmHg, and grade IV: >25 mmHg) (3). In contrast to that, the ACS presupposes per definition a new organ dysfunction and hypertension with a pressure of more than 20 mmHg within the abdominal cavity (3, 12).

Surgical Standard

In our hospital, laparotomy is performed at the point of an intraabdominal pressure of 20 mmHg or above, combined with clinical symptoms of ACS as anuria or insufficiency of perfusion through ECMO.

The standard procedure monitoring IAP in our patients at risk in the ICU was the measurement of pressure within the bladder 30–60 s after the instillation of 25 ml of normal saline through the urinary catheter every 8 h.

Methods of creating an OA at our hospital:

1. Applying NPWT with PU foam and visceral protective film underneath with or without redressing fasciorrhaphy.
2. Interposition of a Vicryl-mesh onto the visceral protective film for the redression of the fascia instead of redressing sutures and usage of a commercially NPWT set.

Other kinds of therapy like the Wittman patch or the Bogota bag were not deployed in our hospital. The choice of wound closure depended on the surgeons' preference.

The standard suction magnitude was 75 or 80 mmHg. Dressing changes for NPWT were performed every 3 days at our hospital.

Depending on the hemodynamical stability of the patient, the surgical creation of the laparostoma was either performed in our central operation room or in ICU.

Outcome Parameter

The outcome parameters of the study were patient-related parameters like sex, age, height, weight, and indications for ECMO as well as outcome parameters like successful fascial closure rate, mortality, length of stay in ICU after closure and in total, length and kind of OA therapy, number of surgical procedures performed, number of dressing changes concerning NPWT, and number of surgical revisions.

Statistics

The data were prepared and analyzed in Microsoft Excel Version 14.1.0 (Microsoft Corp., Redmond, WA, United States). Data of continuous variables are expressed as minimum, maximum, and

TABLE 1 | Patient related data.

Patient	Sex*	Age**	Height (cm)	Weight (kg)	BMI (kg/m^2)	Indications for ECMO
1	-	11–15	162	60	22.9	ARDS after pulmonary aspiration during CPR
2	-	31–35	185	85	24.0	Secondary ARDS (severe pancreatitis)
3	-	61–65	160	70	26.7	COPD
4	-	66–70	180	80	24.7	Thoracic trauma
5	-	61–65	178	92	29.0	Secondary ARDS due to severe pancreatitis
6	-	76–80	165	95	34.9	Ruptured pars membranacea (trachea) while tracheotomy
7	-	51–55	160	65	25.4	Viral pneumonia, (Influenza A, H1N1)
8	-	36–40	163	89	33.5	Bilateral, nosocomial, bacterial pneumonia
In total	*m* = 4 (50%) *f* = 4 (50%)***	56 (14–77)****	164 (160–180)****	82.5 (60–95)****	26.1 (22.9–34.9)****	

**Only summarized data.*
***Presenting as a range (11–15, 16–20, 21–25, 26–30...).*
****Counts (Percentage).*
*****Median (Min–Max).*
m, Male; f, Female; BMI, Body mass index; ECMO, Extra corporeal membrane oxygenation; ARDS, Acute respiratory distress syndrome; CPR, Cardio pulmonary resuscitation; COPD, Chronic obstructive pulmonary disease.

median. Binary and categorical variables are reported as counts and percentages.

RESULTS

Between July 2015 and April 2020, we treated 421 patients on ECMO in total. Among these, we identified 14 patients who underwent decompressive laparotomy followed by the state of an OA (8/421; 1.9%). In our analysis, only patients on ECMO who developed ACS after cannulation were included (8/14; 57%). **Table 1** depicts data of these patients. All eight patients were supported by veno-venous ECMO; one of them (12.5%) initially was placed on veno-arterial ECMO, which was converted within the 1st day of the ECMO support.

The median age of our male patients was lower than that in our female patients (46.5 vs. 56.0 years).

Outcome data are depicted in **Table 2**. Two of the deceased patients died with a non-closed abdomen (days 5 and 7 of the OA). The other two patients died 1 and 16 days after abdominal closure.

The median age of surviving patients was lower than the median age of the patients who did not (46.5 vs. 56 years); 87.5% (7/8) of the ECMO patients with an OA were treated with NPWT. In 62.5% (5/8), abdominal packing was implemented initially or during the course. One patient was only treated with abdominal packing. In all eight patients, we did not use any other techniques of temporary closure than NPWT or abdominal packing. Observing the four surviving patients, the median duration of laparostoma was 30.5 days. The median number of abdominal surgeries in the patients who survived until final closure (6/8; 75%) was 12.5; the median number of dressing changes during NPWT was 9.5. In three patients, relaparotomy was required. One was due to ACS a few hours after the first attempt of closure. The second was a planned exploration after initial emergency surgery, and the third was due to acute bleeding. In all four patients who did not survive, abdominal packing had to be applied (100%), whereas only one of the four surviving patients (25%) was treated with abdominal packing. In two patients (25%), retroperitoneal hemorrhage appeared, while in one patient, it was after initial trauma and thus not caused by the placement on ECMO; in the second, it occurred after the initiation of ECMO support. All abdominal findings during the initial laparotomy were operable.

The median length of stay in ICU of the surviving patients was 42 days, and the median length of stay in ICU after closure was 20 days.

In six patients (6/8; 75%), laparotomy was the initial procedure to relieve the elevated intraabdominal pressure, once ACS has been diagnosed. In two patients (2/8; 25%), draining of fluids was performed previously by puncture.

In all patients whose OA was finally closed, secondary wound closure was performed in layers. We did not perform closure with a partial defect of the abdominal wall or the usage of a mesh. Complications during the OA such as enterocutaneous fistulas or abscesses could not be found.

DISCUSSION

The huge impact of an increased intraabdominal pressure can be seen in the impaired functions of multiple organs such as the lungs, bowel, and the kidneys. That is why immediate diagnosis and appropriate intervention is of vital concern (8, 9, 12–14). This ranges from medical treatment of IAH to surgical treatment when the patient's condition aggravates or ACS develops (14). To relieve the excess pressure, decompressive laparotomy, which represents a non-anatomical situation, is considerable and leads to an OA in many cases. Other causes for an OA are trauma, the effects of abdominal sepsis, also leading to increased abdominal pressure, and damage control surgery (1, 6, 15, 16). During this surgical treatment, with an increased morbidity and mortality,

TABLE 2 | Outcome parameters.

Patient no.	Deceased	Days on ICU	Days with OA	Days on ICU after closure	Number of surgical procedures	Abdominal packing	Negative pressure wound therapy	Number of dressing changes for NPWT	Number of revisions
1	No	66	33	33	15	Yes	Yes	11	1
2	No	73	71	1	26	No	Yes	23	1
3	Yes*	115	9	16	4	Yes	Yes	2	0
4	Yes*	12	12	12	5	Yes	Yes	4	0
5	No	41	28	23	10	No	Yes	8	0
6	No	43	22	17	9	No	Yes	7	0
7	Yes**	25	5	n.a.	2	Yes	Yes	0	0
8	Yes**	30	7	n.a.	2	Yes	No	n.a.	1
In total	• No = 4 (50%) • Yes = 4 (50%)***	42 (12–115)****	17 (5–71)****	16.5 (1–33)****	7 (2–26)****	• No = 3 (37.5%) • Yes = 5 (62.5%)***	• No = 1 (12.5%) • Yes = 7 (87.5%)***	7 (0–23)****	0 (0–1)****

*Death after fascial closure.
**Death before fascial closure.
***Counts (Percentage).
****Median (Min–Max).
ICU, Intensive care unit; OA, Open abdomen; NPWT, Negative pressure wound therapy.

the loss of fluids and temperature, as well as the desiccation of the bowels, must be considered (6).

Multiple ways to manage an OA using temporary or, if possible, final closing techniques are described in the literature. Most of the temporary abdominal closure techniques, providing protection to the abdominal viscera during the time the fascia remains open, include negative pressure therapy techniques such as vacuum packing and vacuum-assisted therapy (1, 17–19). One major objective over the course of laparostoma is to prevent the fascia from retraction, which leads to the impossibility of final closure of the fascia. To prevent this or even to redress the fascia gradually, a mesh can be sewn into the defect. Other options are the sandwich and zipper technique, as well as the artificial burr device or the Wittmann Patch. Although these techniques finally provide a high primary closure rate, they may lead to a remaining gap in the fascia (17, 20–22). Some authors describe the Bogota bag or dynamic retention sutures to be considerable options for temporary closure of the OA (17, 23). In general, closure is recommended to be achieved at the earliest expected time (1).

Depending on the cause for an OA in a given case, distinct conditions can impair primary abdominal closure. These include visceral edema, the inability to control a source of infection, the necessity for second-look surgery or completion of previous treatment, and severe cases of abdominal wall damage, especially given in patients with penetrating trauma (15, 24). Patients who fail primary closure may require a biologic fascial bridge with subsequent fascia repair in the future (4).

In patients on ECMO, IAH can be detected by a reduced flow in the return canula and generates end-organ malperfusion. That is why ACS, followed by the performance of decompressive laparotomy, should be considered in cases of hemodynamic impairment or ECMO dysfunction, to diminish complications (10, 11).

There is a paucity of literature about the development of an ACS followed by laparostoma in ECMO patients, even though ECMO is a risk factor for an increased intraabdominal pressure. Due to the low number of cases, information about this subject, especially about the duration of an OA including the number and kind of surgical procedures in patients on ECMO, is rare. This study gives an insight into the courses of disease for our patients and their outcomes. We found a mortality rate of 50% and a final closure rate of 75% (25% died before, 25% after final closure). Only one patient (12.5%) required an unpredictable surgical procedure on account of a major bleeding event. The techniques used for temporary closure were NPWT and abdominal packing. According to our research, abdominal packing seems to be a risk factor with a potentially fatal outcome. As the OA in ECMO patients is known to be a rare condition, the number of patients we found was correspondingly not high enough to gather universally valid information, but to provide data of a barely investigated thematic area.

In the literature, we found a few studies referring to related substances. McCann et al. performed a retrospective, single-center cohort study with 355 patients on ECMO in 2019 (25). The prevalence of emergency laparotomy in this study was 3.7% (13/355). In six patients (6/13), the abdomen was closed in the same procedure; in two patients (2/13), NPWT was used; and in five patients (5/13), the Bogota bag was used. The mortality rate was 69% among patients with emergency laparotomy until hospital discharge. They described intraoperative major hemorrhage to be rare (2/13; 15.4%). Among our patients, two cases of bleeding could be identified, of which none was intraoperative. One was due to initial trauma and one was during ECMO support. In 2018, Glowka et al. analyzed 175 patients who underwent ECMO support. Eleven out of 175 patients developed an ACS and underwent decompressive laparotomy (11/175; 6.3%). In four of these patients (4/11), ECMO support

was performed as veno-venous, and in seven patients (7/11), it was veno-arterial. Eight of them (8/11; 72%) died while in the hospital, and age was described as a risk factor (15). In comparison, the prevalence of laparotomy and the mortality in our patient group was lower (1.9 vs. 3.7% and 6.3%; 50 vs. 69% and 72%). As our median patient age was lower in the ones who survived, we also suggest age to be a risk factor for a fatal outcome. In all of our patients who did not survive, abdominal packing was performed. That is why we believe abdominal packing to be a risk factor with a potentially fatal outcome. However, there is also a bias, since patients requiring abdominal packing are usually in a worse condition than those who do not. The low number of eligible patients in all these studies including our analysis is an indication of the rare incidence of ACS in this patient group rather than a significant quality of medical therapy.

We did not find any literature giving a more precise indication about the state of an OA from the surgical point of view, like type, duration, and number of surgical procedures in patients on ECMO. Since none of our patients has had any kind of outpatient follow-up after the inpatient stay, our study cannot describe any long-term complications after the abdominal closure.

CONCLUSION

The development of ACS, leading to the necessity of decompressive laparotomy followed by an OA, is a rare complication of patients on ECMO support, but has a relevant mortality. On the other hand, the secondary closure rate of the fascia is very high. The need of abdominal packing seems to be a risk factor for a fatal outcome. However, the small number of our includable eight patients limits any conclusion. Accordingly, a prospective multicenter study with more patients is necessary to confirm our results.

DATA AVAILABILITY STATEMENT

All datasets generated for this study are included in the article/supplementary material.

AUTHOR CONTRIBUTIONS

S-AS, SS, and DB conceived the idea and designed this study. S-AS, SS, PT, and DB did the statistical analysis and drafted the manuscript. DR, CK, and MH contributed to the data interpretation and critically revised the manuscript. All authors have seen and approved the final manuscript.

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REFERENCES

1. Sartelli M, Abu-Zidan FM, Ansaloni L, Bala M, Beltran MA, Biffl WL, et al. The role of the open abdomen procedure in managing severe abdominal sepsis: WSES position paper. *World J Emerg Surg.* (2015) 10:35. doi: 10.1186/s13017-015-0032-7
2. Rollins MD, Deamorim-Filho J, Scaife ER, Hubbard A, Barnhart DC. Decompressive laparotomy for abdominal compartment syndrome in children on ECMO: effect on support and survival. *J Pediatr Surg.* (2013) 48:1509–13. doi: 10.1016/j.jpedsurg.2012.10.052
3. Kirkpatrick AW, Roberts DJ, De Waele J, Jaeschke R, Malbrain ML, De Keulenaer B, 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. doi: 10.1007/s00134-013-2906-z
4. Regner JL, Kobayashi L, Coimbra R. Surgical strategies for management of the open abdomen. *World J Surg.* (2012) 36:497–510. doi: 10.1007/s00268-011-1203-7
5. Balogh ZJ, Leppaniemi A. Patient populations at risk for intra-abdominal hypertension and abdominal compartment syndrome. *Am Surg.* (2011) 77(Suppl.1):S12–6.
6. Shanmugakrishnan RR, Loh CYY, Wakure A, El-Muttardi N. Serial abdominal closure with Gore-tex mesh and Rives-Stoppa for an open abdomen secondary to intra-abdominal hypertension in burns. *Indian J Plast Surg.* (2018) 51:324–6. doi: 10.4103/ijps.IJPS_75_18
7. Holodinsky JK, Roberts DJ, Ball CG, Blaser AR, Starkopf J, Zygun DA, et al. Risk factors for intra-abdominal hypertension and abdominal compartment syndrome among adult intensive care unit patients: a systematic review and meta-analysis. *Crit Care.* (2013) 17:R249. doi: 10.1186/cc13075
8. Coccolini F, Roberts D, Ansaloni L, Ivatury R, Gamberini E, Kluger Y, et al. The open abdomen in trauma and non-trauma patients: WSES guidelines. *World J Emerg Surg.* (2018) 13:7. doi: 10.1186/s13017-018-0167-4
9. Rogers WK, Garcia L. Intraabdominal hypertension, abdominal compartment syndrome, and the open abdomen. *Chest.* (2018) 153:238–50. doi: 10.1016/j.chest.2017.07.023
10. Augustin P, Lasocki S, Dufour G, Rode J, Karsenti A, Al-Attar N, et al. Abdominal compartment syndrome due to extracorporeal membrane oxygenation in adults. *Ann Thorac Surg.* (2010) 90:e40–1. doi: 10.1016/j.athoracsur.2010.06.039
11. Boulos FM, Pasrija C, DiChiacchio L, Rouse M, Raithel M, Mackowick K, et al. Early decompressive laparotomy for intra-abdominal hypertension following initiation of venovenous extracorporeal membrane oxygenation. *Asaio J.* (2019) 66:520–3. doi: 10.1097/MAT.0000000000001045
12. Bailey J, Shapiro MJ. Abdominal compartment syndrome. *Crit Care.* (2000) 4:23–9. doi: 10.1186/cc646
13. Sun K, Hancock BJ, Logsetty S. Ischemic bowel as a late sequela of abdominal compartment syndrome secondary to severe burn injury. *Plast Surg.* (2015) 23:218–20. doi: 10.1177/229255031502300407
14. Nirula R. Two case studies of cardiopulmonary effects of intra-abdominal hypertension. *Surg Clin North Am.* (2012) 92:1679–84. doi: 10.1016/j.suc.2012.08.017
15. Glowka TR, Schewe JC, Muenster S, Putensen C, Kalff JC, Pantelis D. Decompressive laparotomy for the treatment of the abdominal compartment syndrome during extracorporeal membrane oxygenation support. *J Crit Care.* (2018) 47:274–9. doi: 10.1016/j.jcrc.2018.07.024
16. Godat L, Kobayashi L, Costantini T, Coimbra R. Abdominal damage control surgery and reconstruction: world society of emergency surgery position paper. *World J Emerg Surg.* (2013) 8:53. doi: 10.1186/1749-7922-8-53
17. Kreis BE, de Mol van Otterloo AJ, Kreis RW. Open abdomen management: a review of its history and a proposed management algorithm. *Med Sci Monit.* (2013) 19:524–33. doi: 10.12659/MSM.883966
18. Leppäniemi AK. Laparostomy: why and when? *Critical Care.* (2010) 14:216. doi: 10.1186/cc8857
19. Davis J, Caruso DM, Foster KN, Matthews MR. A novel approach to sealing the denuded dermis of the abdominal wall with a negative pressure wound

device after a decompressive laparotomy. *J Burn Care Res.* (2018) 39:838–42. doi: 10.1097/BCR.0000000000000615
20. 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. doi: 10.1002/bjs.1800730514
21. Keramati M, Srivastava A, Sakabu S, Rumbolo P, Smock M, Pollack J, et al. The Wittmann Patch s a temporary abdominal closure device after decompressive celiotomy for abdominal compartment syndrome following burn. *Burns.* (2008) 34:493–7. doi: 10.1016/j.burns.2007.06.024
22. Koss W, Ho HC, Yu M, Edwards K, Ghows M, Tan A, 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. doi: 10.1016/j.jsurg.2008.12.003
23. Muhammad Y, Gondal KM, Khan UA. Use of the "bogota bag" for closure of open abdominal wound after exploratory laparotomy—our experience at Mayo Hospital Lahore. *J Pak Med Assoc.* (2016) 66:980–3.
24. Beale EW, Janis JE, Minei JP, Elliott AC, Phelan HA. Predictors of failed primary abdominal closure in the trauma patient with an open abdomen. *South Med J.* (2013) 106:327–31. doi: 10.1097/SMJ.0b013e31829243ed
25. McCann C, Adams K, Schizas A, George M, Barrett NA, Wyncoll DLA, et al. Outcomes of emergency laparotomy in patients on extracorporeal membrane oxygenation for severe respiratory failure: a retrospective, observational cohort study. *J Crit Care.* (2019) 53:253–7. doi: 10.1016/j.jcrc.2019.06.021

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Dynamic Fascial Closure With Vacuum-Assisted Wound Closure and Mesh-Mediated Fascial Traction (VAWCM) Treatment of the Open Abdomen—An Updated Systematic Review

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Introduction: Several different temporary abdominal closure techniques are described in the context of open abdomen treatment. Techniques based on dynamic fascial closure combined with negative pressure therapy have gained popularity and seem to result in the highest fascial closure rates without increased complications and are highlighted in recent guidelines and recommendations. One dynamic closure technique is the vacuum-assisted wound closure and mesh-mediated fascial traction (VAWCM) technique, first described in 2007. The aim of this systematic review was to evaluate the VAWCM technique regarding a number of short- and long-term results.

Materials and Methods: A systematic literature search was performed in PubMed, EMBASE, and Cochrane Library databases for articles published between January 1, 2006 and May 8, 2020. The review was independently performed by the two authors according to the PRISMA statements for reporting systematic reviews and meta-analyses. Results were pooled for presentation of weighted means when applicable.

Results: A total of 220 articles were screened by title and abstract. Thirty-two articles were assessed for eligibility by full-text review and 15 articles finally remained for review. A total of 600 patients treated with VAWCM were included. The pooled weighted means were as follows: fascial closure, 83.5%; enteroatmospheric fistula, 5.6%; planned ventral hernia, 6.2%; in-hospital survival, 72%; and incisional hernia incidence, 40.5%. Long-term survival ranged between 22 and 72%. Quality of life (SF-36) was reported in two studies showing lower scores than the population mean especially in physical domains. Incisional hernia resulted in lower scores in one but not in the other study.

Discussion: The results of 600 VAWCM-treated patients from 15 studies were evaluated in this systematic review. Earlier findings with high fascial closure rates, low

enteroatmospheric fistula, and planned ventral hernia rates as well as high incisional hernia incidences were underlined. Permanent mesh for efficient fascial traction and reinforcement at fascial closure seem to be the next step in evolving an optimal temporary closure technique in open abdomen treatment.

Keywords: open abdomen, negative pressure wound therapy (NPWT), vacuum assisted wound closure and mesh-mediated fascial traction, VAWCM, dynamic closure technique, temporary abdominal closure (TAC)

INTRODUCTION

Emergency conditions sometimes force surgeons to leave an abdominal incision unclosed and thereby initiating a period of open abdomen (OA) therapy. Meanwhile, a temporary abdominal closure (TAC) technique is used to protect the abdominal contents and to facilitate closure whenever intraabdominal and patient's overall condition is suitable. Causes for OA treatment can roughly be classified into four categories: (1) visceral edema and/or intraabdominal/retroperitoneal swelling with reduced intraabdominal space, making it mechanically impossible to close the abdomen; (2) intraabdominal deep infection/peritonitis needing active drainage; (3) damage control and/or planned second look operation; and (4) indication for decompression in case of abdominal hypertension or compartment syndrome (1). Due to the critical conditions in these patients, it is important that the utilized TAC technique minimizes the risk of complications related to the OA, since prolonged periods of treatment are associated with increased morbidity and mortality. Older static TAC techniques, e.g., Bogota bag or placement of a temporary mesh, did not facilitate closure and frequently resulted in large planned ventral hernias and concomitant morbidity.

With the introduction of negative pressure wound therapy (NPWT), the OA treatment techniques started to evolve. The novel vacuum-assisted wound closure and mesh-mediated facial traction (VAWCM) technique, combining negative pressure wound therapy and fascial traction, was described from our department in 2007 (2). The VAWCM technique was evaluated in a prospective multi-center cohort study presenting a fascial closure rate per protocol of 89%. However, long-term follow up showed a 54% incisional hernia (IH) incident in patients surviving 5 years, with a need for surgical repair in one third (3).

After the introduction of the VAWCM technique, several authors have adopted the technique and published their results. In a review article in 2017 (4), 11 studies evaluating the VAWCM technique was included with high fascial closure rates reported in most populations, while long-term IH development was only reported in 3. In these populations, high IH incidence after VAWCM was evident.

The European Hernia Society (EHS) published guidelines for OA treatment in 2018 (5), recommending the use of dynamic closure techniques. A recent review (6) on articles including short-term outcome of dynamic closure techniques published during the last 3 years updated the search done in the EHS guidelines and reported similar results for the different included dynamic closure techniques. In that review, the VAWCM technique dominated among the dynamic closure techniques. Furthermore, the World Society of Emergency Surgery (WSES) together with the Abdominal Compartment Society (WSACS) also recommend a dynamic closure technique with VAWCM to be used for OA treatment (7). The review and guideline articles share the conclusion that evidence in OA treatment is weak (5–7). A probable explanation is the low incidence of OA treatment per center together with the vast heterogeneity among OA patients and thereby great difficulties in performing randomized trials.

When fascial closure can be achieved in a high number of patients, the importance of evaluation of long-term results becomes evident. The purpose of this systematic review, performed in accordance with the PRISMA recommendations, is to update the present evidence for OA treatment with the VAWCM technique regarding short- and long-term results, with special attention to long-term outcome.

MATERIALS AND METHODS

Electronic database searches from January 1, 2006 to May 8, 2020 were conducted in MEDLINE (PubMed), EMBASE, and Cochrane Library Online with the purpose to identify all publications in English on OA treatment with the VAWCM technique. For detailed search terms, see **Supplementary Material**.

The review was performed according to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines (8). The articles identified from the searches were initially screened for removal of duplicates and thereafter for inclusion on titles and abstracts. Full-text articles were assessed for eligibility whereafter the reference lists of these papers were scrutinized for additional eligible articles. Furthermore, reference lists from identified guideline articles on the matter were scrutinized. All articles, regardless of evidence level, were considered eligible for inclusion. Case reports with <5 patients, reviews, and guidelines were excluded. Furthermore, articles where major modifications of the VAWCM technique were utilized were excluded. The selection process was done by the two authors independently, and articles were included in mutual agreement.

Patient characteristics for the study populations (age, number of patients, and pathogenesis) were noted. Outcome variables of interest were fascial closure rate, time to fascial closure, number of dressing changes, enteroatmospheric fistula (EAF), and planned ventral hernia incidence, in-hospital survival and mortality, follow-up time, IH development and repair, long-time survival rate, and quality of life (QoL). Absence of data on some of the abovementioned outcome variables was not

cause for exclusion. In some studies, another TAC technique besides VAWCM was used for some of the patients. From such articles, the results for VAWCM-treated patients were extracted and included.

The Vacuum-Assisted Wound Closure and Mesh-Mediated Facial Traction (VAWCM) Technique

The VAWCM technique was described in detail by Petersson et al. (2). In summary, if an OA cannot be closed at the first dressing change, the mesh is applied and mesh-mediated fascial traction is started. A heavyweight polypropylene mesh is divided into two halves and sutured with a 2–0 running polypropylene suture with narrow bites to the fascial edges in an in-lay position on each side, whereafter the intraabdominal visceral protection layer of the NPWT system is applied. It is crucial that the visceral protection layer is tucked out as far laterally as possible to prevent adhesion formation between the intraabdominal content and the abdominal wall. The two mesh halves are thereafter pulled together under tension and sutured in the midline. The mesh-mediated tension on the abdominal wall prevents retraction of the lateral muscles, facilitating closure. The subcutaneous polyurethane foam is then placed between the abdominal wall edges, whereafter occlusive self-adhesive polyethylene films are applied to seal the wound. The tubing set is then applied, and the therapy unit of the NPWT system is set to −125 to −150 mmHg with continuous pressure.

Every 48–72 h, the abdominal dressing is changed. The tubing set, occlusive self-adhesive polyethylene films, and subcutaneous polyurethane foams are removed, and the mesh halves are opened in the midline. The intraabdominal visceral protection layer is removed. When the abdominal cavity has been carefully inspected and loose adhesions are divided, a new intraabdominal visceral protection layer is placed, and the mesh halves are re-sutured under tension in the midline. It is important to try to reduce the diastasis at each dressing change.

When the fascial edges can be aligned in the midline, the mesh is removed by cutting the running suture holding the mesh in the in-lay position and the incision is then closed by a running absorbable suture, carefully following the principles of a suture-to-wound ratio of 4:1.

Statistics

Data from the different studies were pooled for description of weighted averages when applicable.

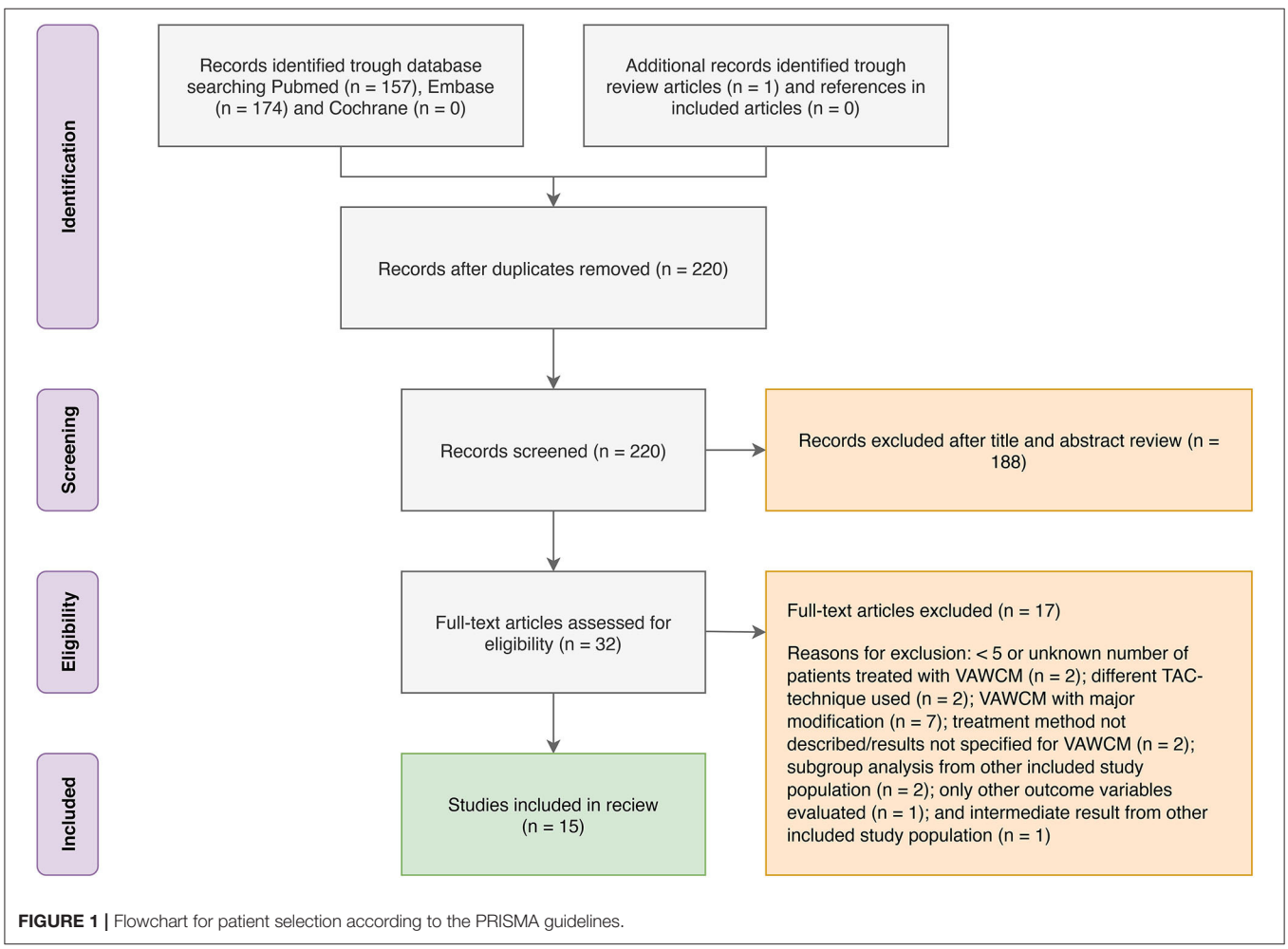

FIGURE 1 | Flowchart for patient selection according to the PRISMA guidelines.

RESULTS

The MEDLINE (PubMed) search yielded 157 articles, the EMBASE search yielded 174 articles, and the Cochrane Library search yielded 0 articles. The identified articles were screened for duplicates, and the remaining 220 articles were screened by title and abstract. Of those, 32 articles were assessed for eligibility by full-text review. After exclusion, 15 articles were included in the review. Some of the articles only included parts of the outcome variables of interest for this review. Reasons for exclusion of full-text reviewed articles were as follows: <5 or unknown number of patients treated with VAWCM ($n = 2$); a different TAC technique was used ($n = 2$); VAWCM with major modification ($n = 7$); treatment method not described/results not specified for VAWCM ($n = 2$); subgroup analysis from other included study population ($n = 2$); only other outcome variables evaluated ($n = 1$); and intermediate result from other included study population ($n = 1$). For details, see the PRISMA flow diagram (**Figure 1**).

Study and Patient Characteristics

Of the 15 articles included, 6 were prospective (3, 9–13) and 9 were retrospective (2, 14–21). No study was randomized, and most studies were observational with only one treatment group. Four reports (15, 18, 19, 21) included other techniques beside VAWCM, from which the VAWCM results were extracted. The study populations ranged between 7 and 111 with a mean of 40, and 600 patients were totally included (2, 3, 9–21). Thirteen articles included surgical patients, some in combination with vascular and/or trauma patients, one included only vascular patients, and the last article only included patients with peritonitis. For details on the included articles and patient characteristics, see **Table 1**.

Short-Term Results

Twelve of fifteen articles reported on short-term outcomes (see **Tables 2**, **4**). The fascial closure rate per protocol varied between 50 and 100% (2, 9, 10, 13–21) with a pooled weighted average rate, for 11 studies, of 83.5%. Time to fascial closure varied between 7 and 32 days, and the number of dressing changes between 2 and 10. EAF development was seen in 0–12% (2, 9, 10, 13–17, 20) with a pooled weighted average of 5.6% and planned ventral hernia incidence varied between 0 and 50% (2, 9, 10, 13–16, 18, 20, 21) with a pooled weighted average of 6.2%. The pooled in-hospital survival was 72% with range between 55 and 87% (2, 9, 10, 13–17, 20).

Long-Term Results

Six of fifteen articles reported on long-term outcomes (see **Tables 3**, **4**). The follow-up time was 17–63 months (3, 9, 11, 12, 16, 21). IH rate was 21–54% (3, 9, 11, 16, 21), and the pooled weighted average was 40.5%. IH repair, in the two studies reporting on this, was 33 and 42%, respectively (3, 11). The survival rate at follow-up was reported in four studies and ranged between 22 and 72% (3, 11, 16, 21). Two articles presented data on QoL using the SF-36 questionnaire. In one of the studies (3), both component scores and all subscales except bodily pain were lower than the population mean and correlated with major comorbidity and the presence of a stoma. In that study, no differences in SF-36 scores were found between patients with and without an IH. Neither did abdominal wall discomfort differ in relation to IH, when evaluated with the Ventral Hernia Pain Questionnaire. In the other study (12), lower scores for role physical, physical function, and physical component score were reported and correlated with the complex intensive care score being a surrogate marker of severity of global illness. Patients with an IH scored lower than the total study population as well as the population mean in the same domains.

DISCUSSION

This is an update of the review on VAWCM-treated patients published in 2017 (4). In this review, five additional studies meeting our inclusion criteria have been included (12, 14, 17, 20, 21), adding data on both short- and long-term outcomes. Fifteen articles were included in this review displaying great heterogeneity among patients with different pathogeneses, comorbidities, and causes for OA therapy.

Optimization in the management of OA patients, whether treated with VAWCM or other TAC techniques, is of fundamental importance for the results and must be emphasized. The desire to close the OA as quickly as possible, to prevent complications induced by the OA as such, must be balanced against organ dysfunction needing further decompression, the possibilities of accomplishing negative fluid balance for reducing visceral edema, the need of further drainage, or delayed reconstructive measures. While taking this into consideration, the surgical performance needs to be optimized. For VAWCM, this implies starting the traction early during OA treatment and performing every dressing change and mesh tightening procedure in time with the intention and skill to reduce the fascial diastasis successively, i.e., every 2–3 days, daytime by a surgeon familiar with the technique and for a long enough period of time to achieve fascial medialization and closure. By own experience, we know that it can be hard to comply with these prerequisites for optimal utilization of the VAWCM technique, which, however, must be strived for in order to improve outcome. Besides the almost unanimous compliance with dressing change intervals, it is not possible to evaluate the other important factors in the included studies.

The review revealed per-protocol fascial closure rates between 50 and 100%. Failure of fascial closure necessitates an alternative measure when terminating the OA. The alternatives utilized in the included studies have been leaving the patient with a large planned ventral hernia, closure with mesh bridging, or fascial closure with component separation. The incidence of planned ventral hernias varied between 0 and 50% (2, 9, 10, 13–16, 18, 20, 21) with a pooled weighted average of 6.2%. The use of mesh bridging (10, 16, 18, 21) or component separation (20) lowered the planned ventral hernia rate but was not part of the basic idea of the VAWCM technique and must be considered a failure in evaluation of the technique. This vast variation in closure and planned ventral hernia rates might depend on

TABLE 1 | Included articles and patient characteristics.

References	Article title	Author (year)	Study design	Inclusion period	VAWCM patients (*n*)	Type of patients	Age, years (median)	Long-term follow-up
(2)	Vacuum-assisted wound closure and mesh-mediated fascial traction—a novel technique for late closure of the open abdomen	Petersson et al. (2007)	Retrospective	2005–2006	7	Surgical, vascular, trauma	65	No
(9)	Early results after treatment of open abdomen after aortic surgery with mesh traction and vacuum-assisted wound closure	Seternes et al. (2010)	Prospective	2006–2009	9	Vascular	70	Yes
(10)	Multicenter prospective study of fascial closure rate after open abdomen with vacuum and mesh-mediated fascial traction	Acosta et al. (2011)	Prospective	2006–2009	111	Surgical, vascular, trauma	68	No
(14)	Promising results after vacuum-assisted wound closure and mesh-mediated fascial traction	Kleif et al. (2012)	Retrospective	2009–2011	16	Surgical, non-trauma	66	No
(15)	Vacuum and mesh-mediated fascial traction for primary closure of the open abdomen in critically ill surgical patients	Rasilainen et al. (2012)	Retrospective	2008–2010	50	Surgical (ACS 47%)	60	No
(16)	Vacuum with mesh is a feasible temporary closure device after fascial dehiscence	Bjørsum-Meyer et al. (2013)	Retrospective	2008–2012	18	Surgical	64	Yes
(13)	Management of the open abdomen using vacuum-assisted wound closure and mesh-mediated fascial traction	Willms et al. (2015)	Prospective	2006–2012	53	Surgical, trauma	53 (mean)	No
(3)	Quality of life and hernia development 5 years after open abdomen treatment with vacuum-assisted wound closure and mesh-mediated fascial traction	Petersson et al. (2016)	Prospective	2006–2009	50	Surgical, vascular, trauma	70	Yes
(17)	Retrospective analysis of a VACM (vacuum-assisted closure and mesh-mediated fascial traction) treatment manual for temporary abdominal wall closure—results of 58 consecutive patients	Beltzer et al. (2016)	Retrospective	2007–2008	31	Surgical	67	No
(11)	Abdominal wall integrity after open abdomen: long-term results of vacuum-assisted wound closure and mesh-mediated fascial traction (VAWCM)	Willms et al. (2016)	Prospective	2006–2013	34	Surgical, trauma	56 (mean)	Yes
(18)	Greater success of primary fascial closure of the open abdomen: A retrospective study analyzing applied surgical techniques, success of fascial closure, and variables affecting the results	Kääriäinen et al. (2017)	Retrospective	2009–2013	30	Surgical, Vascular	–	No
(19)	Open abdomen treated with negative pressure wound therapy: Indications, management and survival	Seternes et al. (2017)	Retrospective	2006–2014	92	Vascular, surgical, trauma (ACS 44%)	–	No

(Continued)

TABLE 1 | Continued

References	Article title	Author (year)	Study design	Inclusion period	VAWCM patients (*n*)	Type of patients	Age, years (median)	Long-term follow-up
(20)	Open abdomen with vacuum-assisted wound closure and mesh-mediated fascial traction in patients with complicated diffuse secondary peritonitis: A single-center 8-year experience	Tolonen et al. (2017)	Retrospective	2008–2016	41	Peritonitis	59	No
(12)	Intensive care and health outcomes of open abdominal treatment: long-term results of vacuum-assisted wound closure and mesh-mediated fascial traction (VAWCM)	Willms et al. (2017)	Prospective	2006–2013	27	Surgical, trauma	56 (mean)	Yes
(21)	Blurring the boundary between open abdomen treatment and ventral hernia repair	Käser et al. (2019)	Retrospective	2013–2015	31	Surgical, septic peritonitis	58	Yes

patient and pathogenic heterogeneity, but the ability to utilize and perform the technique in an optimal way in each patient is likely to contribute to the differences to an even larger extent. Nevertheless, the high weighted average closure rate of 83.5% must be considered a good result, implying that the VAWCM technique is reproducible and relatively simple.

A feared complication during OA therapy is the development of an EAF, which has been shown to be a significant predictor of failure of fascial closure and possibly also of mortality in OA patients (10, 22) even if an interim analysis from the International Registry of Open Abdomen did not find any EAF impact on mortality (23). A word of caution was raised when NPWT for OA treatment was popularized (24, 25). A damaging effect of the negative pressure, supposed to propagate to the bowel surface, was proposed to be the pathogenic mechanism. With use of a visceral protective layer, it appears as the negative pressure propagation to the bowel surface is significantly reduced, independently of preset negative pressure, according to the results of an experimental porcine study (26). The concern for NPWT-induced EAF development has later been toned down as a result of increased experience with the technique and succeeding publications stating that the use of NPWT in OA patients, on the contrary, seems to reduce the incidence of EAF compared to non-NPWT-treated patients, especially when combining NPWT with fascial traction (27). In this review, the weighted average for EAF formation was 5.6% (range 0–12%), which is in the lower range of earlier published results for OA treatment, regardless of treatment technique (23, 27). Multiple studies have, as shown in this review, evaluated the VAWCM technique without finding proof of problematic EAF formation rates.

The weighted average for in-hospital survival for patients treated with VAWCM in this review was 72%, i.e., 28% in-hospital mortality, which is in line with other reports. For comparison, a systematic review (28) reported in-hospital mortality rates, from 12 studies including 2733 patients, between 14 and 59% with a weighted average mortality rate of 31.3%.

The short-term results in this updated review strengthen the previously found high fascial closure rates, low planned ventral hernia and EAF rates.

Long-term results were reported in six articles with median follow-up of 17–63 months. IH rates were reported in five studies ranging from 21 to 54% at the latest follow-up occasion (3, 9, 11, 16, 21), resulting in a weighted average of 40.5%. Clinical examination was the basis for IH diagnosis in three of the studies. In two of the three prospective studies, the protocol included a CT scan (3) or an ultrasound (11) contributing to higher sensitivity in IH diagnosis (3). These two studies had a reasonable number of patients eligible for follow-up and reported 54 and 35% IH, respectively (3, 11). The high IH rates and the resulting 30–40% IH repair rate from the former review on the technique was thereby underlined. IH rates in the same range have been reported after use of other fascial traction techniques not including any fascial reinforcement at definitive closure (29, 30).

Long-term survival varied largely, from 22 to 73%, in the four studies reporting on this (3, 11, 16, 21). This most certainly accounts for differences in age, comorbidities, and causes for OA treatment, and a major loss to follow-up must be anticipated whenever OA long-term results are to be evaluated.

Only two articles reported on QoL, and both showed that patients treated with OA had lower SF-36 scores than the population mean (3, 12), but the presence of an IH influenced the scores negatively only in one of the studies. In one of the studies (3), the scores were overall lower than the Swedish population mean and correlated with major comorbidity and the presence of a stoma but not with the presence of an IH. Furthermore, no differences in abdominal wall discomfort were found between patients with and without an IH when evaluated with the Ventral Hernia Pain Questionnaire. In the other study (12), lower scores than the German population mean for physical domains were reported and correlated with the complex intensive care score being a surrogate marker of severity of global illness. Patients

TABLE 2 | Short-term outcome.

References	Author (year)	Patients alive at OA closure	FC per protocol, %*	Time to closure, days (median)	Dressing changes, *n* (median)	EAF (%)*	Closure with mesh bridging (%)†	Closure with adjunct CS (%)	Small fascial defect at closure (%)±	Planned ventral hernia*	In-hospital survival (%)*
(2)	Petersson et al. (2007)	7	100	32	10	0	0	0	0	0	86
(9)	Seternes et al. (2010)	8	100	10.5	3	0	0	0	0	0	66
(10)	Acosta et al. (2011)	95	89.5	14	4	6.3	8.4	0	2.1	0	70
(14)	Kleif et al. (2012)	14	50	10	4	0	0	0	0	50	87
(15)	Rasilainen et al. (2012)	42	92.9	9	3.5	12	0	0	0	7.1	62
(16)	Bjørsum-Meyer et al. (2013)	15	80	21	3	0	13.3	0	0	6.7	83
(13)	Willms et al. (2015)	47	89.4	10	6.2 (mean)	1.8	0	0	0	10.6	87
(17)	Beltzer et al. (2016)	31	61	–	–	6.5	–	–	–	–	55
(18)	Kääriäinen et al. (2017)	30	83.3	20.6 (mean)	–	–	10	0	0	6.7	–
(19)	Seternes et al. (2017)	–	84	–	–	–	–	–	–	–	–
(20)	Tolonen et al. (2017)	36	83.3	7	2	7.3	0	8.3	2.8	5.6	71
(21)	Käser et al. (2019)	31	58	–	5	–	42	0	0	0	–

*FC, Facia closure; EAF, enteroatmospheric fistula; CS, component separation. *Outcome included in the pooled data presented in **Table 4**. †Closure with mesh bridging when fascial closure was not possible. ‡Facial closure without mesh was achieved after component separation. ±Fascial closure achieved in major part of the incision with smaller fascial defect remaining.*

TABLE 3 | Long-term results.

References	Author (year)	Follow-up time, months (median)	Patients eligible for follow-up (*n*)	IH after FC (%)*	IH repair (% of IH)*	Long-term survival (%)	QoL comments
(9)	Seternes et al. (2010)	17	6	38	–	–	–
(16)	Bjørsum-Meyer et al. (2013)	21	14	21	–	72.2	–
(3)	Petersson et al. (2016)	63	50	54	33	49.5	SF-36: Generally lower scores except BP. No difference between IH and non-IH.
(11)	Willms et al. (2016)	46	34	35	42	73	–
(12)	Willms et al. (2017)	46	–	–	–	–	SF-36: Lower physical domains. Hernia patients had lower PF, GH, and PCS than others.
(21)	Käser et al. (2019)	24	9	22	–	22	–

*IH, Incisional hernia; QoL, Quality of Life. *Outcome included in the pooled data presented in **Table 4**.*

TABLE 4 | Pooled data.

Outcome variable	Pooled result* (%)
Fascia closure rate per protocol	83.5
Enteroatmospheric fistula	5.6
Planned ventral hernia	6.2
In-hospital survival	72.0
Incisional hernia after fascia closure	40.5
Incisional hernia repair	35.8

See **Tables 2, **3** for included article.*

with an IH scored lower than the total study population as well as population mean in the same domains. In view of the sparse information on QoL after OA treatment found in the literature, it is of importance to include QoL evaluation in upcoming study protocols.

Articles reporting on long-term results was six, which is twice the number compared to the earlier review (4). A high IH rate was underlined, but data on QoL were only added from one study indicating a lower QoL after OA treatment than in the population mean.

Reporting weighted averages or pooled outcomes provides a more accurate view of the combined results from many studies with a wide range of included patients, but this review also has several weaknesses attached. No article on the VAWCM technique was randomized, and more than half of the articles were retrospective with low to very low evidence level. Heterogeneity in pathogenesis, severity of illness, and patient characteristics together with a relatively infrequent use of OA at a single institution are reflected in the quality of many of the included studies and also inflict problems in conducting good RCTs and thereby improve the level of evidence in this research area. Four reports (15, 18, 19, 21) included other techniques beside VAWCM, and results for VAWCM had to be extracted, which may inflict a risk of misinterpretation of data. Intention-to-treat analyses were not possible due to missing data, and therefore, results per protocol on patients surviving until fascial closure was attempted were the only option for many of the outcome variables. There is also a minor risk that a small number of patients may be reported in more than one article, but where the suspicion was obvious, only one of the reports were included.

Conclusion

Dynamic fascial closure combined with NPWT, as in the VAWCM technique, seems to provide the best OA treatment results according to today's knowledge, albeit mostly based on weak evidence (5–7). The VAWCM technique is not the only technique based on this combination but mesh-mediated fascial traction plus NPWT is today best evaluated with high fascial closure rates, low EAF and planned ventral hernia rates, but high IH rates. The future challenges for mesh-mediated fascial traction plus NPWT-based techniques are short term to further increase fascial closure and long term to reduce IH rates. Permanent mesh for traction and reinforcement at fascial closure may solve both of these problems but need to be prospectively evaluated (1, 31, 32).

DATA AVAILABILITY STATEMENT

The original contributions generated for the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

AUTHOR CONTRIBUTIONS

PP and UP: contribution to the conception of the work, the acquisition, analysis, and interpretation of data, drafting the work, final approval of the version to be published, and

agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors contributed to the article and approved the submitted version.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fsurg.2020.577104/full#supplementary-material

REFERENCES

1. Petersson P, Montgomery A, Petersson U. Vacuum-assisted wound closure and permanent onlay mesh–mediated fascial traction: a novel technique for the prevention of incisional hernia after open abdomen therapy including results from a retrospective case series. *Scand J Surg.* (2018) 108:1457496918818979. doi: 10.1177/1457496918818979
2. 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. doi: 10.1007/s00268-007-9222-0
3. Petersson U, Bjarnason T, Bjorck M, Montgomery A, Rogmark P, Svensson M, et al. Quality of life and hernia development 5 years after open abdomen treatment with vacuum-assisted wound closure and mesh-mediated fascial traction. *Hernia.* (2016) 20:755–64. doi: 10.1007/s10029-016-1516-4
4. Acosta S, Björck M, Petersson U. Vacuum-assisted wound closure and mesh-mediated fascial traction for open abdomen therapy — a systematic review. *Anaesthesiol Intensive Ther.* (2016) 49:139–45. doi: 10.5603/AIT.a2017.0023
5. López-Cano M, García-Alamino JM, Antoniou SA, Bennet D, Dietz UA, Ferreira F, et al. EHS clinical guidelines on the management of the abdominal wall in the context of the open or burst abdomen. *Hernia.* (2018) 22:921–39. doi: 10.1007/s10029-018-1818-9
6. Poortmans N, Berrevoet F. Dynamic closure techniques for treatment of an open abdomen: an update. *Hernia.* (2020) 24:325–31. doi: 10.1007/s10029-020-02130-9
7. Coccolini F, Roberts D, Ansaloni L, Ivatury R, Gamberini E, Kluger Y, et al. The open abdomen in trauma and non-trauma patients: WSES guidelines. *World J Emerg Surg.* (2018) 13:7. doi: 10.1186/s13017-018-0167-4
8. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Bmj Clin Res Ed.* (2009) 339:b2535. doi: 10.1136/bmj.b2535
9. 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.* (2010) 40:60–64. doi: 10.1016/j.ejvs.2010.02.018
10. Acosta S, Bjarnason T, Petersson U, Palsson B, Wanhainen A, Svensson M, et al. Multicentre prospective study of fascial closure rate after open abdomen with vacuum and mesh-mediated fascial traction. *Brit J Surg.* (2011) 98:735–43. doi: 10.1002/bjs.7383
11. Willms A, Schaaf S, Schwab R, Richardsen I, Bieler D, Wagner B, et al. Abdominal wall integrity after open abdomen: long-term results of vacuum-assisted wound closure and mesh-mediated fascial traction (VAWCM). *Hernia.* (2016) 20:849–58. doi: 10.1007/s10029-016-1534-2
12. Willms A, Schaaf S, Schwab R, Richardsen I, Jänig C, Bieler D, et al. Intensive care and health outcomes of open abdominal treatment: long-term results of vacuum-assisted wound closure and mesh-mediated fascial traction (VAWCM). *Langenbeck's Arch Surg.* (2017) 402:481–92. doi: 10.1007/s00423-017-1575-8
13. Willms A, Güsgen C, Schaaf S, Bieler D, Websky M, Schwab R. Management of the open abdomen using vacuum-assisted wound closure and mesh-mediated fascial traction. *Langenbeck's Arch Surg.* (2015) 400:91–9. doi: 10.1007/s00423-014-1240-4
14. Kleif J, Fabricius R, Bertelsen CA, Bruun J, Gogenur I. Promising results after vacuum-assisted wound closure and mesh-mediated fascial traction. *Danish Med J.* (2012) 59:A4495.
15. Rasilainen SK, Mentula PJ, Leppäniemi 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. doi: 10.1002/bjs.8914
16. Bjørsum-Meyer T, Skarbye M, Jensen KH. Vacuum with mesh is a feasible temporary closure device after fascial dehiscence. *Dan Med J.* (2013) 60:A4719.
17. Beltzer C, Eisenächer A, Badendieck S, Doll D, Küper M, Lenz S, et al. Retrospective analysis of a VACM (vacuum-assisted closure and mesh-mediated fascial traction) treatment manual for temporary abdominal wall closure – results of 58 consecutive patients. *Gms Interdiscip Plastic Reconstr Surg DGPW.* (2016) 5:Doc19. doi: 10.3205/iprs000098
18. Kaariainen M, Kuuskeri M, Helminen M, Kuokkanen H. Greater success of primary fascial closure of the open abdomen: a retrospective study analyzing applied surgical techniques, success of fascial closure, and variables affecting the results. *Scand J Surg.* (2017) 106:145–51. doi: 10.1177/1457496916665542
19. Seternes A, Rekstad LC, Mo S, Klepstad P, Halvorsen DL, Dahl T, et al. Open abdomen treated with negative pressure wound therapy: indications, management and survival. *World J Surg.* (2017) 41:152–61. doi: 10.1007/s00268-016-3694-8
20. Tolonen M, Mentula P, Sallinen V, Rasilainen S, Bäcklund M, Leppäniemi A. Open abdomen with vacuum-assisted wound closure and mesh-mediated fascial traction in patients with complicated diffuse secondary peritonitis: a single-center 8-year experience. *J Trauma Acute Care Surg.* (2017) 82:1100–5. doi: 10.1097/TA.0000000000001452
21. Kaser SA, Brosi P, Clavien PA, Vonlanthen R. Blurring the boundary between open abdomen treatment and ventral hernia repair. *Langenbeck's Arch Surg.* (2019) 404:489–94. doi: 10.1007/s00423-019-01757-2
22. Acosta S, Seternes A, Venermo M, Vikatmaa L, Sörelius K, Wanhainen A, et al. Open abdomen therapy with vacuum and mesh mediated fascial traction after aortic repair: an international multicentre study. *European J Vasc Endovasc Surg.* (2017) 54:697–705. doi: 10.1016/j.ejvs.2017.09.002
23. Coccolini F, Ceresoli M, Kluger Y, Kirkpatrick A, Montori G, Salvetti F, et al. Open abdomen and entero-atmospheric fistulae: an interim analysis from the international register of open abdomen (IROA). *Injury.* (2019) 50:160–6. doi: 10.1016/j.injury.2018.09.040
24. Barker JA, Carlson GL. Managing the open wound: indications for topical negative pressure therapy. *Surg Oxf.* (2011) 29:507–12. doi: 10.1016/j.mpsur.2011.06.008
25. 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. doi: 10.1111/j.1463-1318.2006.01154.x
26. 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. doi: 10.1007/s00268-010-0937-y
27. Atema JJ, Gans SL, Boermeester MA. Systematic review and meta-analysis of the open abdomen and temporary abdominal closure techniques in non-trauma patients. *World J Surg.* (2015) 39:912–25. doi: 10.1007/s00268-014-2883-6
28. Cristaudo A, Jennings S, Gunnarsson R, DeCosta A. Complications and mortality associated with temporary abdominal closure techniques: a systematic review and meta-analysis. *Am Surg.* (2017) 83:191–216. doi: 10.1177/000313481708300220
29. Brandl A, Laimer E, Perathoner A, Zitt M, Pratschke J, Kafka-Ritsch R. Incisional hernia rate after open abdomen treatment with negative pressure and delayed primary fascia closure. *Hernia.* (2014) 18:105–11. doi: 10.1007/s10029-013-1064-0
30. Hofmann AT, Gruber-Blum S, Lechner M, Petter-Puchner A, Glaser K, Fortelny R. Delayed closure of open abdomen in septic patients treated with negative pressure wound therapy and dynamic fascial

suture: the long-term follow-up study. *Surg Endosc.* (2017) 31:4717–24. doi: 10.1007/s00464-017-5547-4

31. Jakob MO, Schwarz C, Haltmeier T, Zindel J, Pinworasarn T, Candinas D, et al. Mesh-augmented versus direct abdominal closure in patients undergoing open abdomen treatment. *Hernia.* (2018) 22:785–92. doi: 10.1007/s10029-018-1798-9
32. Salamone G, Licari L, Guercio G, Comelli A, Mangiapane M, Falco N, et al. Vacuum-assisted wound closure with mesh-mediated fascial traction achieves better outcomes than vacuum-assisted wound closure alone: a comparative study. *World J Surg.* (2018) 42:1679–86. doi: 10.1007/s00268-017-4354-3

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METHODS
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Prophylactic Onlay Mesh Implantation During Definitive Fascial Closure After Open Abdomen Therapy (PROMOAT): Absorbable or Non-absorbable? Methodical Description and Results of a Feasibility Study

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Introduction: Incisional hernia development after open abdomen therapy (OAT) remains a common complication in the long run. To demonstrate the feasibility, we describe our method of prophylactic onlay mesh implantation with definitive fascial closure after open abdomen therapy (PROMOAT). To display the feasibility of this concept, we evaluated the short-term outcome after absorbable and non-absorbable synthetic mesh implantation as prophylactic onlay.

Material and Methods: Ten patients were prospectively enrolled, and prophylactic onlay mesh (long-term absorbable or non-absorbable) was implanted at the definitive fascial closure operation. The cohort was followed up with a special focus on incisional hernia development and complications.

Results: OAT duration was 21.0 ± 12.6 days (95% CI: 16.9–25.1). Definitive fascial closure was achieved in all cases. No incisional hernias were present during a follow-up interval of 12.4 ± 10.8 months (range 1–30 months). Two seromas and one infected hematoma occurred. The outcome did not differ between mesh types.

Conclusion: The prophylactic onlay mesh implantation of alloplastic, long-term absorbable, or non-absorbable meshes in OAT showed promising results and only a few complications that were of minor concern. Incisional hernias did not occur during follow-up. To validate the feasibility and safety of prophylactic onlay mesh implantation long-term data and large-scaled prospective trials are needed to give recommendations on prophylactic onlay mesh implantation after OAT.

Keywords: open abdomen, prophylactic mesh, incisional hernia, onlay, laparotomy

INTRODUCTION

Open abdomen therapy (OAT) is defined as the deliberate decision not to close the fascia at the end of laparotomy (1). This treatment strategy is an established cornerstone in the surgical management of critically ill patients with intraabdominal pathologies to reduce surgical traumatization. It has been shown that OAT reduces morbidity and mortality in patients with depleted systemic resources due to severe abdominal trauma or gastrointestinal disease (2).

The primary treatment goal is the sequential control of infectious or traumatic foci. Secondarily, the key issues are swift fascial closure and the prevention of enteroatmospheric fistulas (1). Vacuum-assisted wound closure nd mesh-mediated fascial traction (VAWCM) and other OAT techniques, which combine the synergistic effects of negative pressure wound therapy and dynamic fascial traction are the best available options for OAT nowadays (3). However, repetitive abdominal surgeries are necessary, which results in reasonable cumulative traumatization of the abdominal wall.

Incisional hernias are common complications of abdominal surgery with a reported incidence of at least 3–20% after laparotomies (4). Little is published on the specific aspects of incisional hernia development after OAT; however some monocentric retrospective studies showed the incisional hernia incidence after OAT to be far higher (35–66%) than after regular laparotomies (5–9). The development of incisional hernias depends on various factors such as surgical technique (e.g., incision type, suture technique, and material) or comorbidity (i.e., aortic aneurysm, obesity) (10, 11).

Incisional hernia development is associated with an impaired outcome, as the functional properties of the abdominal wall are altered, incarceration and emergency surgeries are omnipresent risks, and pain is a frequent symptom (12). Research data showed the reduced quality of life (SF36 questionnaire) in patients with an incisional hernia after OAT (5). Moreover, hernia repair itself comes with remarkable perioperative risks, especially if complex abdominal wall reconstruction becomes necessary due to giant hernias with an intestinal loss of domain condition (13).

Prophylactic mesh implantation is shown to be beneficial in high-risk patients with midline laparotomies (14, 15). Risk factors in that context are considered to be either patient-specific or surgery-relates. The former ones include factors such as obesity, connective tissue disorders or aortic aneurysms, diabetes, smoking, and corticosteroid medication (16). The most relevant factor associated with the surgical procedure itself is the actual technique of how fascial closure is obtained. The European Hernia Society has given recommendations on fascial closure, which involve the use of long-term absorbable sutures and a suture length to wound length (SL:WL) ratio of at least 4:1 (9, 11, 17).

A remarkable amount of evidence on prophylactic mesh implantation in high-risk patients after laparotomies has been grown (14, 17). Borab et al., for example, reported a reduction of incisional hernia risk of 85% (15). However, this comes at the cost of a higher seroma rate. These results were recently confirmed for emergency laparotomies, as well (16). Put these findings together; it seems reasonable to suppose that the fascial closure after OAT is a similar high-risk situation, both in terms of patient-specific or surgical-technical factors (11).

Currently, there is no evidence on prophylactic mesh implantation during delayed primary fascial closure operation after OAT. To display the feasibility of prophylactic onlay mesh implantation after OAT (PROMOAT), we evaluated the short-term outcome after absorbable and non-absorbable synthetic mesh implantation as prophylactic onlay.

MATERIALS AND METHODS

Description of Surgical Technique

The original technique of OAT (Koblenz Algorithm) has been described in detail previously (18). In this study, we present an amended method as a prophylactic onlay mesh is implanted at the delayed primary fascial closure operation (Koblenz Algorithm 2.0, **Figure 1**).

Patients with the indication for OAT and in whom primary fascial closure is impossible during the abdominal surgery are treated with a commercially available OAT dressing kit (ABThera^{TM} SensaTRAC^{TM} Open Abdomen Dressing, KCI Medical/3M, Maplewood, MN, United States). To protect the viscera from serosal lesions and prevent enteroatmospheric fistulas, a visceral protective layer integrated into the abdominal vacuum foam is implanted (19). It is placed deep laterally in the paracolic spaces to prevent lateral adhesions.

A scheduled second-look operation after 48–72 h is performed, and the decision is made whether it is possible to close the abdomen or to continue OAT. This initial period was considered the acute phase; hence in the former case, the abdominal fascia is closed following the recommendations by the EHS (17) but without a prophylactic onlay mesh. If the OAT has to be continued, an alloplastic non-resorbable mesh is sutured in inlay position to the fascial edges to achieve mesh-mediated fascial traction (VAWCM). The mesh is divided in the midline, and each half is sutured to the fascial edges with a resorbable running suture until it was sutured in the midline maintaining continuous moderate traction of the fascia. In the next step, another vacuum foam is cut to the size of the laparostomy and placed on the mesh. Then, the wound is closed with adhesive foil, and the suction is applied. Usually, a negative pressure of 75–100 mmHg is reasonable, but in special conditions (i.e., impaired coagulation), this is reduced to 25 mmHg.

During the next operation, the mesh is was re-opened in the midline, and the surgical revision is obtained. Depending on the intrabdominal pressure and swelling of the intestines, the fascial dehiscence is reduced by suturing the mesh tighter in the midline. This leads to continuous and progressive fascial traction and hence facilitates the delayed primary fascial closure.

As soon as it is considered possible, the mesh is removed, and the abdominal fascia is closed with a slowly absorbable running suture (Monomax®, poly-4-hydroxybutyrate, B. Braun, Melsungen, Germany) following EHS guidelines of the abdominal wall closure (17). This condition is defined as definitive fascia closure, i.e., the complete closure of the fascia edges with no remaining fascial gap (fascia-to-fascia closure) and

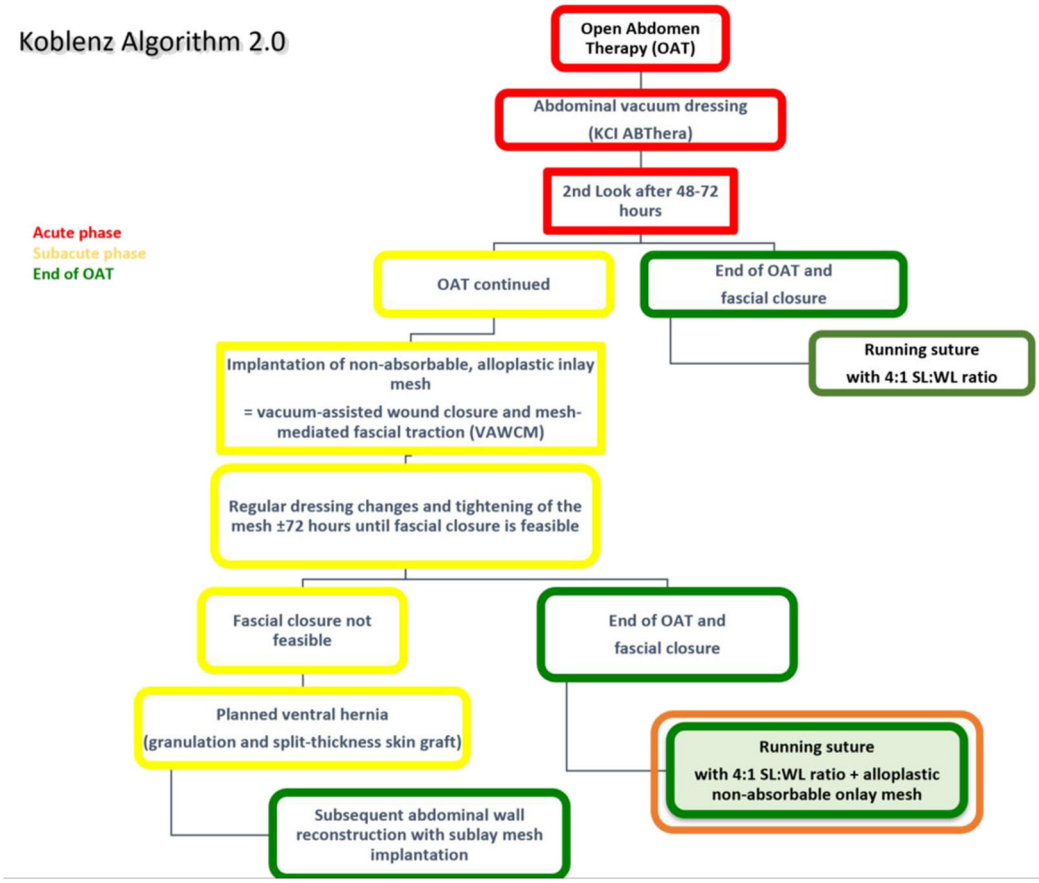

FIGURE 1 | The amended Koblenz Algorithm (2.0) with special focus on the prophylactic onlay mesh implantation at the end of OAT.

is a pre-requisite for onlay mesh augmentation and inclusion in this study.

To prepare the abdominal wall for onlay mesh implantation, a sufficient dissection is done to warrant an epifascial overlap of at least 5 cm in all directions from the fascia-to-fascia closure. Either an alloplastic long-term absorbable mesh (TIGR® Matrix, Novus Scientific, Uppsala, Sweden) or an alloplastic non-absorbable mesh (Dynamesh CICAT, Dahlhausen, Aachen, Germany) is used for augmentation in onlay position in this study cohort. The reason for using two different mesh types was to check for feasibility in the OAT setting, and not to compare the outcomes. As the implantation of alloplastic material in patients with the history of peritonitis seemed potentially risky, we chose a two-step approach. Initially, the long-term absorbable mesh was implanted. After we observed no complications requiring invasive treatment, we also tried the implantation of the non-absorbable mesh because there is recent evidence that the risk of mesh infection and the need for explantation depends on the specific mesh material (20).

The mesh is fixed to the fascial tissue underneath with an absorbable running suture (Vicryl, polyglactin, B. Braun, Melsungen, Germany) and a negative pressure wound therapy (NPWT) is applied with continuous suction of 100 mmHg. NPWT dressings are changed at least two times until the onlay mesh is sufficiently integrated with granulating tissue, as we assume the mesh-associated seroma/hematoma risk to be lower. Afterwards, secondary wound closure with the placement of suction drains is performed (**Figure 2**). In particular, secondary wound closure is obtained in two layers with a subepidermal slowly absorbable suture and non-absorbable single epidermal stitches after subtle excision of the dermal wound edges. Additionally, **Figure 3** shows the post-operative course after definitive fascial closure.

Patient Population and Study Design

Patients have been prospectively included in this study.

Inclusion criteria were as follows:

- OAT at our facility between July 2017 and March 2020 (**Figure 4**)
- Definitive fascial closure (no remaining fascial gap) was possible, and a prophylactic onlay mesh has been implanted (PROMOAT)

Patients were excluded due to these reasons if the prophylactic onlay mesh implantation has been considered unfeasible:

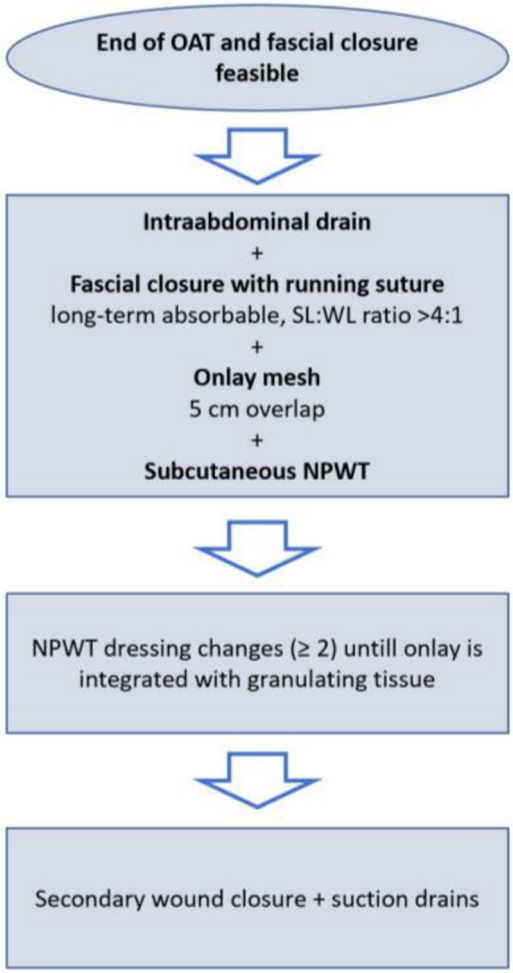

FIGURE 2 | Detailed procedure of delayed primary fascial closure and prophylactic onlay mesh implantation.

- Surgeon's individual decision
- Expected survival was less than half a year
- End of OAT and definitive fascial closure was possible yet at the second look operation (acute phase of Koblenz Algorithm)
- Further abdominal surgery (e.g., ostomy reversal) was scheduled

The primary endpoint of this study was the occurrence of an incisional hernia during follow-up. Secondary endpoints were post-operative complications like seromas, hematomas, bleeding, burst abdomen, surgical site infections (SSI), and any complication with the indication for a redo surgery. Surgical site infections were defined by the CDC criteria (21). In this study, every CDC type of SSI (superficial, deep, and organ space) was considered a SSI. Complications have been classified following Clavien and Dindo (22). Invasive treatment of a complication was considered Clavien-Dindo grade III or higher, whereas non-invasive actions that had to be taken were grades I and II.

Patients' age, sex, and BMI, as well as the underlying disease and current surgical history, have been retrieved from the charts. Furthermore, surgery-related data, e.g., remaining dehiscence/fascial gap length and width, type of mesh, size, and fixation, have been documented. Lastly, the post-operative pain was rated with the numerical rating scale (NRS), 0 no pain; 10 worst pain). This scale is a simple 11-item scale that is commonly used as a pain assessment tool in the clinical routine and research (23). The patients were asked to rate their level of pain on a scale of 0 to 10.

Data Management and Statistical Analysis

The collected data has been stored after pseudonymization. Informed consent has been obtained from the patients or their legal representatives. The local ethics committee approved this study (No. 2020-14884 of 25 March 2020).

The data analysis has been done with Excel (Excel 2016, Microsoft Corp., Redmont, United States) and SPSS (SPSS Statistics 20, IBM, Armonk, United States). Descriptive statistics have been calculated. Metric data is given in means ± standard deviation and 95% confidence interval. Categorical data are reported as proportions (percentages).Due to the low n, we assumed the data not to be normally distributed. Therefore, differences between groups were tested with either contingency tables (Chi-square or Fisher's exact test) or with the non-parametric Mann–Whitney-*U*-test depending on the data scale. The level of significance was set with $p < 0.05$.

RESULTS

Ten patients were included in this analysis and were treated with PROMOAT. The majority of the patients were males (90%). The mean age was 49.4 ± 15.9 years (95% CI: 60.4–71.1). The patients had a mean body mass index (BMI) of 26.2 ± 6.2 kg/m² (95% CI: 24.7–28.8). These parameters did not differ between the two mesh groups.

The indications for OAT were trauma (2 cases, 20%), peritonitis (4 cases, 40%), and ACS or burst abdomen (4 cases, 40%) (**Figure 5**). There was no trauma among the long-term absorbable mesh patients. Underlying diagnoses are given in **Table 1**.

OAT duration was 21.0 ± 12.6 days (95% CI: 16.9–25.1). Definitive fascial closure was achieved in all cases. In 5 cases (case no. 1–5; 50%), a long-term absorbable alloplastic mesh was implanted and a non-absorbable alloplastic mesh in the remaining cases (case no. 6–10; 50%). OAT duration was for the long-term absorbable mesh group 28.3 ± 11.9 days (95% CI: 22.4–34.1) and for the non-absorbable mesh group 19.2 ± 12.6 days (95% CI: 13.6–24.7). This difference was not statistically significant ($p = 0.111$).

The mesh and fascial gap sizes are given in **Table 2**. The dimensions of the implanted meshes were 3- to 5 fold the sizes of the remaining fascial defect when definitive fascial closure was performed. **Figure 6** visualizes the relations of mesh overlap.

The follow-up interval was in mean 12.4 ± 10.8 months (range 2–30 months). The long-term absorbable mesh group

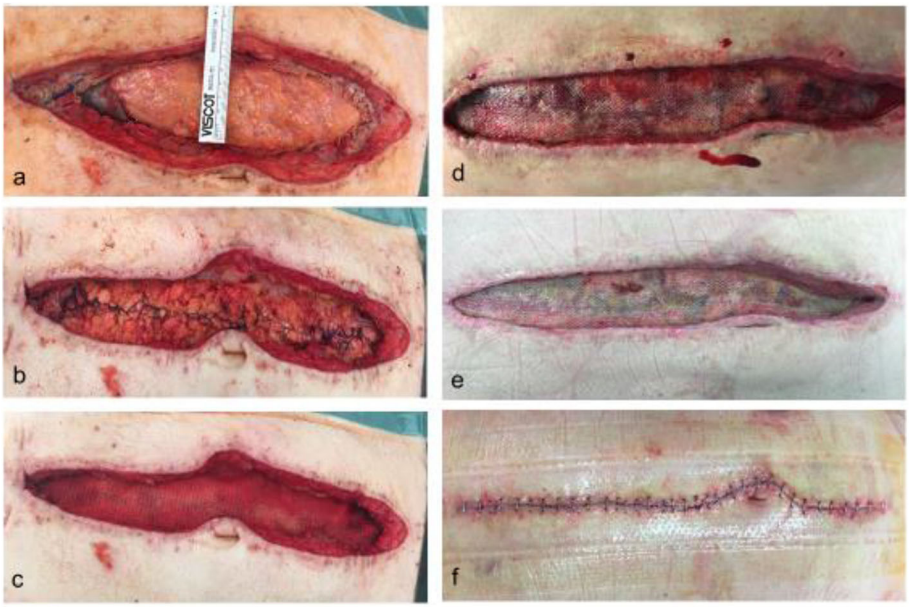

FIGURE 3 | Post-operative course after definitive fascial closure with prophylactic onlay mesh. Picture a shows the residual fascial dehiscence at the of 15 days of OAT in a 75 yo male **(a)**. The indication for OAT was ACS following massive bleeding and transfusion. The fascial defect was sutured with a long-term absorbable running suture maintaining a suture length to wound length ratio of at least 4:1 **(b)**. After dissection of a proper epifascial space, a 30 × 10 cm long-term resorbable mesh was placed in onlay position and fixated with a non-absorbable running suture and a subcutaneous vacuum dressing was applied **(c)**. Intraabdominal drains had been placed previously. Picture **(d)** shows the situs at day 4 after definitve fascial closure with clean conditions and initial integration of the mesh by granulating tissue. On day 8 the mesh and the wound was well granulated, hence secondary wound closure was performed **(e)**. Lastly, **(f)** shows the wound 20 days after definitive fascial closure and end of OAT.

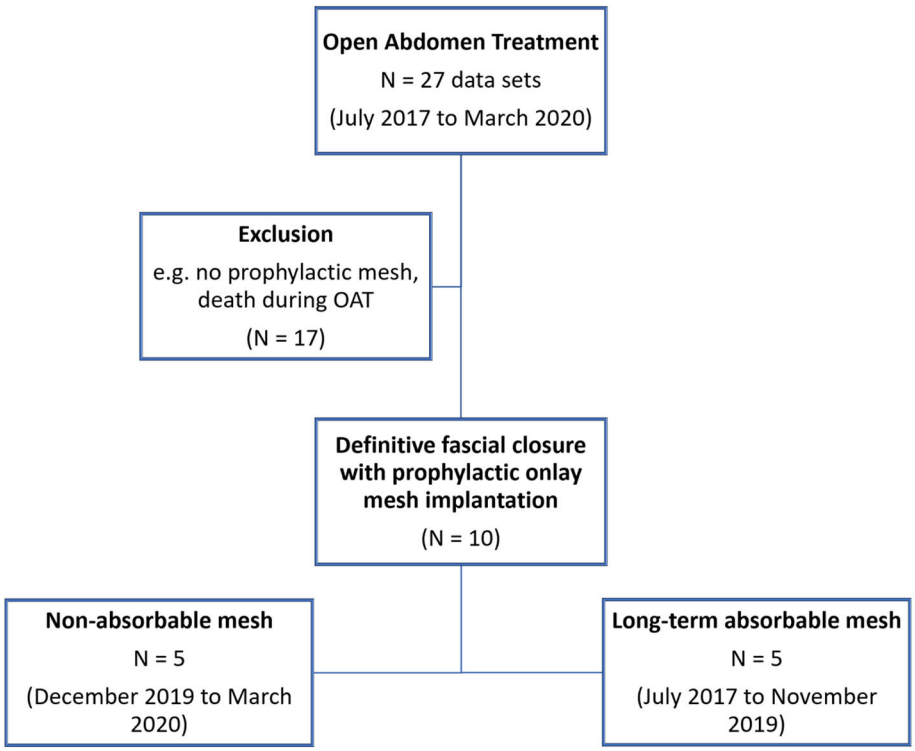

FIGURE 4 | Flow chart of patient inclusion in the study.

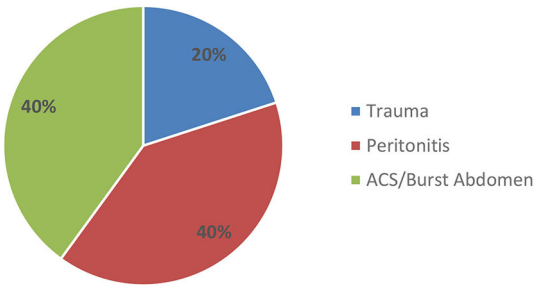

FIGURE 5 | Indications for OAT. ACS, abdominal compartment syndrome.

TABLE 1 | Overview of diagnoses and OAT indications.

Case no.	Diagnosis	OAT indication
1	Severe sepsis (pneumonia)	ACS/burst abdomen
2	Abdominal aortic aneurysm repair (EVAR) with post-interventional bleeding	ACS/burst abdomen
3	Strangulated incisional hernia with sigmoid volvolus	Peritonitis
4	Serosal leak after sigmoid colectomy	Peritonitis
5	Severe sepsis (pneumonia)	ACS/burst abdomen
6	Sigmoid diverticulitis with free perforation	Peritonitis
7	Motor vehicle accident with blunt abdominal trauma and gastric perforation	Trauma
8	Motor vehicle accident with blunt abdominal trauma and hepatic and splenic laceration	Trauma
9	Capillary leak syndrome after urinary bladder resection (urothelial cell carcinoma)	ACS/burst abdomen
10	Intraabdominal abscess following colonic perforation	Peritonitis

EVAR, endovascular aortic aneurysm repair; ACS, abdominal compartment syndrome.

had a longer follow-up period (23.5 ± 6.3 months, range 15–30 months) as this mesh type was implanted at the beginning of the study. The non-absorbable mesh group was followed up after 3.6 ± 1.0 months (range 2–5). During the follow-up period, complications were reported in three cases (30%). All of them were classified as Clavien-Dindo grade II (complications requiring non-surgical/pharmacological treatment). In one case, the complication was an infected seroma (long-term resorbable mesh), and in two cases, it was a superficial surgical site infection (both non-absorbable mesh group). None of the complications required invasive or surgical treatment. Apart from this, no other complications, especially no incisional hernias, were present.

At the follow-up exam, the overall pain was rated for all patients 2.3 ± 1.4 (95% CI: 1.9–2.8), for long-term resorbable meshes 1.8 ± 1.8 (95% CI: 0.9–2.6) and for non-absorbable meshes 2.8 ± 0.8 days (95% CI: 2.4–3.2). At rest pain was rated for all 1.0 ± 1.2 (95% CI: 0.6–1.4), for long-term absorbable meshes 1.8 ± 1.3 (95% CI: 1.1–2.4) and for non-absorbable meshes 0.4 ± 0.5 (95% CI: 0.2–0.6). Under strain all patients rated the pain 4.2 ± 1.0 (95% CI: 3.4–4.6), the patients with the long-term absorbable meshes rated 4.0 ± 1.2 (95% CI: 3.4–4.6) and patients with the non-absorbable mesh rated 4.4 ± 0.8 (95% CI: 4.1–4.7). None of the differences were statistically significant.

DISCUSSION

The results of this cohort study are promising. They might support the hypothesis that prophylactic onlay mesh implantation is feasible and safe after OAT, irrespective of whether a long-term absorbable or a non-absorbable mesh is used. During the follow-up period, no incisional hernias were observed, and the occurred complications in both groups were of minor concern and healed without invasive measures (Clavien-Dindo II).

Numerous studies evaluated the effect of prophylactic mesh implantation after laparotomies, and their results favored the prophylactic mesh implantation in high-risk patients over suture-only fascial closure (14, 15). For example, Jairam et al. conducted a randomized controlled trial (PRIMA trial) and found an incisional hernia incidence of 13% for the prophylactic onlay mesh compared to 31% for suture-only (14). The included patients had risk factors like aortic aneurysms and obesity. Seromas occurred in approximately one-quarter of the cases in the onlay mesh group. As in our study, those seromas had no impact on reoperations, invasive treatment, or surgical site infections. Muysoms et al. reported similar results in aortic aneurysm patients and prophylactic sublay mesh implantation (24).

In line with the findings for prophylactic onlay and sublay mesh implantation, Kohler et al. reported a reduced incisional hernia rate for prophylactic IPOM (intraperitoneal onlay mesh) implantation (7.2%) compared to suture-only (18.5%) (25). Patients in the IPOM group complained of more post-operative pain and had a longer duration of wound healing, however. For a similar technique, prophylactic implantation of a 7.5 cm wide IPOM stripe were incisional hernia rates of 17% after 2 years and 26% after a 5 year period reported (26, 27).

Borab et al. calculated an incisional hernia risk reduction of 85% in high-risk patients with elective laparotomies and prophylactic mesh implantation in a systematic review (15). Moreover, they found an increased rate of post-operative seromas, especially for onlay position of the mesh and polypropylene material, and more post-operative pain compared to suture-only fascial closure. Likewise, a meta-analysis by Indrakusuma et al. found a substantial incisional hernia risk reduction in aortic aneurysms repair patients and prophylactic mesh implantation (28). They reported no difference in the reoperation rate (i.e., due to hernia repair later on) between prophylactic mesh and suture-only groups, though. Concerning this study, Wanhainen emphasized there is level-A evidence for the prophylactic mesh implantation in open abdominal aortic aneurysm repair. Still, yet this is not represented in treatment guidelines, and it is not common in the daily routine (29). Wanhainen supposed most surgeons are hesitant to implant

TABLE 2 | Comparison of study data across mesh groups.

	All (n = 10)	Long-term absorbable mesh (*n* = 5)	Non-absorbable mesh (*n* = 5)	p
Age [years]	49.6 ± 15.9 (95% CI: 44.4–54.8)	56.9 ± 13.4 (95% CI: 51.0–62.8)	43.7 ± 15.3 (95% CI: 37.1–50.4)	0.413
Sex (m/f)	9 (90%)/1 (10%)	5 (100%)/0 (0%)	4 (80%)/1 (20%)	0.556
BMI [kg/m²]	26.8 ± 6.2 (95% CI: 24.7–28.8)	30.4 ± 7.2 (95% CI: 27.2–33.5)	23.8 ± 3.1 (95% CI: 22.5–25.2)	0.286
Gap width [cm]	4.2 ± 1.4 (95% CI: 3.8–4.7)	5.3 ± 1.5 (95% CI: 4.5–6.0)	3.4 ± 0.6 (95% CI: 3.2–3.6)	0.111
Gap length [cm]	18.4 ± 4.3 (95% CI: 17.0–19.8)	19.1 ± 4.2 (95% CI: 17.1–21.2)	17.8 ± 4.1 (95% CI: 16.0–19.6)	0.905
Gap area [cm²]	81.1 ± 42.3 (95% CI: 67.2–94.9)	105.8 ± 48.4 (95% CI: 82.0–129.5)	61.3 ± 20.6 (95% CI: 52.3–70.3)	0.286
Mesh width [cm]	9.5 ± 2.2 (95% CI: 8.8–10.2)	9.4 ± 3.3 (95% CI: 7.8–11.0)	9.6 ± 0.8 (95% CI: 9.3–9.9)	0.286
Mesh length [cm]	29.1 ± 3.4 (95% CI: 28.0–30.2)	28.8 ± 1.3 (95% CI: 28.1–29.4)	29.4 ± 4.1 (95% CI: 27.6–31.2)	1.000
Mesh area [cm²]	277.6 ± 76.5 (95% CI: 252.6–302.6)	272.4 ± 105.3 (95% CI: 220.8–324.0)	281.8 ± 39.9 (95% CI: 264.3–299.3)	0.556
Mesh/gap area ratio	4.3 ± 1.8 (95% CI: 3.7–4.9)	3.5 ± 2.2 (95% CI: 2.4–4.6)	4.9 ± 1.0 (95% CI: 4.5–5.4)	0.413
Incisional hernia	0%	0%	0%	1.000
Pain [NRS]	2.3 ± 1.4 (95% CI: 1.9–2.8)	1.8 ± 1.8 (95% CI: 0.9–2.6)	2.8 ± 0.8 (95% CI: 2.4–3.2)	0.556
Complications	3 (30%)	1 (20%; infected seroma)	2 (40%; superficial SSI)	0.655

prophylactic meshes as long-term data is still lacking, and there might be only little individual experience in prophylactic mesh implantation. There are only a few studies with quite a long follow-up interval of about 5 years. However, these studies did not report any severe or frequent complications following prophylactic onlay mesh implantation (27, 30).

Eventually, there are several well-designed studies that support the beneficial role of prophylactic mesh implantation in high-risk patients with elective laparotomies (14, 15, 25, 28, 29). This will likely be reflected in upcoming updates of guidelines on abdominal surgery. However, small bites technique, a suture length to wound length ratio of >4:1 with a long-term or non-absorbable running suture is still the current state of the art of abdominal wall closure following the European Hernia Society guidelines of the abdominal wall closure (9, 11, 17).

Less research has yet been done on prophylactic mesh implantation in emergency laparotomies. But this is an important aspect, as the midline laparotomy is usually the first-choice abdominal incision in the emergency situation. Alternative methods like minimally invasive procedures with their inherently reduced incisional hernia risk, are hardly feasible. Burns et al. recently published a meta-analysis with 299 pooled patients and found substantially reduced incisional hernia risks and no remarkable differences concerning post-operative complications (31).

Put together; we hypothesized that the high-risk conditions in terms of incisional hernia development are similar or even worse in OAT patients (11). Firstly, OAT patients are equally likely to have intrinsic or patient-specific risk factors like aortic aneurysm or obesity. Secondly, the index operation at the initiation of OAT is usually an emergency operation. Thirdly, the repetitive traumatization of the abdominal fascia, caused by multiple reoperations and fascial traction, serves as a particular risk factor for incisional hernia development. And lastly, several pathophysiological factors (e.g., extended ICU stay, hemodynamic instability, malnutrition, catabolic nutritional status, and prolonged immobilization) are very likely to impair fascial viability, healing capabilities, and long-term resistance against hernia development. Hence, the pathophysiological conditions of elective or emergency laparotomies, for which the impact of prophylactic mesh implantation has already been studied, can be compared only to a limited degree. Nevertheless, as the incisional hernia rates after OAT are high, we supposed a positive impact of PROMOAT on incisional hernia rate (11).

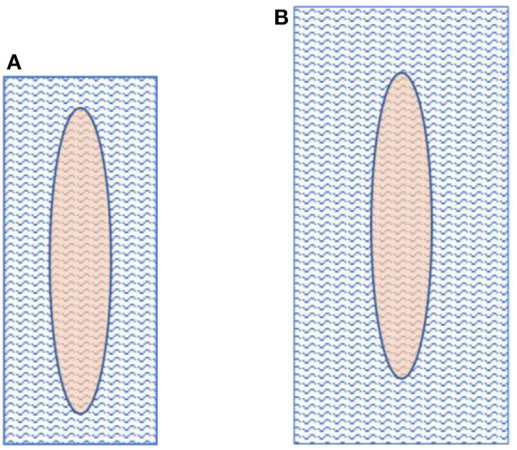

FIGURE 6 | Fascial gap size in comparison to mesh size. The left image **(A)** depicts a mesh-to-gap ratio of 3 and the right one **(B)** a mesh-to-gap ratio of 5.

Guidelines by the European Hernia Society on the fascial closure recommend mesh reinforcement in OAT or burst abdomen at the definitive fascial closure operation to reduce the incisional hernia rate (9). This recommendation was given based on weak evidence, as there were only very heterogeneous case series available. However, the guideline authors conducted a pooled analysis and found an incisional hernia rate of 19.4%. That was a substantial reduction compared to reported incisional hernia rates of 35–66% after OAT (9). Moreover, the pooled analysis revealed a rate of surgical site occurrences (surgical site infections, hematomas, and seromas) of 31.9%, which was higher

in comparison to closure techniques without the use of mesh. Finally, the expert panel concluded there was expert guidance for mesh reinforcement at the definitive facial closure operation after OAT. The individual decision is up to the surgeon, though, in the context of increased risk for surgical site occurrences. (9, 11)

Only two studies were found, which prospectively evaluated prophylactic mesh implantation in OAT patients. The first one was published by Jakob et al. and evaluated the VAC-IPOM technique (32). With this, an IPOM is used for fascial traction in the VAWCM concept. Complete fascia-to-fascia closure was not mandatory, as the IPOM was considered stable even if there was residual fascia dehiscence at the end of OAT. Eventually, they reported a fascial closure rate of only 26% in the VAC-IPOM group compared to 74% in the VAWCM group. Nevertheless, in the VAC-IPOM group, longer hernia-free survival, and fewer reoperation were observed. The rate of post-operative wound infections was substantially higher in the VAC-IPOM group.

In our opinion, a prophylactic alloplastic IPOM should not be the treatment of the first choice since anatomical, functional abdominal wall reconstruction is advisable. Furthermore, IPOM should be implanted with caution due to the risk of an acute or chronic mesh infection, if potentially infectious intrabdominal foci are evident. Therefore, the implantation of a mesh in onlay position at the end of OAT (PROMOAT) is considered safe, as control of the infectious disease is then usually achieved. We would also suppose, the onlay mesh implantation is technically more straightforward than the IPOM implantation in an early stage of OAT (11, 14). But it has to be considered that there is currently no evidence to conclude on the appropriate mesh position (onlay, sublay, IPOM) for prophylactic implantation after OAT (11).

The second study on prophylactic mesh implantation in OAT patients was published by Petersson et al. (33). This report described a novel technique; the vacuum-assisted wound closure and permanent onlay mesh mediated fascial traction (VAWCPOM) for temporary and final closure of the open abdomen. The main difference to conventional VAWCM technique lies in the fact that the mesh, which is used for fascial traction during OAT, is placed in onlay position, is left there, and readapted in the midline with a suture when definitive fascial closure is performed. Moreover, the fascial edges are previously reinforced using a non-absorbable suture (reinforced tension line). At the end of OAT, the definitive fascial closure is obtained with a running suture, and the previously implanted mesh augments the stitches and the fascial edges. The authors reported an incisional hernia rate of 22.2% after a mean follow-up of 467 days and only minor complications without the need for invasive treatment.

The study by Petersson et al. describes a technically similar concept of augmenting the abdominal fascia with a prophylactic onlay mesh after OAT. Moreover, they found no substantial complications and a low incisional hernia rate. These results are in line with our findings. The higher incisional hernia rate of 22.2 vs. 0% in our study should be interpreted with caution, as our follow-up period is somewhat shorter, and incisional hernias are known to occur not necessarily shortly after definitive fascial closure. Probably, the midline incision and suturing of the prophylactic mesh might impair the mechanical properties, which might explain the higher incisional hernia rate by Petersson et al.

We suppose two further factors are of importance with regard to the prophylactic onlay mesh implantation. Firstly, as alloplastic meshes were used, we would favor implantation only in clean wound conditions with definitively controlled intraabdominal septic foci. And secondly, the mandatory NPWT of at least two changes after the onlay mesh implantation seems necessary, as seromas are a common and potentially infective complication following onlay mesh implantation. Our data showed only one seroma (11.1%), which is quite a low rate compared to other studies (14–16).

The question of which mesh material should be used for prophylactic onlay mesh implantation cannot be answered based on the scarcity of published data (11). Our study findings suggest there is no difference between long-term absorbable and non-absorbable mesh material. Still, of course, the power of this small case series is not sufficient, and long-term data are lacking to conclude on that. Hence, the choice of the mesh material should be made upon the surgeon's experiences. The current evidence on mesh materials confirms alloplastic non-absorbable meshes to be safe for prophylactic implantation (10, 11).

Study limitations comprise of the low power due to the small sample size. That hampers the possible conclusions drawn from this case series results. Moreover, there were differences between the mesh groups in the demographics and some operative variables (e.g., the gap width, mesh size). Though these differences were not statistically significant in this analysis, that is likely to be caused by the low sample size. Due to the short and unequal follow-up period, the reported outcome has to be interpreted with caution.

In conclusion, the prophylactic onlay mesh implantation of alloplastic, long-term absorbable, or non-absorbable meshes in OAT showed promising results and only a few complications that were of minor concern. Incisional hernias did not occur during follow-up. To validate the feasibility and safety of prophylactic onlay mesh implantation after OAT, long-term data and large-scaled prospective trials are needed.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethikkommission der Landesärztekammer Rheinland-Pfalz. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

REFERENCES

1. Coccolini F, Montori G, Ceresoli M, Catena F, Moore EE, Ivatury R, et al. The role of open abdomen in non-trauma patient: WSES consensus paper. *World J Emerg Surg.* (2017) 12:39. doi: 10.1186/s13017-017-0146-1
2. Sartelli M, Abu-Zidan FM, Ansaloni L, Bala M, Beltrán MA, Biffl WL, et al. The role of the open abdomen procedure in managing severe abdominal sepsis: WSES position paper. *World J Emerg Surg.* (2015) 10:35. doi: 10.1186/s13017-015-0032-7
3. Atema JJ, Gans SL, Boermeester MA. Systematic review and meta-analysis of the open abdomen and temporary abdominal closure techniques in non-trauma patients. *World J Surg.* (2015) 39:912–25. doi: 10.1007/s00268-014-2883-6
4. Brown SR, Goodfellow PB. Transverse verses midline incisions for abdominal surgery. *Cochrane Database Syst Rev.* (2005) 4:CD005199. doi: 10.1002/14651858.CD005199.pub2
5. Willms A, Schaaf S, Schwab R, Richardsen I, Jänig C, Bieler D, et al. Intensive care and health outcomes of open abdominal treatment: long-term results of vacuum-assisted wound closure and mesh-mediated fascial traction (VAWCM). *Langenbecks Arch Surg.* (2017) 402:481–92. doi: 10.1007/s00423-017-1575-8
6. Bjarnason T, Montgomery A, Ekberg O, Acosta S, Svensson M, Wanhainen A, 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. doi: 10.1007/s00268-013-2082-x
7. Brandl A, Laimer E, Perathoner A, Zitt M, Pratschke J, Kafka-Ritsch R. Incisional hernia rate after open abdomen treatment with negative pressure and delayed primary fascia closure. *Hernia.* (2014) 18:105–11. doi: 10.1007/s10029-013-1064-0
8. Willms A, Schaaf S, Schwab R, Richardsen I, Bieler D, Wagner B, et al. Abdominal wall integrity after open abdomen: long-term results of vacuum-assisted wound closure and mesh-mediated fascial traction (VAWCM). *Hernia.* (2016) 20:849–58. doi: 10.1007/s10029-016-1534-2
9. López-Cano M, García-Alamino JM, Antoniou SA, Bennet D, Dietz UA, Ferreira F, et al. EHS clinical guidelines on the management of the abdominal wall in the context of the open or burst abdomen. *Hernia.* (2018) 22:921–39. doi: 10.1007/s10029-018-1818-9
10. Muysoms FE, Dietz UA. Prophylaktische netze an der bauchdecke. *Chirurg.* (2016) 87:751–61. doi: 10.1007/s00104-016-0245-7
11. Berrevoet F. Prevention of incisional hernias after open abdomen treatment. *Front Surg.* (2018) 5:11. doi: 10.3389/fsurg.2018.00011
12. Bleier JIS, Resnick AS. Complications of incisional hernia repair. *Semin Colon Rect Surg.* (2009) 20:125–30. doi: 10.1053/j.scrs.2009.06.004
13. Azar FK, Crawford TC, Poruk KE, Farrow N, Cornell P, Nadra O, et al. Ventral hernia repair in patients with abdominal loss of domain: an observational study of one institution's experience. *Hernia.* (2017) 21:245–52. doi: 10.1007/s10029-017-1576-0
14. Jairam AP, Timmermans L, Eker HH, Pierik RE, van Klaveren D, Steyerberg EW, et al. Prevention of incisional hernia with prophylactic onlay and sublay mesh reinforcement versus primary suture only in midline laparotomies (PRIMA):2-year follow-up of a multicentre, double-blind, randomised controlled trial. *Lancet.* (2017) 390:567–76. doi: 10.1016/S0140-6736(17)31332-6
15. Borab ZM, Shakir S, Lanni MA, Tecce MG, MacDonald J, Hope WW, et al. Does prophylactic mesh placement in elective, midline laparotomy reduce the incidence of incisional hernia? a systematic review and meta-analysis. *Surgery.* (2017) 161:1149–63. doi: 10.1016/j.surg.2016.09.036
16. Payne R, Aldwinckle J, Ward S. Meta-analysis of randomised trials comparing the use of prophylactic mesh to standard midline closure in the reduction of incisional herniae. *Hernia.* (2017) 21:843–53. doi: 10.1007/s10029-017-1653-4
17. Muysoms FE, Antoniou SA, Bury K, Campanelli G, Conze J, Cuccurullo D, et al. European Hernia Society guidelines on the closure of abdominal wall incisions. *Hernia.* (2015) 19:1–24. doi: 10.1007/s10029-014-1342-5
18. Willms A, Güsgen C, Schaaf S, Bieler D, Websky M von, Schwab R. Management of the open abdomen using vacuum-assisted wound closure and mesh-mediated fascial traction. *Langenbecks Arch Surg.* (2015) 400:91–9. doi: 10.1007/s00423-014-1240-4
19. Willms AG, Schaaf S, Zimmermann N, Schwab R, Güsgen C, Vilz TO, et al. The significance of visceral protection in preventing enteroatmospheric fistulae during open abdomen treatment in patients with secondary peritonitis: a propensity score-matched case-control analysis. *Ann Surg.* (2019). doi: 10.1097/SLA.0000000000003440. [Epub ahead of print].
20. Bueno-Lledó J, Torregrosa-Gallud A, Sala-Hernandez A, Carbonell-Tatay F, Pastor PG, Diana SB, et al. Predictors of mesh infection and explantation after abdominal wall hernia repair. *Am J Surg.* (2017) 213:50–7. doi: 10.1016/j.amjsurg.2016.03.007
21. National Healthcare Safety Network, Centers for Disease Control and Prevention. *Surgical Site Infection (SSI) event*. (2017). Available online at: http://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf (accessed July 27, 2020).
22. Clavien PA, Barkun J, Oliveira ML, de Vauthey JN, Dindo D, Schulick RD, et al. The clavien-dindo classification of surgical complications: five-year experience. *Ann Surg.* (2009) 250:187–96. doi: 10.1097/SLA.0b013e3181b13ca2
23. Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: visual analog scale for pain (VAS Pain), numeric rating scale for pain (NRS Pain), mcgill pain questionnaire (MPQ), short-form mcgill pain questionnaire (SF-MPQ), chronic pain grade scale (CPGS), short form-36 bodily pain scale (SF-36 BPS), and measure of intermittent and constant osteoarthritis pain (ICOAP). *Arthritis Care Res.* (2011) 63 (Suppl. 11):S240–52. doi: 10.1002/acr.20543
24. Muysoms FE, Detry O, Vierendeels T, Huyghe M, Miserez M, Ruppert M, et al. Prevention of incisional hernias by prophylactic mesh-augmented reinforcement of midline laparotomies for abdominal aortic aneurysm treatment: a randomized controlled trial. *Ann Surg.* (2016) 263:638–45. doi: 10.1097/SLA.0000000000001369
25. Kohler A, Lavanchy JL, Lenoir U, Kurmann A, Candinas D, Beldi G. Effectiveness of prophylactic intraperitoneal mesh implantation for prevention of incisional hernia in patients undergoing open abdominal surgery: a randomized clinical trial. *JAMA Surg.* (2019) 154:109–15. doi: 10.1001/jamasurg.2018.4221
26. Brosi P, Glauser PM, Speich B, Käser SA, Maurer CA. Prophylactic intraperitoneal onlay mesh reinforcement reduces the risk of incisional hernia, two-year results of a randomized clinical trial. *World J Surg.* (2018) 42:1687–94. doi: 10.1007/s00268-017-4363-2
27. Glauser PM, Brosi P, Speich B, Käser SA, Heigl A, Rosenberg R, et al. Prophylactic intraperitoneal onlay mesh following midline laparotomy-long-term results of a randomized controlled trial. *World J Surg.* (2019) 43:1669–75. doi: 10.1007/s00268-019-04964-6
28. Indrakusuma R, Jalalzadeh H, van der Meij JE, Balm R, Koelemay MJ. Prophylactic mesh reinforcement versus sutured closure to prevent incisional hernias after open abdominal aortic aneurysm repair via midline laparotomy: a systematic review and meta-analysis. *Eur J Vasc Endovasc Surg.* (2018) 56:120–8. doi: 10.1016/j.ejvs.2018.03.021
29. Wanhainen A. To mesh or not to mesh? that is the question! *Eur J Vasc Endovasc Surg.* (2018) 56:129. doi: 10.1016/j.ejvs.2018.04.010
30. San Miguel C, Melero D, Jiménez E, López P, Robin Á, Blázquez LA, et al. Long-term outcomes after prophylactic use of onlay mesh in midline laparotomy. *Hernia.* (2018) 22:1113–22. doi: 10.1007/s10029-018-1833-x
31. Burns FA, Heywood EG, Challand CP, Lee MJ. Is there a role for prophylactic mesh in abdominal wall closure after emergency laparotomy?

a systematic review and meta-analysis. *Hernia*. (2020) 24:441–7. doi: 10.1007/s10029-019-02060-1

32. Jakob MO, Schwarz C, Haltmeier T, Zindel J, Pinworasarn T, Candinas D, et al. Mesh-augmented versus direct abdominal closure in patients undergoing open abdomen treatment. *Hernia*. (2018) 22:785–92. doi: 10.1007/s10029-018-1798-9
33. Petersson P, Montgomery A, Petersson U. Vacuum-assisted wound closure and permanent onlay mesh-mediated fascial traction: a novel technique for the prevention of incisional hernia after open abdomen therapy including results from a retrospective case series. *Scand J Surg*. (2019) 108:216–26. doi: 10.1177/1457496918818979

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Open Abdomen Treatment in Acute Pancreatitis

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Background: Severe acute pancreatitis (SAP) is a heterogeneous and life-threatening disease. While recent guidelines recommend a stepwise approach starting with non-surgical techniques, emergency laparotomy remains inevitable in certain situations. Open abdomen treatment (OAT) may follow, potentially resulting in additional risks for severe morbidity. Causative factors and clinical impact of OAT in SAP are poorly understood and therefore issue of the present study.

Materials and Methods: A retrospective analysis of patients admitted to the Department of General, Visceral, Thoracic and Vascular Surgery at University of Bonn suffering from acute pancreatitis (ICD K.85) between 2005 and 2020 was performed. Medical records were screened for demographic, clinical and outcome parameters. Patients who received primary fascial closure (PFC) were compared to those patients requiring OAT. SAP-specific scores were calculated, and data statistically analyzed ($P = 0.05$).

Results: Among 430 patients included, 54 patients (13%) had to undergo emergency laparotomy for SAP. Patients were dominantly male (72%) with a median age of 51 years. Indications for surgery were infected necrosis (40%), suspected bowel perforation (7%), abdominal compartment syndrome (5%), and acute intra-abdominal hemorrhage (3%). While 22 patients (40%) had PFC within initial surgery, 33 patients (60%) required OAT including a median of 12 subsequent operations (SD: 6, range: 1–24). Compared to patients with PFC, patients in the OAT group had significantly fewer biliary SAP ($P = 0.031$), higher preoperative leukocyte counts ($P = 0.017$), higher rates of colon resections ($P = 0.048$), prolonged ICU stays ($P = 0.0001$), and higher morbidity according to Clavien–Dindo Classification ($P = 0.002$). Additionally, BISAP score correlated positively with the number of days spent at ICU and morbidity ($P = 0.001$ and $P = 0.000002$). Both groups had equal mortality rates.

Discussion: Our data suggest that preoperative factors in surgically treated SAP may indicate the need for OAT. The procedure itself appears safe with equal hospitalization days and mortality rates compared to patients with PFC. However, OAT may significantly increase morbidity through longer ICU stays and more bowel resections. Thus, minimally invasive options should be promoted for an uncomplicated and rapid recovery in this severe disease. Emergency laparotomy will remain ultima ratio in SAP while patient selection seems to be crucial for improved clinical outcomes.

Keywords: acute pancreatitis, severe acute pancreatitis, abdominal compartment syndrome, risk analysis, open abdomen treatment

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INTRODUCTION

Acute pancreatitis (AP) is a frequent cause of emergency admissions with rising incidence over the last years (1). Although various parameters have been identified contributing to onset and progression of disease, cholelithiasis and excessive alcohol consumption are the two predominant risk factors (2). According to the Atlanta Classification, AP clinically ranges from "mild" over "moderately severe" to "severe" (3). While most patients experience a rather uncomplicated course of disease, severe acute pancreatitis (SAP) is observed in 20–30 % of individuals with an alarming lethality of 15%. SAP is defined as a life-threatening clinical condition with persistent organ failure resulting from aggravated comorbidities (3, 4). In particular, the respiratory, cardiovascular, and renal systems are affected, why their functions need to be closely monitored in the course of disease (3). Moreover, extensive peripancreatic necrosis observed in up to 10% of AP patients harbors the risk for significant morbidity, especially in the presence of infection (5). In fact, controlling pancreatic necrosis and associated sepsis has been an essential task in SAP management and comprises the use of broad-spectrum antibiotics, radiological, and endoscopic interventions, as well as surgical measures (6).

Regarding the operative spectrum, early cholecystectomy is still highly recommended in patients with biliary pancreatitis. However, indication and optimal timing of other surgical interventions and especially of laparotomy, operative necrosectomy, and peritoneal lavage has been a matter of vivid debates (6). Generally, a "step-up" approach is nowadays favored for the treatment of SAP ranging from initial minimally invasive interventions such as CT or endoscopic drainage to open surgery reserved for complicated cases (7). In fact, various pathophysiological mechanisms of SAP result in essentially three main indications for emergency laparotomy: Firstly, SAP frequently induces systemic inflammatory response syndrome (SIRS), resulting in increased vascular permeability, the urge for excessive intravenous fluid substitution, and generalized edema while on intensive care unit (ICU). This in turn leads to high intraperitoneal pressure (IAP) culminating in an abdominal compartment syndrome (ACS), which is regularly treated with decompressive laparotomy (8, 9). Furthermore, acute intra-abdominal hemorrhage and otherwise not controllable infected necrosis are two other frequent causes for open surgery (10).

Whenever primary fascial closure (PFC) within initial surgery is impossible or unintended, patients need to undergo subsequent scheduled operations within "open abdomen treatment" (OAT). OAT relates to intentionally dispensing fascial approximation to allow continuous observation and treatment of intra-abdominal disease. Obvious advantages are paralleled by significant clinical risks such as abdominal wall hernia, entero-atmospheric fistulas, and increased mortality (11). Current guidelines support an individualized management stressing a meticulous selection of patients suitable for laparotomy and OAT (12) while an evidence-based approach reliably guiding surgical decision making in SAP is thus far not available. To stratify therapy decisions in SAP for an optimized outcome in this severe condition, we conducted single-center and retrospective analysis of patients from our tertiary referral center for pancreatic diseases who underwent operative therapy and, in part, OAT for SAP.

MATERIALS AND METHODS

Patient Cohort

A retrospective analysis of patients admitted to the Department of General, Visceral, Thoracic and Vascular Surgery, University Hospital Bonn (Bonn, Germany), with the diagnosis of AP (ICD K.85) between 2005 and 2020 was performed. Patients with multiple admissions for AP were included as single cases respecting their first admission. Medical records were manually screened for patients that had undergone emergency laparotomy for SAP. Patients then were subdivided into two groups; firstly, patients who received PFC within their emergency laparotomy and secondly patients who received OAT. Demographic and clinical data (i.e., age at operation, gender, and comorbidities) were extracted, and the recent literature was scrutinized for additional relevant SAP and OAT-specific parameters to be included into our analysis. Etiologic factors for pancreatitis (i.e., cholelithiasis, alcohol, iatrogenic, and uncertain), pancreatitis-specific scores (i.e., BISAP, Atlanta), and relevant laboratory parameters [e.g., leukocyte count, (LC), c-reactive protein (CRP), procalcitonin (PCT), pancreas-specific lipase, and amylase] were documented (3, 13). Indications for emergency laparotomy (i.e., therapy-refractory infected necrosis, suspected bowel perforation, ACS, and acute hemorrhage) and reasons for OAT (i.e., peritonitis, fascial retraction, and other), as well as the numbers of subsequent reoperations, days of OAT, and OAT technique (vicryl mesh, visceral protection layer, and negative pressure) were charted. To determine the specific outcome of OAT, we assessed morbidity by Clavien–Dindo classification and evaluated the need for colon resection, the duration at ICU, and general hospitalization (14). Furthermore, in-house hospital mortality was calculated.

Statistics

Descriptive and inferential statistics were used in data analysis using SPSS Statistics (IBM, Armonk, New York, USA). Intergroup differences were calculated using CHI-squared- and Student's *t*-test. Pre-, intra-, and postoperative parameters were analyzed for possible correlations using the Pearson correlation coefficient. Findings were compared with recent treatment guidelines and literature. *P*-values were 2-sided, and statistical significance was set at 0.05.

RESULTS

Patients, Comorbidities, and SAP

Of 430 patients with AP treated between 01.01.2005 and 01.01.2020, 54 patients (13%) needed emergency laparotomy because of SAP. The PFC group included 22 (41%) patients and the OAT group 32 (59%) patients. **Table 1** summarizes both groups, their composition, and their relevant comorbidities. Neither sex nor age showed significant intergroup differences ($P > 0.05$). With the exception of significantly more pulmonary diseases in the PFC group ($P = 0.02$), comorbidities did not differ

significantly. While no patient of the PFC group had undergone previous laparotomy, four patients (13%) of the OAT group had a history of abdominal operations.

While cholelithiasis ($N = 18$, 33%) and alcohol abuse ($N = 18$, 33%) accounted for the most frequent etiologic factors, iatrogenic pancreatitis occurred in six patients (11%). In the remainder, the exact cause remained elusive ($N = 12$, 22%). In the OAT group, biliary SAP was significant less frequent ($P = 0.03$) and there was a tendency for more unclarified etiologies ($P = 0.054$). Emergency laparotomy was in most patients performed for therapy-refractory-infected necrosis ($N = 39$, 72%). Suspected bowel perforation with free intra-abdominal air on CT scans was indication for surgery in seven patients (13%). Decompressive laparotomy for ACS was required in five patients (9%), and operative exploration for acute severe hemorrhage in three individuals (6%). While ACS showed a trend to lead to OAT at a higher rate ($P = 0.055$), no such coherences were observed for other surgical indications. Compared to the PFC group, in OAT patients preoperative LC and CRP levels were significantly increased ($P = 0.015$ and $P = 0.048$), whereas no differences were observed for other serum parameters such as PCT, lipase, and amylase. Median BISAP scores for PFC and OAT groups were 1.5 (range 0–4) and 2 (range 0–4), and median Atlanta Classification was 2 (range 1–3) and 3 (range 2-3), respectively. No significant differences were measured regarding both scores.

Post-laparotomy Treatment and Outcome

Operation protocols stated two distinct reasons leading to OAT: Most frequently, severe peritonitis with abdominal sepsis present in 12 patients (38%) demanded second-look operations and prevented the surgeon from closing the abdominal cavity. The second cause was fascia retraction and dehiscence precluding primary fascial closure which was found in eight individuals (25%); including five cases in which ACS triggered initial laparotomy. A median of 12 subsequent reoperations were necessary in the OAT cohort, resulting in a median of 27 days until the final surgical intervention. Intestinal damage was a recurring complication ($N = 11$, 20%) and significantly higher in the OAT cohort reflected by more colon resections ($P = 0.048$) and a higher rate of enteric stomata ($P = 0.032$). Abdominal wall was temporarily closed with vicryl mesh interposition in 17 OAT patients (53%) of which 4 (13%) were supported with a protective visceral layer and 2 (6%) with vacuum wound therapy. Most patients ($N = 22$, 569%) were dismissed with planned ventral hernia (e.g., dry secondary wound closure, suture of skin above secondary healing abdominal wall), whereas delayed primary closure was performed in 10 patients (31%).

Median ICU stay was 14 days and 45 days for the PFC and the OAT group, respectively, with significantly longer ICU stays in the OAT cohort ($P = 0.0002$). As shown in **Figure 1**, LC and BISAP correlated positively with the lengths of ICU stays; however, only correlation between BISAP and ICU stay was statistically significant ($P = 0.06$ and $P = 0.001$). SAP patients were hospitalized for a median of 71 days (range 8–217). Despite longer ICU treatment, OAT patients did not spend longer time in hospital compared to PFC patients ($P = 0.12$). An overall longer hospital stay was not significantly related to any preoperative parameter included. None of the remaining preoperative parameters correlated relevantly with length of ICU stay or overall hospitalization.

Overall, the mean grade of complication (or morbidity) according to Clavien–Dindo classification was 4 (range 1–5), while the OAT group had increased morbidity with significantly higher Clavien–Dindo scores ($P = 0.0015$). LC and BISAP showed positive correlation with Clavien–Dindo classification **Figure 2** with significance for BISAP score. All other parameters showed no relevant impact on morbidity.

Overall mortality was 7% ($N = 4$) and showed no intergroup difference. The small number of patients precluded valid statistical analyses for risk factor analysis. Deceased patients were all male and had a median age at operation of 49 years (range 29–74). Half had no prior comorbidities (50%) with varying causes for SAP [alcohol ($N = 2$), bile stone ($N = 1$), and iatrogenic ($N = 1$)]. Cause of death was sepsis triggered multi-organ failure in all four patients.

DISCUSSION

The incidence of AP is currently on the rise in western countries while particularly elderly patients are affected with most individuals being in their 70s (15). Not surprisingly, a higher disease-related mortality could be evidenced in these compared to younger patients (16). In contrast, it is the middle-aged adults who were reported to have the highest risk for aggravated disease, which is in concordance with the mean age of 52 years in our analysis (17). Furthermore, evidence is emerging that preexisting comorbidities rather than age *per se* seem to trigger adverse outcomes. The demographic shift will increase the number of endangered patients and therefore we should expect AP to gain further clinical relevance with a potentially growing financial burden to our health care system both justifying scientific dedication to that topic (1).

Adequate treatment of AP is laboriously studied, and distinct focus lies on the prevailing question when to intervene in SAP since any unnecessary therapy might cause further significant morbidity in these severely ill patients. Especially, periprocedural trauma caused by abdominal surgery results in increased risk for severe morbidity and mortality and therefore needs to be avoided (18). Thus, minimally invasive approaches such as endoscopic and interventional radiological techniques have been developed over the past two decades and resulted in the least trauma for maximum impact (19). When comparing different interventions, three randomized controlled trials all favored endoscopic over percutaneous drainage. On the other hand, inconsistent results were reported when comparing endoscopic with surgical treatment of infected necrosis (7, 20, 21).

Surgical Treatment

Emerging evidence in this clinical field has still not provided precise algorithms unequivocally guiding surgical therapy in SAP. Thus, indication for surgery is heavily debated upon and depends on the experience and preference of the interdisciplinary team. In concordance to Jacob et al. therapy-refractory-infected necrosis was the major cause for laparotomy

TABLE 1 | Baseline characteristics of all patients, divided into PFC and OAT group.

	PFC group		OAT group		*P*	OR/mean difference	CI95	
All (*n*, %)	22	41	32	59				
Sex m (*n*, %)	15	68	23	72	0.716	1.193	0.365	3.892
Sex w (*n*, %)	7	32	9	28	0.716	0.839	0.257	2.736
Age (mean days, range)	54	26–74	49	25–80	0.221	4.591	−2.863	12.045
Any comorbidity (*n*, %)	17	77	23	72	0.657	0.752	0.213	2.650
Hypertension (*n*, %)	10	45	12	38	0.559	0.720	0.239	2.169
Cardiac disease (*n*, %)	7	32	7	22	0.413	0.600	0.176	2.048
Diabetes (*n*, %)	6	27	4	13	0.170	0.381	0.093	1.555
Hepatic disease (*n*, %)	4	18	6	19	0.958	1.038	0.256	4.214
Malignant disease (*n*, %)	1	5	3	9	0.506	2.172	0.211	22.368
Pulmonary disease (*n*, %)	5	23	1	3	**0.024**	**0.110**	**0.012**	**1.017**
Renal disease (*n*, %)	0	0	0	0	–	–	–	–
Other (*n*, %)	13	59	13	41	0.182	0.474	0.157	1.429
Previous laparotomy (*n*, %)	0	0	4	13	0.085	1.429	0.238	8.571
Cause								
Uncertain (*n*, %)	2	9	10	31	0.054	4.545	0.887	23.304
Iatrogenic (*n*, %)	3	14	3	9	0.624	0.655	0.119	3.592
Cholelithiasis (*n*, %)	11	50	7	22	**0.031**	**0.280**	**0.086**	**0.915**
Alcohol (*n*, %)	6	27	12	38	0.433	1.600	0.492	5.207
LC (mean G/l, range)	12	2–28	17	5–46	**0.015**	**5.586**	**1.15**	**10.02**
CRP (mean mg/l, range)	129	25–215	195	74–347	**0.048**	**66.045**	**0.61**	**131.48**
PCT (mean μg/l, range)	3	0–8	36	0–345	0.304	33.610	−35.404	102.624
Lipase (mean U/l, range)	233	41–809	676	3–5191	0.169	442.995	−202.901	1,088.892
Amylase (mean U/l, range)	68	22–170	113	7–770	0.254	44.170	−33.415	121.756
BISAP (mean, range)	2	0–4	2	0–4	0.179	0.491	−0.235	1.218
Atlanta (mean, range)	2	1–3	3	2–3	0.200	0.199	−0.109	0.507
Indication								
Infected necrosis (*n*, %)	18	82	21	66	0.567	0.424	0.115	1.566
ACS (*n*, %)	0	0	5	16	0.056	–	–	–
Bowel perforation (*n*, %)	2	9	5	16	0.509	1.852	0.325	10.538
Acute hemorrhage (*n*, %)	2	9	1	3	0.332	0.323	0.027	3.796
Colon resection (*n*, %)	3	14	8	25	**0.048**	**2.111**	**0.492**	**9.063**
Enteric stoma (*n*, %)	1	5	8	25	**0.032**	**7.000**	**0.807**	**60.684**
Hospital stay (mean days, range)	65	8–184	84	24–217	0.116	19.043	−4.949	43.034
ICU stay (mean days, range)	14	0–100	45	3–120	**0.001**	**31.097**	**15.85**	**46.34**
Clavien–Dindo (mean, range)	3	1–5	4	3.5–5	**0.002**	**1.078**	**0.45**	**1.71**
Mortality (*n*, %)	3	14	1	3	0.138	0.204	0.020	2.108

For dichotomous variables the odds ratio (OR) and for continuous variables, the mean difference is stated. CI 95=95% confidence interval. Characteristics with significant differences between the two groups are printed bold.

in our cohort followed by suspected bowel perforation, ACS, and acute intra-abdominal hemorrhage (22). Supporting recent recommendations, our findings stress the need for sparing certain patients with infected necrosis from surgery to reduce periprocedural morbidity. However, recent guidelines recommend decompressive laparotomy as treatment of choice in cases of ACS. Here a rapid laparotomy is frequently unavoidable and is sometimes performed at ICU, for example, if the patient transport appears risky (9). Since our meticulous literature study failed to reveal any relevant data on bowel perforation in SAP, we can only share our single-center experience. As in other conditions, surgery is the standard treatment in case of free abdominal air why percutaneous drainage merely can be performed as a bridging strategy before definitive surgical treatment.

The clinical concept of OAT emerged over the past three decades, while surgeons left the dogma of PFC in favor of benefits associated with the open abdomen. In general, two main scenarios lead to an inability to perform PFC: on the one hand, generalized edema leads to fascial dehiscence in which approximation is impossible and the surgeon is left with virtually no choice. This scenario is typically applied in ACS. On the other hand, definitive closure of the abdominal cavity is postponed due to the need for revision operations. Here,

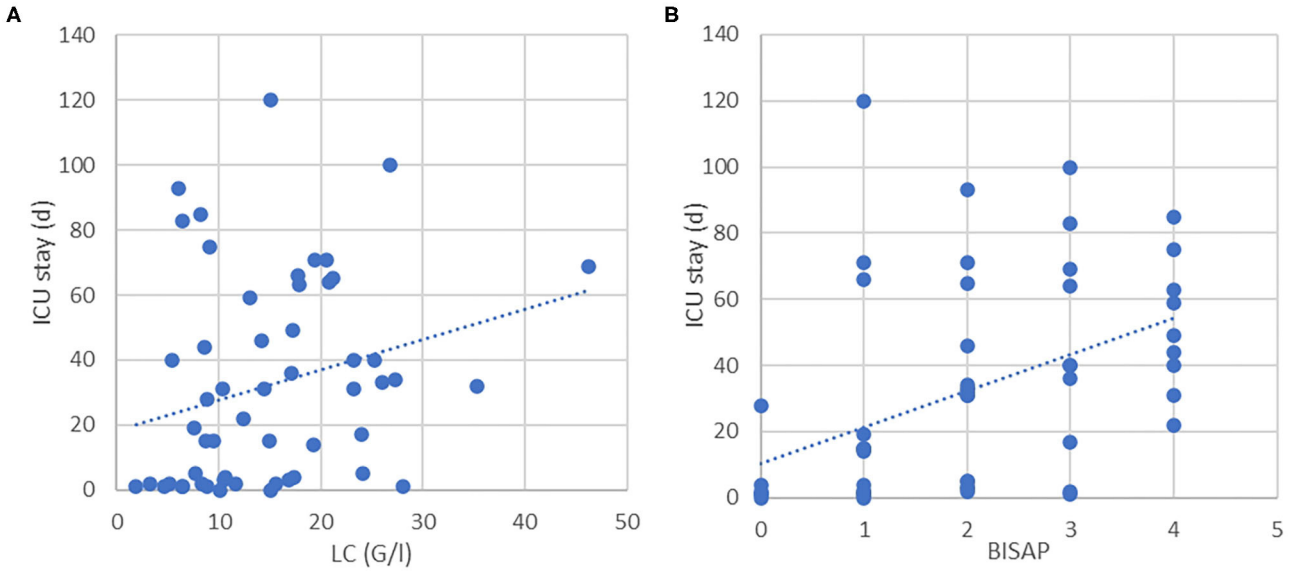

FIGURE 1 | (A) Correlation between LC and ICU stay ($P = 0.062$). **(B)** Correlation between BISAP and ICU ($P < 0.001$).

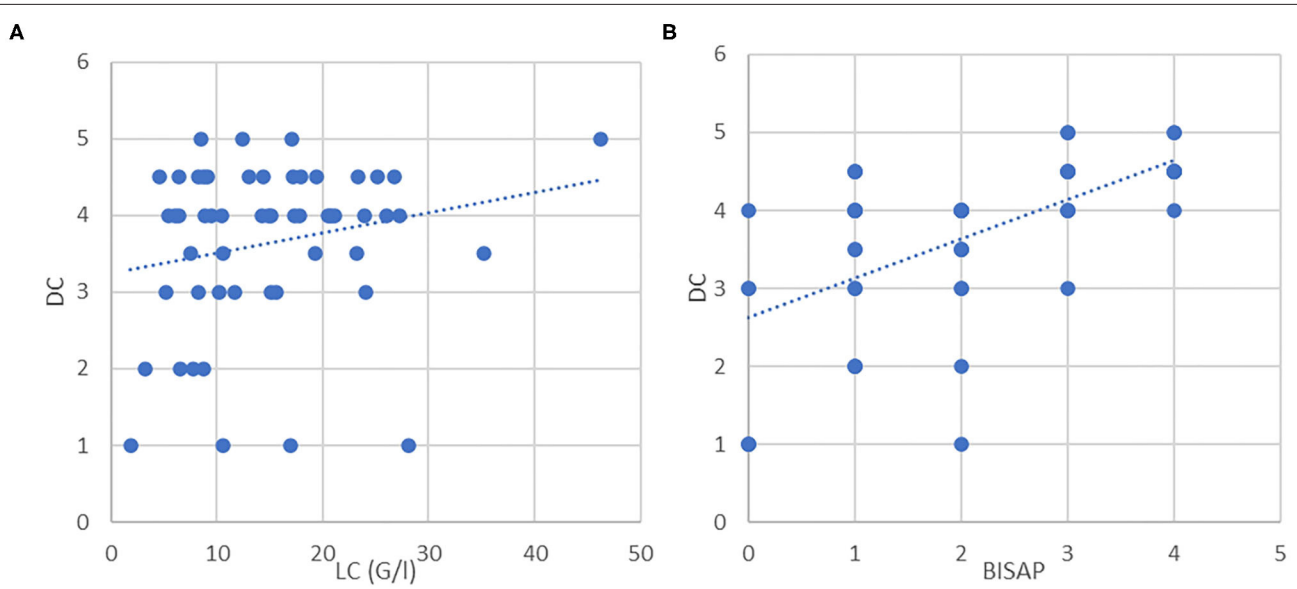

FIGURE 2 | (A) Correlation between LC and DC ($P = 0.122$). **(B)** Correlation between BISAP and DC ($P < 0.001$).

consideration is heavily based on the experience of surgical team and therefore remains poorly objectifiable. While fortunately continuous improvements broadened our spectrum of surgical therapy in these critically ill patients, our findings suggest that laparotomy and OAT independently contribute to morbidity (23). Unsuitably, even repetitive fascial approximation may lead to secondary wound healing. To allow a timely fascial closure and to prevent formation of a large ventral defect, various techniques have been reported. Mesh-mediated fascial traction represents one of the most used techniques and is also standard at our center (24). Additionally, a combination of mesh-mediated fascial traction and negative wound pressure (e.g., vacuum assisted systems) is generally accepted as best practice, leading to highest rates of fascial closure (25). Hereby, the unacceptable high rates of ventral hernia can be decreased and therefore given techniques are highly recommended. For various reasons and especially in the early era, only half of our OAT patients were treated by this contemporary standard. Finally, innovative approaches such as "fasciotens" or "ABTHERA" are currently being evaluated to allow complete fascial closure before demission (26, 27).

Despite all dedication to improved results, OAT significantly increases risk for morbidity when compared to PFC and secondary morbidity following ICU treatment and possible extensive reconstructive operations must be taken into consideration additionally if the attempt at delayed primary fascial closure fails. Reported mortality in surgically treated SAP patients ranges up to a horrifying 65% (28). Overall, we detected a much lower rate which may indicate a safe procedure when patients are carefully selected. In literature, OAT patients independently from genesis were received less excessive surgical treatment than our OAT patients. This may be seen as another expression of the unfavorable combination of SAP and surgical interventions (23, 29, 30).

Risk Factor Analysis

Until now, there are no established risk factors to determine in an early phase which patients will benefit from surgery or likely require OAT. Starting with demographic factors, reported increased mortality above the age of 70 cannot be supported by our data. In contrast to large population-based studies, two thirds of our SAP cohort are represented by men and therefore male sex seems to represent a decisive factor for severity of AP (31). Moreover, etiology-specific outcomes have been observed in AP and, in line with recent literature, bile stones and alcohol were the most common causes for SAP in our cohort. Previous data linking alcohol-induced AP to higher morbidity and mortality could not be supported by our study (32). Individuals in the OAT group had fewer cholelithiasis-induced SAP and suffered more often from idiopathic disease, although the latter did not reach statistical significance. This finding is in line with Zhu et al. who evidenced that AP caused by bile stones shows milder disease while severe and complicating diseases were mainly observed in idiopathic cases (33). The more favorable course of biliary pancreatitis can be related to the opportunity for eliminating the causative factors through ERCP/cholecystectomy allowing a rapid and full recovery. Since biliary pancreatitis is more common in women, data suggest female sex as a protective factor for OAT (34).

Because BISAP score was designed to predict mortality in SAP and showed its efficiency in a large population-based study (13), we evaluated the score's use in prediction of OAT. Though BISAP correlated significantly with ICU stay and Clavien–Dindo classification in both groups and therefore seems to be an appropriate marker for morbidity, no significant difference in BISAP was observed between the OAT and PFC groups. Although LC represents an unspecific value, it differentiated the most between both groups and may therefore indicate or even predict OAT. Moreover, Stirling et al. conducted a retrospective study for severity stratification in SAP patients and concluded that large changes in, and excessive, CRP levels predict severe disease (35). Accordingly, our OAT group expressed significantly higher CRP levels, suggesting that CRP may indicate a more critical course suggesting the need for OAT. Our data could not confirm the usefulness of PCT in severity prediction, which is in line with inconsistent results reported in literature (36).

For further validation of presented and identification of additional risk parameters of OAT in SAP, prospective randomized multicenter trials are needed. With ever growing medical data, new bioinformatic techniques of data analysis (e.g., artificial intelligence) seems most appropriate for this urgent task.

Limitations

We acknowledge several limitations in our study, mainly with respect to study design and patient cohort. The retrospective design and the relatively small number of patients, even if treated at our tertiary referral center for pancreatic diseases, reduce the level of evidence of our findings. Additionally, missing clinical data reasoned by a study period of 15 years further limits the statistical power. Furthermore, data was retrieved from a single center, with the potential risk for selection bias. Since OAT is a therapeutic concept underlying constant improvements, no uniform standard has been applied in this historic cohort hampering direct comparison of treatment. To provide sufficient evidence for this crucial field, future studies need to leverage the power of created registries (37).

Conclusion

Our data suggest that preoperative factors in surgically treated SAP may indicate the need for OAT and predict the postoperative outcome. Using these parameters, OAT patients may in the future ideally be triaged, and their management scheduled in an early phase. OAT itself appears to be a safe option with equal mortality and hospital stay compared to PFC. However, OAT may significantly increase morbidity with longer ICU stays and higher chance of bowel resection. A minimally invasive step-up approach has been shown superior to open surgery for the treatment of SAP. In combination with presented data, we suggest avoiding open surgery and particularly OAT in the treatment of SAP, whenever possible. Besides clear indication, e.g., for ACS and bowel perforation, emergency laparotomy remains the ultima ratio in SAP-related infections and evidence-based indications should be aimed in future for best patient outcomes. OAT cannot entirely be eliminated in the interdisciplinary management of SAP why respective knowledge and technical skills are mandatory for the abdominal surgeon.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

JH, MW, and HM contributed to conception and designed the study. JH and HM drafted the manuscript. All the authors contributed to manuscript revision and approved the manuscript.

REFERENCES

1. Peery AF, Crockett SD, Barritt AS, Dellon ES, Eluri S, Gangarosa LM, et al. Burden of gastrointestinal, liver, and pancreatic diseases in the United States. *Gastroenterology*. (2015) 149:1731–41.e3. doi: 10.1053/j.gastro.2015.08.045
2. Krishna SG, Kamboj AK, Hart PA, Hinton A, Conwell DL. The changing epidemiology of acute pancreatitis hospitalizations: a decade of trends and the impact of chronic pancreatitis. *Pancreas*. (2017) 46:482–8. doi: 10.1097/MPA.0000000000000783
3. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis-—2012: revision of the Atlanta classification and definitions by international consensus. *Gut*. (2013) 62:102–111. doi: 10.1136/gutjnl-2012-302779
4. Agarwal S, George J, Padhan RK, Vadiraja PK, Behera S, Hasan A, et al. Reduction in mortality in severe acute pancreatitis: a time trend analysis over 16 years. *Pancreatology*. (2016) 16:194–9. doi: 10.1016/j.pan.2016.01.012
5. Petrov MS, Shanbhag S, Chakraborty M, Phillips ARJ, Windsor JA. Organ failure and infection of pancreatic necrosis as determinants of mortality in patients with acute pancreatitis. *Gastroenterology*. (2010) 139:813–20. doi: 10.1053/j.gastro.2010.06.010
6. Hoffmeister A, Mayerle J, Beglinger C, Büchler MW, Bufler P, Dathe K, et al. S3-leitlinie chronische pankreatitis: definition, ätiologie, diagnostik, konservative, interventionell endoskopische und operative therapie der chronischen pankreatitis. Leitlinie der Deutschen Gesellschaft für Verdauungs- und Stoffwechselkrankheiten (DGV). *Z Gastroenterol*. (2012) 50:1176–224. doi: 10.1055/s-0032-1325479
7. van Santvoort HC, Besselink MG, Bakker OJ, Hofker HS, Boermeester MA, Dejong CH, et al. A step-up approach or open necrosectomy for necrotizing pancreatitis. *N Engl J Med*. (2010) 362:1491–502. doi: 10.1056/NEJMoa0908821
8. Sartelli M, Abu-Zidan FM, Ansaloni L, Bala M, Beltrán MA, Biffl WL, et al. The role of the open abdomen procedure in managing severe abdominal sepsis: WSES position paper. *World J Emerg Surg*. (2015) 10:35. doi: 10.1186/s13017-015-0032-7
9. Kirkpatrick AW, Roberts DJ, De Waele J, Jaeschke R, Malbrain MLNG, De Keulenaer B, 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. doi: 10.1007/s00134-013-2906-z
10. van Santvoort HC, Bakker OJ, Bollen TL, Besselink MG, Ahmed Ali U, Schrijver AM, et al. A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. *Gastroenterology*. (2011) 141:1254–63. doi: 10.1053/j.gastro.2011.06.073
11. Coccolini F, Roberts D, Ansaloni L, Ivatury R, Gamberini E, Kluger Y, et al. The open abdomen in trauma and non-trauma patients: WSES guidelines. *World J Emerg Surg*. (2018) 13:1–16. doi: 10.1186/s13017-018-0167-4
12. Leppäniemi A, Tolonen M, Tarasconi A, Segovia-Lohse H, Gamberini E, Kirkpatrick AW, et al. 2019 WSES guidelines for the management of severe acute pancreatitis. *World J Emerg Surg*. (2019) 14:27. doi: 10.1186/s13017-019-0247-0
13. Wu BU, Johannes RS, Sun X, Tabak Y, Conwell DL, Banks PA. The early prediction of mortality in acute pancreatitis: a large population-based study. *Gut*. (2008) 57:1698–703. doi: 10.1136/gut.2008.152702
14. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. (2004) 240:205–13. doi: 10.1097/01.sla.0000133083.54934.ae
15. Pendharkar SA, Mathew J, Zhao J, Windsor JA, Exeter J, Petrov MS. Ethnic and geographic of pancreatitis and post- mellitus in New Zealand : a nationwide population- based study. *N Z Med J*. (2017) 130:55–68. Available online at: https://www.nzma.org.nz/journal-articles/ethnic-and-geographic-variations-in-the-incidence-of-pancreatitis-and-post-pancreatitis-diabetes-mellitus-in-new-zealand-a-nationwide-population-based-study
16. Márta K, Lazarescu AM, Farkas N, Mátrai P, Cazacu I, Ottóffy M, et al. Aging and comorbidities in acute pancreatitis I: a meta-analysis and systematic review based on 194,702 patients. *Front Physiol*. (2019) 10:328. doi: 10.3389/fphys.2019.00328
17. Szakács Z, Gede N, Pécsi D, Izbéki F, Papp M, Kovács G, et al. Aging and comorbidities in acute pancreatitis II: a cohort-analysis of 1203 prospectively collected cases. *Front Physiol*. (2019) 10: 1776. doi: 10.3389/fphys.2018.01776
18. Strik C, van den Beukel B, van Rijckevorsel D, Stommel MWJ, ten Broek RPG, van Goor H. Risk of pain and gastrointestinal complaints at 6months after elective abdominal surgery. *J Pain*. (2019) 20:38–46. doi: 10.1016/j.jpain.2018.07.010
19. Keane MG, Sze SF, Cieplik N, Murray S, Johnson GJ, Webster GJ, et al. Endoscopic versus percutaneous drainage of symptomatic pancreatic fluid collections: a 14-year experience from a tertiary hepatobiliary centre. *Surg Endosc*. (2016) 30:3730–40. doi: 10.1007/s00464-015-4668-x
20. van Brunschot S, van Grinsven J, van Santvoort HC, Bakker OJ, Besselink MG, Boermeester MA, et al. Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial. *Lancet*. (2018) 391:51–8. doi: 10.1016/S0140-6736(18)31189-9
21. Bang JY, Arnoletti JP, Holt BA, Sutton B, Hasan MK, Navaneethan U, et al. An endoscopic transluminal approach, compared with minimally invasive surgery, reduces complications and costs for patients with necrotizing pancreatitis. *Gastroenterology*. (2019) 156:1027–40.e3. doi: 10.1053/j.gastro.2018.11.031
22. Jacob AO, Stewart P, Jacob O. Early surgical intervention in severe acute pancreatitis: Central Australian experience. *ANZ J Surg*. (2016) 86:805–10. doi: 10.1111/ans.12707
23. Miller PR, Meredith JW, Johnson JC, Chang MC, Fabian TC, Maxwell R, et al. Prospective evaluation of vacuum-assisted fascial closure after open abdomen: planned ventral hernia rate is substantially reduced. *Ann Surg*. (2004) 239:608–16. doi: 10.1097/01.sla.0000124291.09032.bf
24. López-Cano M, García-Alamino JM, Antoniou SA, Bennet D, Dietz UA, Ferreira F, et al. EHS clinical guidelines on the management of the abdominal wall in the context of the open or burst abdomen. *Hernia*. (2018) 22:921–39. doi: 10.1007/s10029-018-1818-9
25. Willms A, Güsgen C, Schaaf S, Bieler D, von Websky M, Schwab R. Management of the open abdomen using vacuum-assisted wound closure and mesh-mediated fascial traction. *Langenbeck's Arch Surg*. (2014) 400:91–9. doi: 10.1007/s00423-014-1240-4
26. Frazee RC, Abernathy SW, Jupiter DC, Hendricks JC, Davis M, Regner JL, et al. Are commercial negative pressure systems worth the cost in open abdomen management? *J Am Coll Surg*. (2013) 216:730–3. doi: 10.1016/j.jamcollsurg.2012.12.035
27. Fung SN, Vaghiri S, Ashmawy H, Kropil F, Rehders A, Wt K. Case Report Fasciotens © Abdomen ICU : Novel Device Prevents Abominal Wall Retraction and Facilitates Early Abdominal Wall Closure of Septic Open Abdomen. (2019), 354–8.
28. Portelli M, Jones CD. Severe acute pancreatitis: pathogenesis, diagnosis and surgical management. *Hepatobiliary Pancreat Dis Int*. (2017) 16:155–9. doi: 10.1016/S1499-3872(16)60163-7
29. Perez D, Wildi S, Demartines N, Bramkamp M, Koehler C, Clavien PA. Prospective evaluation of vacuum-assisted closure in abdominal compartment syndrome and severe abdominal sepsis. *J Am Coll Surg*. (2007) 205:586–92. doi: 10.1016/j.jamcollsurg.2007.05.015
30. Verdam FJ, Dolmans DEJGJ, Loos MJ, Raber MH, De Wit RJ, Charbon JA, et al. Delayed primary closure of the septic open abdomen with a dynamic closure system. *World J Surg*. (2011) 35:2348–55. doi: 10.1007/s00268-011-1210-8
31. Xiao AY, Tan MLY, Wu LM, Asrani VM, Windsor JA, Yadav D, et al. Global incidence and mortality of pancreatic diseases: a systematic review, meta-analysis, and meta-regression of population-based cohort studies. *Lancet Gastroenterol Hepatol*. (2016) 1:45–55. doi: 10.1016/S2468-1253(16)30004-8
32. Lankisch PG, Assmus C, Pflichthofer D, Struckmann K, Lehnick D. Which etiology causes the most severe acute pancreatitis? *Int J Gastrointest Cancer*. (1999) 26:55–7. doi: 10.1007/BF02781731
33. Zhu Y, Pan X, Zeng H, He W, Xia L, Liu P, et al. A study on the etiology, severity, and mortality of 3260 patients with acute pancreatitis according to the revised atlanta classification in Jiangxi, China over an 8-year period. *Pancreas*. (2017) 46:504–9. doi: 10.1097/MPA.0000000000000776
34. Weitz G, Woitalla J, Wellhöner P, Schmidt K, Büning J, Fellermann K. Does etiology of acute pancreatitis matter? A review of 391 consecutive episodes. *JOP*. (2015) 16:171–5. doi: 10.6092/1590-8577/2959

35. Stirling AD, Moran NR, Kelly ME, Ridgway PF, Conlon KC. The predictive value of C-reactive protein (CRP) in acute pancreatitis – is interval change in CRP an additional indicator of severity? *Hpb.* (2017) 19:874–80. doi: 10.1016/j.hpb.2017.06.001
36. Staubli SM, Oertli D, Nebiker CA. Laboratory markers predicting severity of acute pancreatitis. *Crit Rev Clin Lab Sci.* (2015) 52:273–83. doi: 10.3109/10408363.2015.1051659
37. Willms A, Muysoms F, Güsgen C, Schwab R, Lock J, Schaaf S, et al. The Open Abdomen Route by EuraHS: introduction of the data set and initial results of procedures and procedure-related complications. *Hernia.* (2017) 21:279–89. doi: 10.1007/s10029-017-1572-4

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METHODS
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Delayed Closure of Open Abdomen in Septic Patients Treated With Negative Pressure Vacuum Therapy and Dynamic Sutures: A 10-Years Follow-Up on Long-Term Complications

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Introduction: Patients with open abdomen after surgical interventions associated with the complication of secondary peritonitis are successfully treated with negative pressure wound therapy. The use of dynamic fascial sutures reduces fascial lateralization and increases successful delayed fascial closure after open abdomen treatment.

Methods: In 2017 we published the follow-up results of 38 survivors out of 87 open abdomen patients treated with negative pressure wound therapy and dynamic fascial sutures between 2007 and 2012. In our current study we present the 10-years follow-up results regarding long-term complications with the focus on incisional hernias and pain. Since 2017 seven more patients have died, hence 31 patients were included in the current study. The patients were asked to answer questions about specific long-term complications of OA treatment including pain, the presence of incisional hernias and subsequent surgical interventions. Demographic data and data regarding fascial closure after open abdomen treatment were collected. All results were analyzed quantitatively. The follow-up period was 8–13 years.

Results: The median age was 69 (30–90) years, and 15 (48.4%) were females. Twenty-four patients (77.4%) responded to the questionnaire: Three patients (12.5%) suffered from pain in the original operating field, all three at rest but not during exercise. None of the patients required analgesic treatment. Eleven patients (45.8%) were found to have incisional hernias. Five out of 11 hernias (45.5%) were treated by surgery and did not declare any pain in the operating field. Among the patients with incisional hernias lower MPI (Mannheimer Peritonitis Index) at the time of primary surgery but more reoperations and treatment days were found. The technique of fascial closure was heterogenic and no differences in the occurrence of incisional hernia could be detected.

Conclusion: The incidence of incisional hernias after open abdomen treatment is still high, but are associated with little pain in the original operating field. Further studies are required to investigate methods for fascial closure techniques after OA treatment.

Keywords: open abdomen, negative pressure wound therapy, delayed fascial closure, dynamic fascial suture, incisional hernia

INTRODUCTION

The treatment of patients with open abdomen (OA) and the subsequent fascial closure (FC) are still challenging clinical problems. The mortality rate in patients with abdominal sepsis remains between 20 and 60% (1). Several techniques for the treatment of OA were introduced over the last years, but most of them did not lead to the anticipated success and were already abandoned [e.g., Marlex® Zipper (2), plastic bags (the Bogota technique) (3), Velcro adhesive sheets (4), sandwich technique (5), modified Barker Vacuum Bag (6)]. Negative pressure wound therapy (NPWT) proved to significantly decrease morbidity and mortality in patients with secondary peritonitis and OA treatment. NPWT activates wound healing, acts as wound fluid drainage, reduces infection and abdominal compartment syndrome (7–9). A "frozen abdomen" and entero-atmospheric fistulas are among possible complications of OA treated with NPWT (10, 11). The retraction of the fascial edges can lead to failure of delayed primarily fascial closure and patients end up with planed hernias (12). Different techniques were established to minimize fascial retraction and facilitate FC like mesh mediated facial traction (13), retention sutured sequential FC (14), or Wittmann patching (15). Dynamical fascial sutures (DFS) reduce fascial retraction and are associated with a high incidence of FC after OA treatment (16, 17).

The duration of OA treatment and the closure technique (component separation, suture technique) influence the outcome of OA treatment (9). Early abdominal closure can lead to reinfection and relaparotomy with subsequent destruction of the fascia, whereas late closure lead to recuts muscle lateralization and complications of abdominal wall reconstruction (1). The prognosis of OA treatment can significantly be improved by NPWT and dynamic closure techniques (18).

Up to know there are some studies in the literature that describe quality of life and incidence of incisional hernias (IH) after OA treatment with NPWT for up to 5 years (19–21). However, long-term outcome studies up to 10 years are rarely found.

In 2017 we published long-term follow-up results of 38 survivors out of 87 patients treated with NPWT and DFS between 2007 and 2012: The median age was 60.9 (25.2–86.1) years, and 17 (44.7%) were females. Twenty-one patients (55.3%) answered the questions about specific long-term complications of OA treatment regarding pain and incisional hernias. Six patients (28.6%) suffered from pain in the previous operating field. Seven (33.3%) patients developed incisional hernias. Three out of seven hernias (42.9%) were treated by surgery.

The aim of the present study was to follow-up these patients and to assess their condition 8–13 years after OA treatment with NPWT and DFS (**Figure 1**). Thirty-eight patients were included in the recent study according to the protocol of our last publication in 2017 (20). After a mean follow-up period of 8–13 years patients were again questioned about long-term complications of OA treatment such as pain, incisional hernia and additional surgical interventions.

Demographic data and further causes of incisional hernias after NPWT therapy were analyzed.

To the best of our knowledge this the longest follow-up study investigating long-term complications of OA treatment with NPWT and DFS.

METHODS

Study Population

Thirty-eight patients, all survivors from our last study in 2017, were included in the current investigation (20). Inclusion criteria were secondary peritonitis and OA treated with NPWT and DFS between 2007 and 2012 in our hospital. Exclusion criteria were hemorrhage, localized peritonitis, or the ability to perform sufficient source control during the initial procedure in stable patients (17).

Because of the prospective but non-randomized and non-comparative character of the study, the local ethical committee waived responsibility.

Surgical Technique

The surgical technique of OA treatment with NPWT and DFS has been described in detail in our first publication in 2013 (17).

In brief, after treatment of the source of the initially present secondary peritonitis an intraabdominal vacuum dressing was placed. In order to prevent abdominal muscle lateralization elastic loops were sutured to the fascia in large bites. Patients were admitted to ICU (intensive care unit) and planned reoperations were performed not later than 48 h. After successful NPWT the vacuum dressing and DFS were removed and the abdomen closed with either interrupted or running sutures. Thirty patients out of the included 38 patients in the previous study (78.9%) received FC. In four patients (10.6%) the fascia was not primarily closed and ended up with planned hernias (skin or split- thickness skin graft closure). Fascial closure was performed with running sutures in 26 patients (68.4%), in four patients the fascia was

Abbreviations: OA, Open Abdomen; NPWT, Negative Pressure Wound Therapy; DFS, Dynamic Fascial Sutures; FC, Fascial Closure; IH, Incisional Hernia; MPI, Mannheimer Peritonitis Index; SAPS, Simplified Acute Physiology Score; ASA, American Society of Anesthesiologists; ICU, Intensive care unit; VAS, Visual Analog Scale.

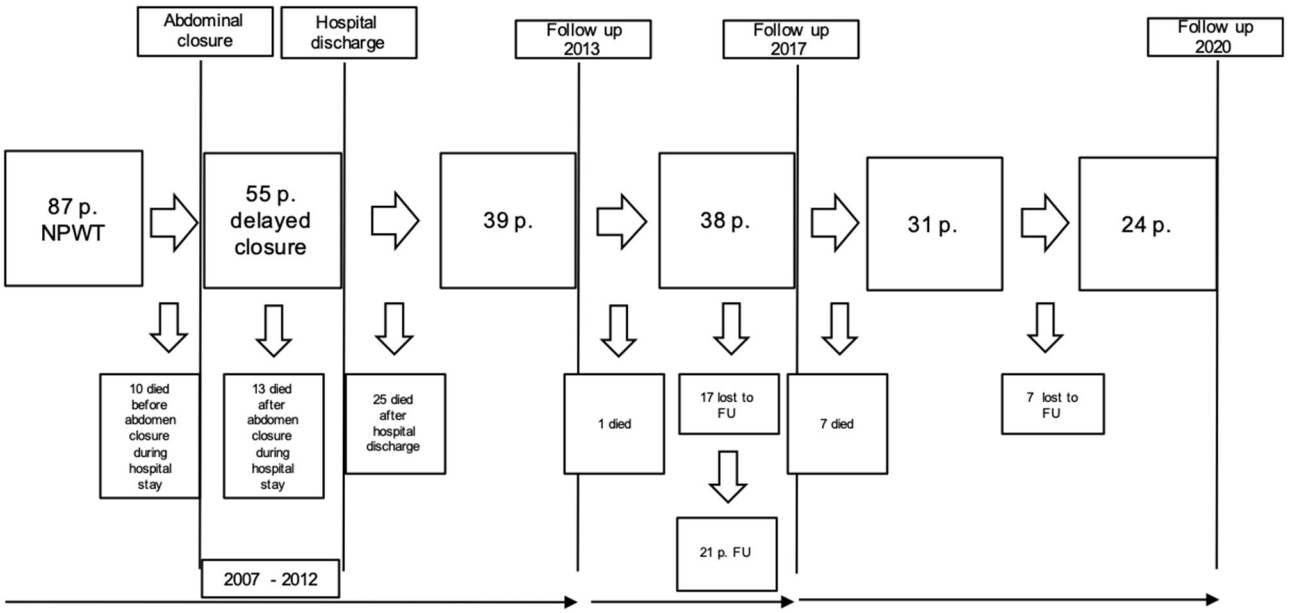

FIGURE 1 | Time line of follow-up (FU): Figure shows number of excluded and included patients over time.

closed using interrupted sutures. In four patients the applied technique was not sufficiently documented (20).

Questionnaire

A questionnaire regarding long-term complications of OA treatment due to secondary peritonitis between 2007 and 2012 were sent to the included patients. Patients were asked about pain in the operating field differentiating between acute and chronic pain and the necessity of analgesic treatment. The questionnaire further targeted potential IH after DFS, hernia diagnostics and treatment or other surgeries in the previous operating field. In case of not returned questionnaire within 4 weeks the patients were contacted for an oral interview. Questions are listed in **Figure 2**. Patients we were not able to get in touch with were lost to follow-up.

Data Collection

We collected the following data: patients' demographics, MPI, ASA classification (American Society of Anesthesiologists), Simplified Acute Physiology Score (SAPS), number of NPWT changes, duration of NPWT, and duration of ICU stay in days.

The results were analyzed quantitatively and presented as median and range, unless otherwise stated.

Statistical testing was carried out using the Kolmogorov–Smirnov Test for Gaussian distribution. *t*-test was used when comparing two groups and when data were normally distributed, Mann–Whitney test when data were not normally distributed. Contingency was tested with Chi-square (>2 variables) and Fisher's tests (two variables, low n). *p*-values of <0.05 were considered to indicate statistical significance.

RESULTS

Demographic Data

Since our study in 2017 seven more patients had deceased (four women, three men) with a median age of 78 years (69–96 years). The causes of death were not documented, but the main reason might have been natural death due to the patients' high age.

Thirty-one patients were included in the current study, 15 patients were females (48.4%) and 16 were males (51.6%) with a median age of 69 years (33–90 years). The overall mortality rate after the follow-up duration starting in 2007 with 87 included patients was 64.4%. The median MPI as index for intraperitoneal peritonitis at the timepoint of the initial surgery was 14 (5–26), the median ASA as index for co-morbidities was 2 (1–4) and the SAPS as index for physiological health was 8 (0–28) in the current study population (**Table 1**).

The source of infection at the initial surgery was the upper GI (gastrointestinal) tract (stomach, duodenum, small bowel) in 10 patients (32.3%), the lower GI tract (colon, rectum) in 19 patients (61.3%) and pancreas in two cases (6.5%) (**Figure 3**).

The follow-up period was 8–13 years.

NPWT and Delayed Closure

The median NPWT duration was 6.5 days (3–62) with a median of 3 (1–16) reoperations (**Table 1**). In 27 patients (87.1%) FC could be performed, in four patients (12.9%) FC was not possible: in two patients the skin only could be closed, in one case split-thickness skin grafts were used for abdominal closure. These three patients had planned hernias after discharge from hospital. One patient received plastic abdominal wall reconstruction.

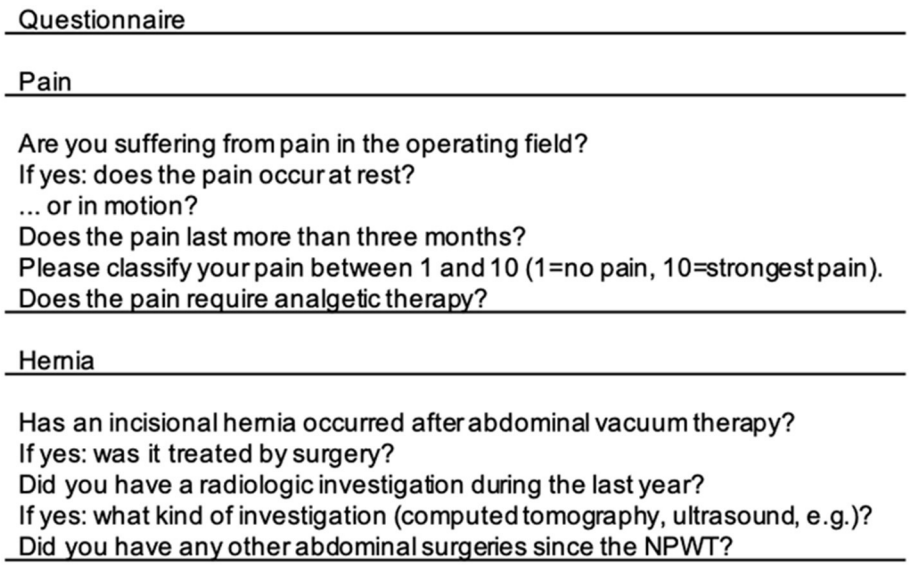

FIGURE 2 | Questionnaire about long-term complications after OA and NPWT. OA, open abdomen; NPWT, negative pressure wound therapy.

TABLE 1 | Patients demographic data.

Population	31
Male sex	16 (51.6%)
Female sex	15 (48.4%)
Age	69 (33–90)
Source of Infection	
Upper GI	10 (32.2%)
Lower GI	19 (61.3%)
Pancreas	2 (6.5%)
MPI	14 (5–26)
SAPS	8 (0–28)
ASA	2 (1–4)
Reoperations	3 (1–16)
NPWT duration	6.5 (3–62)
ICU stay	13 (3–74)

GI, Gastrointestinal tract; MPI, Mannheimer Peritonitis score; SAPS, Simplified Acute Physiology Score; ASA, American Society of Anesthesiologists; NPWT, Negative Pressure Wound Therapy; ICU, Intensive care unit.

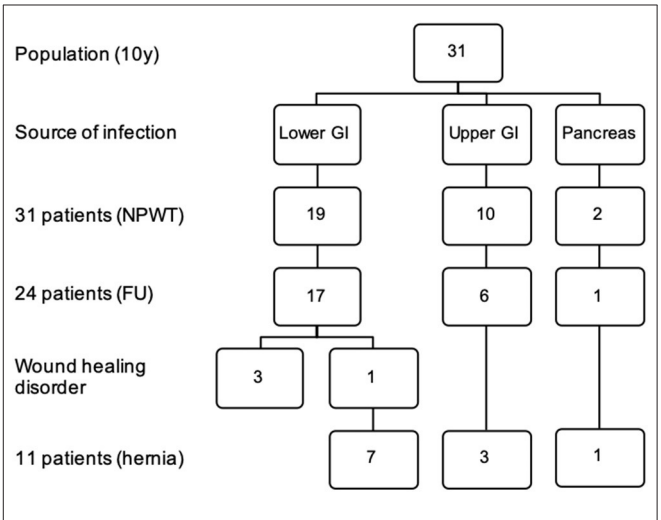

FIGURE 3 | Source of infection, wound healing disorder and incisional hernia in a 10 years follow up. FU, follow-up; NPWT, negative pressure wound therapy; GI, gastrointestinal tract.

Fascial closure with running sutures was performed in 22 patients: Six with Monomax® 0 (Braun, Melsungen, Germany), three with Monomax® 1 (Braun, Melsungen, Germany), eight with PDS® (Ethicon, Norderstedt, Germany), two with MaxonPlus® (Braun, Melsungen, Germany), and three with Prolene® (Ethicon, Norderstedt, Germany). In two patients the fascia was closed with interrupted sutures using Vicryl® (Ethicon, Norderstedt, Germany). In three patients the applied technique was not sufficiently documented (**Figure 4**). The median stay at the ICU was 13 (3–74) days.

Questionnaire

Among the 31 included patients 24 (77.4%) answered the questionnaire (**Figure 2**).

Three patients (12.5%) were still suffering from pain in the operating field. All three patients were having pain at rest but not during exercise typical of the respective patient's age and for more than 3 months (chronic pain). None of the patients required analgesic treatment. The mean VAS score was 3 (3–4). Twenty-one patients (87.5%) did not feel any pain in the original operating field (**Table 2**).

Among the 24 patients, 11 patients (45.8%) have developed an IH, whereas three patients suffered from planned IH after skin closure only or split thickness skin grafts. Six hernias (54.5%) were diagnosed radiologically (computed tomography, magnetic resonance imaging, ultrasound), the other five hernias

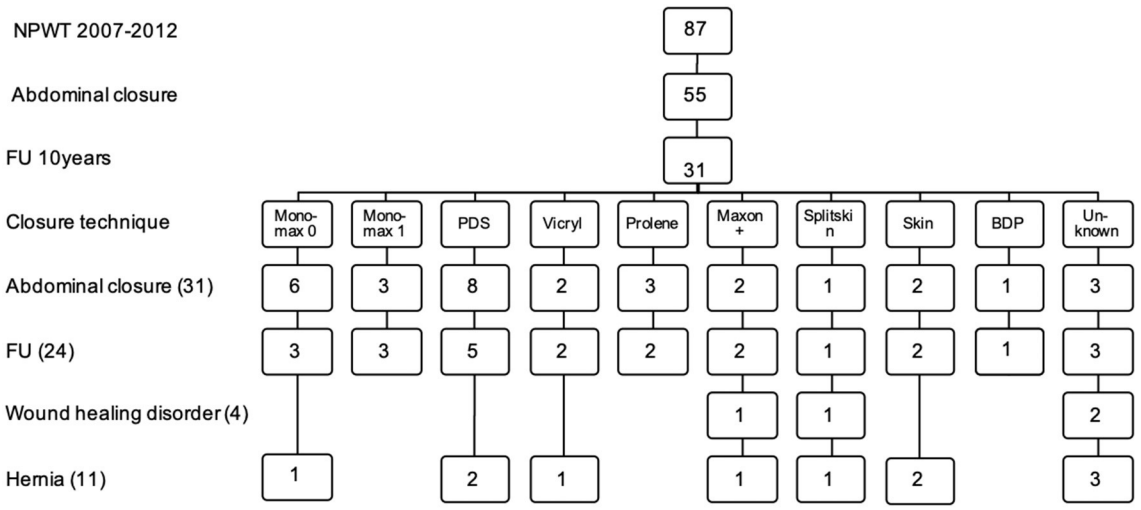

FIGURE 4 | Techinque of delayed abdominal closure, wound healing disorder and incisional hernia in a 10 years follow up. FU, follow-up; NPWT, negative pressure wound therapy.

TABLE 2 | Results of the questionnaire answered by 24 patients.

Pain	3	12.5%
Pain at rest	3	
Pain in motion	0	
Chronic pain (>3 months)	3	
VAS (1–10)	3.3	3–4
Analgetic therapy required	0	
Incisional hernia	11	45.8%
Clinically detected	5	45.5%
Radiologically detected	6	54.5%
Hernia repair	5	45.5%
Recurrence	1	
Other abdominal surgeries after NPWT	6	25%

TABLE 3 | Answers regarding incisional hernias, with and without repair and pain.

	Pain (3)	**No pain (21)**
Hernia (11)	2 (18.2%)	9 (81.8%)
No hernia (13)	1 (7.7%)	12 (92.3%)
Hernia (w. repair) (5)	0	5 (100%)
Hernia (wo. repair) (6)	2 (33.3%)	4 (66.7%)

(45.5%) were diagnosed by clinical examination. Five patients (45.5%) with hernias underwent surgical hernia repair, with one recurrence hernia among the operated patients. None of these patients claimed pain in the operating field (**Table 3**).

Among the 11 IH patients nine (81.8%) were found to have an asymptomatic hernia and two (18.2%) symptomatic hernias. Two out of three patients with pain in the operating field (66.6%) still had an IH and did not have hernia repair (**Table 3**, **Figure 5**).

Six patients (25%) underwent additional abdominal surgery after NPWT and fascial or skin closure: one prostatectomy, two stoma surgeries, one scar correction, one cholecystectomy, one reason for surgery was not reported.

The reason for loss to follow-up were changes in address and/or phone number, or personal reason not to answer our questionnaire.

Incisional Hernia

We compared the technique of fascial closure, the source of infection, delayed wound healing in patients that developed an IH after NPWT with DFS.

Among the 24 patients, 11 patients (45.8%) were found to have an IH. Four patients (36.4%) received FC with running sutures: one with Monomax® 0 (9%), two with PDS® (18.2%) and one with MaxonPlus® (9%). In one patient (9%) the fascia was closed with interrupted sutures (Vicryl®). In three patients the technique of FC was not documented (27.3%). Three patients did not receive FC after NPWT therapy but skin closure only or split thickness grafts (27.3%) (**Figure 4**).

One patient that was found to have an IH after NPWT has died since our last publication and was excluded in the present study.

The source of infection of the secondary peritonitis among the IH patients was documented: In three out of ten patients (30%) with the upper GI tract (stomach, duodenum, small bowel), in seven among 19 patients (36.8%) with the lower GI (colon, rectum) and in one out of two patients (50%) with the pancreas as source of infection an IH was diagnosed (**Figure 3**). No significant relation could be shown between source of peritonitis and the development of IH.

Four patients suffered delayed wound healing after NPWT, one of these patients did not receive FC but skin closure and one patient with delayed wound healing developed an IH. All four patients had the lower GI as source of infection (**Figure 3**), but not all of these were found to have an IH.

Delayed abdominal closure in patients with IH was achieved after 10 (3–62) days with 4 (1–16) reoperations. Patients without

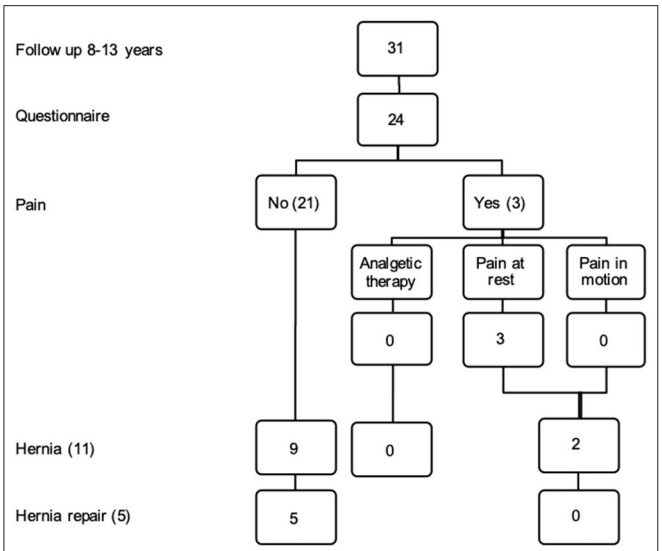

FIGURE 5 | Twenty-four patients were available for follow up. Flow chart regarding pain incisional hernia and hernia repair.

TABLE 4 | Possible risk factors for the development of incisional hernia (IH) after NPWT.

	IH	No IH
NPWT (days)	10 (3–62)	6 (3–38)
Reoperations	4 (1–16)	3 (1–10)
ICU (days)	13 (3–74)	15 (11–39)
MPI	11 (5–26)	15 (9–25)
SAPS	7 (1–15)	11 (4–28)
ASA	1 (1–3)	2 (1–4)
BMI	28 (16–44)	27 (18–35)

MPI, Mannheimer Peritonitis score; SAPS, Simplified Acute Physiology Score; ASA, American Society of Anesthesiologists; NPWT, Negative Pressure Wound Therapy; ICU, Intensive care unit; BMI, Body Mass Index.

IH received delayed closure after 6 (3–38) days with 3 (1–10) reoperations (**Table 4**). No significant differences were detected between treatment days, reoperations and the development of IH ($p = 0.302$ and $p = 0.238$). The mean MPI in patients that developed an IH [11 (5–26)] was lower compared to the patients without IH [15(9–25)] but failed to be significant ($p = 0.107$). The mean SAPS and ASA score was lower in patients that have developed an incisional hernia [7 (1–15) vs. 11 (4–28), 1 (1–3) vs. 2 (1–4)] ($p = 0.66$, $p = 0.92$). The mean stay at ICU was lower in patients with IH [13 (3–74) vs. 15 (11–39)] ($p = 0.1$) (**Table 4**). The mean BMI was higher in patients with IH [28 (16–44)] compared to patients without IH [27 (18–35)] but without significant differences ($p = 0.564$).

DISCUSSION

After a follow-up period of 8–13 years 31 out of 87 primarily included patients (35.6%) were still alive. Seven more patients died since our last study in 2017. The overall mortality rate over the whole follow-up period is 64.4%, whereas 26.4% of the patients already died during the hospital stay. We already described a high early mortality rate and detected significantly higher MPI, ASA and SAPS scores in the patient population that did not survive until the first follow-up. After these first critical months OA and NPWT is accompanied by a satisfying survival rate (20). Currently there are no data in the literature about survival rates over a follow-up period of 10 years.

In the current study 24 among 31 patients (77.4%) were available for follow-up compared to 21 out of 36 (55.3%) in our study in 2017. In 11 patients an incisional hernia was diagnosed (45.8%). In our previous study a lower IH rate with seven hernias among 21 patients (33.3%) were detected. Additionally, two of the IH patients died since 2017 and were excluded in the present study. The higher rate of IH can be explained by two recently diagnosed hernias and four patients with hernias that were not available for follow-up in the previous study.

The hernia rate of 45.8% after a period of 8–13 years is still lower than described by Petersson et al. who found an IH rate of 62% in a 5-years follow-up after OA treatment with vacuum assisted wound closure and mesh mediated fascial traction. The mean time of hernia diagnosis was 11 months, either by clinical investigation (36%) or CT scan or laparotomy in further 30%. The earlier development of IH can be explained by a more extensive injury to the fascia caused by suturing the mesh to the fascial edges (19).

Brandl et al. (12) found an IH rate of 35% at a median follow-up time of 26 (12–81) months using NPWT for OA treatment without DFS or other devices to reduce fascial lateralization. The Kaplan-Meier analysis estimated a hernia rate of 66% after five years, which is higher compared to our study with 45.8% after 7–13 years. They described the best results with running sutures and a slow absorbable material for DFS and the highest IH rate with interrupted sutures and absorbable material (Vicryl®). They discuss a certain selection bias with a higher rate of Vicryl® use in patients with a higher extent of fascial contamination and injury, and higher degree of tension at closure. In our study DFS were applied to reduce fascial lateralization to lower the consecutive tension at the time of FC. The higher fascial tension and the use of different closure techniques can explain the differences in IH rates described by Brandl et al. (12). A follow-up study with recent data might be of interest.

The recommended closure technique for midline closure described by Israelsson et al. is a running suture in small bite technique with 5:1 or 6:1 suture-to-wound length (22–24). We changed closure technique according to the recommendations from interrupted sutures with multifilament, resorbable and non-resorbable material *(Vicryl®, Ethibond®)* to large bite and small bite technique with monofilament, non-resorbable *(Prolene®)* and late resorbable sutures *(PDS®, MaxonPlus®, MonoMax®)*. This change caused a heterogeneity in closure technique in our study, thus recommendations for FC according to our study results are hardly possible.

Petersson et al. performed FC with PDS® achieving a suture to wound ratio of at least 4:1 after mesh mediated fascial traction and found higher IH rates compared to our study (19). This

might well be due to the above mentioned more extensive fascial injury rather than to the actual suture technique.

Jakob et al. described a new technique for abdominal closure after OA treatment. After an initial period with NPWT they implanted an intraperitoneal onlay mesh (VAC-IPOM). The fascia was partially or completely closed with running sutures using PDS® and NPWT was applied to the mesh. NPWT was kept until an adequate formation of granulation tissue was achieved. They compared their new technique with vacuum-assisted wound closure and mesh-mediated fascial traction (VAWCM) with direct fascial closure using absorbable loops. They described less re-operations and reduced hospital and ICU stay after VAC-IPOM therapy. Complete fascial closure using VAC-IPOM was achieved in only 26% compared to 74.2% using VAWCM. 25.8% of patients with VAWCM were left with a planned hernia. They described a significantly longer hernia-free survival using their new technique caused by a possible sufficient stabilization using the IPOM mesh without direct fascial closure and a subsequent reduction of extensive fascial tension. This reduced fascial tension and the possible fascial injury as well as the use of resorbable material in the VAWCM group can explain the difference in hernia incidence (21). A comparison to our study is hardly possible, because the authors do not offer an IH rate at a given time point.

Willms et al. recently published a multi-center multivariable analysis of data from the Open Abdomen Route of the European Hernia Society. They found a significant improvement of prognosis of OA and a positive correlation of fascial closure with NPWT and dynamic closure techniques. A high intraabdominal contamination and long treatment before facial closure was found to be negative correlated with fascial closure (18).

In our previous study we found significantly fewer NPWT treatment days and reoperations in patients without IH (20). These findings indicate a possible negative influence of OA and NPWT on hernia development. In the recent study patients with IH achieved delayed abdominal closure after 10 (3–62 days) and 4 (1–16) reoperations. Patients without IH were again found to have fewer NPWT treatment days [6 (3–38)] and reoperations [3 (1–10)]. Nevertheless, after a mean of 10 years no significant differences could be detected between treatment days, reoperations and the development of hernias, although we still see a clear trend. Interestingly and in contrast to the results regarding reoperations and treatment days, we detected a lower MPI, lower ASA and SAPS scores and fewer days at ICU in patients that developed an incisional hernia over a time period of 8–13 years. Hence, patients without IH had a higher MPI but a shorter treatment period. These findings might support a trend to fewer reoperations and treatment days despite distinct secondary peritonitis at the time of acute primary surgery. The BMI at time of primary surgery was lower in patients that did not develop an incisional hernia without significant differences. Bjarnason also did not find a significant association between known risk factors of IH (e.g., obesity) and the development of IH one year after OA treatment but discussed a possible type II statistical error (25). Interestingly, all four patients with wound healing disorder had the lower GI as source of infection, but not all of these patients were found to have an IH in the FU. Wound healing disorder is a well-known risk factor for IH, but might lose its importance in the development of IH in a long-term FU.

Three out of 24 patients were still suffering from pain in the original operating field, one patient had three further abdominal surgeries, the other two patients achieved abdominal closure after NPWT with split skin grafts and planned hernias. None of the patients required ongoing pain medication. Five patients with IH had undergone incisional hernia repair. In contrast to our previous study none of the patients complained of pain in the operating field. Among the six patients that did not have hernia repair four do not claim pain in the operating field. We reported of six patients with pain in our previous study with a possible relation of pain and IH. Bjarnason et al. reported similar relations between pain and IH after NPWT and mesh-mediated fascial traction after 1 year (25). Petersson at al found 59% of patients complaining of different symptoms at the abdominal wall without relation to IH in the same study population after 5 years (19). Only 14% reported pain in the original operating field. These findings and our own results suggest a possible reduction of pain over time. Abdominal symptoms might be caused by possible consequences of secondary peritonitis and OA with NPWT (e.g., adhesions).

Incisional hernias remain a serious problem after OA and NPWT. Our long-term follow-up study over up to 13 years underlines the relevance of incisional hernias as a main long-term complication after OA treatment. Nevertheless, the use of dynamic fascial sutures and negative pressure wound therapy lead to high rates of success in delayed fascial closure, fewer hernias and a low incidence of pain compared to other techniques. To the best of our knowledge our study reviews the longest follow-up period of 8–13 years. Due to a seriously ill and elderly patient population we found a high drop-out rate. Recommendations for FC technique in this special case of partly injured fascia and lateralization of the rectus muscle are limited by the heterogeneity of FC in our study.

In conclusion, the incidence of incisional hernias after OA treatment increases over time with 45.9% after a mean follow up of 10 years. In contrast, the number of patients with pain in the original operating field and the use of analgesic treatment decreases over time. Further research is needed to investigate techniques for fascial closure after NPWT and an eventual positive effect with standardized methods has to be hypothesized.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

AH tasks were literature research, send and analyse questionnaires, analyses of all data, and manuscript writing. CM's tasks were writing and proof reading. KG and RF were responsible for support in text writing and analyses, and proof reading. All authors contributed to the article and approved the submitted version.

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REFERENCES

1. Kreis BE, de Mol van Otterloo AJ, Kreis RW. Open abdomen management: a review of its history and a proposed management algorithm. *Med Sci Monit.* (2013) 19:524–33. doi: 10.12659/MSM.883966
2. Garcia-Sabrido JL. Treatment of severe intra-abdominal sepsis and/or necrotic foci by an "open-abdomen" approach. *Arch Surg.* (1988) 123:152. doi: 10.1001/archsurg.1988.01400260032002
3. Howard CA, Turner WW. Successful treatment of early, postoperative, necrotizing infection of the abdominal wall. *Crit Care Med.* (1989) 17:586–7. doi: 10.1097/00003246-198906000-00022
4. 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. doi: 10.1007/BF01664876
5. Schein M, Saadia R, Jamieson JR, Decker GAG. The 'sandwich technique' in the management of the open abdomen. *Br J Surg.* (1986) 73:369–70. doi: 10.1002/bjs.1800730514
6. Montori G, Allievi N, Coccolini F, Solaini L, Campanati L, Ceresoli M, et al. Negative pressure wound therapy versus modified barker vacuum pack as temporary abdominal closure technique for open abdomen management: a four-year experience. *BMC Surg.* (2017) 17:1–6. doi: 10.1186/s12893-017-0281-3
7. Björck M, Bruhin A, Cheatham M, Hinck D, Kaplan M, Manca G, et al. Classification–important step to improve management of patients with an open abdomen. *World J Surg.* (2009) 33:1154–7. doi: 10.1007/s00268-009-9996-3
8. Boele van Hensbroek P, Wind J, Dijkgraaf MGW, Busch ORC, Goslings JC, Carel Goslings J. 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. doi: 10.1007/s00268-008-9867-3
9. Miller PR, Meredith JW, Johnson JC, Chang MC. Prospective evaluation of vacuum-assisted fascial closure after open abdomen. *Ann Surg.* (2004) 239:608–16. doi: 10.1097/01.sla.0000124291.09032.bf
10. 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. doi: 10.1007/s00268-010-0937-y
11. Latifi R, Joseph B, Kulvatunyou N, Wynne JL, O'Keeffe T, Tang A, et al. Enterocutaneous fistulas and a hostile abdomen: reoperative surgical approaches. *World J Surg.* (2012) 36:516–23. doi: 10.1007/s00268-011-1306-1
12. Brandl A, Laimer E, Perathoner a, Zitt M, Pratschke J, Kafka-Ritsch R. Incisional hernia rate after open abdomen treatment with negative pressure and delayed primary fascia closure. *Hernia.* (2014) 18:105–11. doi: 10.1007/s10029-013-1064-0
13. Petersson U, Acosta S, Björck 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. doi: 10.1007/s00268-007-9222-0
14. Pliakos I, Papavramidis TS, Mihalopoulos N, Koulouris H, Kesisoglou I, Sapalidis K, et al. Vacuum-assisted closure in severe abdominal sepsis with or without retention sutured sequential fascial closure: a clinical trial. *Surgery.* (2010) 148:947–53. doi: 10.1016/j.surg.2010.01.021
15. Keramati M, Srivastava A, Sakabu S, Rumbolo P, Smock M, Pollack J, et al. The Wittmann Patch s a temporary abdominal closure device after decompressive celiotomy for abdominal compartment syndrome following burn. *Burns.* (2008) 34:493–7. doi: 10.1016/j.burns.2007.06.024
16. Kafka-Ritsch R, Zitt M, Schorn N, Stroemmer S, Schneeberger S, Pratschke J, 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. doi: 10.1007/s00268-012-1586-0
17. Fortelny RH, Hofmann A, Gruber-Blum S, Petter-Puchner AH, Glaser KS. Delayed closure of open abdomen in septic patients is facilitated by combined negative pressure wound therapy and dynamic fascial suture. *Surg Endosc.* (2014) 28:735–40. doi: 10.1007/s00464-013-3251-6
18. Willms AG, Schwab R, von Websky MW, et al. Factors influencing the fascial closure rate after open abdomen treatment: results from the European Hernia Society (EuraHS). *Registry Hernia*. (2020). doi: 10.1007/s10029-020-02336-x. [Epub ahead of print].
19. Petersson U, Bjarnason T, Björck M, Montgomery A, Rogmark P, Svensson M, et al. Quality of life and hernia development 5 years after open abdomen treatment with vacuum-assisted wound closure and mesh-mediated fascial traction. *Hernia.* (2016) 20:755–64. doi: 10.1007/s10029-016-1516-4
20. Hofmann AT, Gruber-Blum S, Lechner M, Petter-Puchner A, Glaser K, Fortelny R. Delayed closure of open abdomen in septic patients treated with negative pressure wound therapy and dynamic fascial suture: the long-term follow-up study. *Surg Endosc.* (2020) 31:4717–24. doi: 10.1007/s00464-017-5547-4
21. Jakob MO, Schwarz C, Haltmeier T, Zindel J, Pinworasarn T, Candinas D, et al. Mesh-augmented versus direct abdominal closure in patients undergoing open abdomen treatment. *Hernia.* (2018) 22:785–792. doi: 10.1007/s10029-018-1798-9
22. Israelsson LA, Millbourn D. Closing midline abdominal incisions. *Langenbeck's Arch Surg/Dtsch Gesellschaft für Chir.* (2012) 397:1201–7. doi: 10.1007/s00423-012-1019-4
23. Millbourn D, Cengiz Y, Israelsson LA. Risk factors for wound complications in midline abdominal incisions related to the size of stitches. *Hernia.* (2011) 15:261–6. doi: 10.1007/s10029-010-0775-8
24. Millbourn D, Cengiz Y, Israelsson LA. Effect of stitch length on wound complications after closure of midline incisions: a randomized controlled trial. *Arch Surg.* (2009) 144:1056–9. doi: 10.1001/archsurg.2009.189
25. Bjarnason T, Montgomery A, Ekberg O, Acosta S, Svensson M, Wanhainen A, 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. doi: 10.1007/s00268-013-2082-x

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REVIEW
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Technique Advances in Enteroatmospheric Fistula Isolation After Open Abdomen: A Review and Outlook

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Enteroatmospheric fistula (EAF) after open abdomen adds difficulties to the management and increases the morbidity and mortality of patients. As an effective measurement, reconstructing gastrointestinal tract integrity not only reduces digestive juice wasting and wound contamination, but also allows expedient restoration of enteral nutrition and intestinal homeostasis. In this review, we introduce several technologies for the temporary isolation of EAF, including negative pressure wound therapy, fistuloclysis, fistula patch, surgical covered stent, three-dimensional (3D) printing stent, and injection molding stent. The manufacture and implantation procedures of each technique with their pros and cons are described in detail. Moreover, the approach in combination with finger measurement, x-ray imaging, and computerized tomography is used to measure anatomic parameters of fistula and design appropriate 3D printer-recognizable stereolithography files for production of isolation devices. Given the active roles that engineers playing in the technology development, we call on the cooperation between clinicians and engineers and the organization of clinical trials on these techniques.

Keywords: open abdomen, enteroatmospheric fistula, fistula isolation, biomedical device, 3D printing

INTRODUCTION OF OPEN ABDOMEN THERAPY

The open abdomen therapy can be chosen for severe intraabdominal infections and abdominal compartment syndrome (ACS) when no other perceived options exist. This strategy allows surgeons to carry out source control procedures on unexplored abdominal infections and reduce intraabdominal pressure for the prevention of visceral organ ischemia (1). Early closure of abdomen is highly recommended once patients' conditions are improved because open abdomen therapy can alter the normal physiological states of abdomen and cause wound infections, seromas, fistula formation, recurrence of the defect, and even death (2–4). Primary fascia closure is an ideal solution to realize the abdominal closure, but in the presence of large fascia defects, temporary abdominal closure (TAC) can be alternatively applied including Bogotà bag, skin closure, Wittmann patch, Barker vacuum pack, commercial negative pressure wound therapy (NPWT), and commercial NPWT plus mesh-mediated traction (5). A clinical investigation from the International Register of Open Abdomen (IROA) study group indicated that NPWT was the most frequent choice (46.8%) for TAC (6, 7) because it facilitated the formation of wound granulation, prevention of fistula formation, and reduction of wound contaminations (8, 9).

Even with these interventions, the occurrence of enteroatmospheric fistula (EAF) still reached 9% and the overall mortality rate in the entire population was 29.7%. In the subgroup analysis, it was revealed that EAF raised the death rate from 28.8 to 39%, suggesting that EAF was an independent risk factor of mortality as it can lead to the loss of digestive fluid and other complications including wound contamination, water-electrolyte disturbance, troubles in enteral nutrition, and hyper-metabolic conditions as well as chronic intestinal failure (10, 11). Moreover, once the mucosa is protruded, EAF cannot be closed spontaneously and has to be resected until the patient has recovered and the wound completely heals (12). For this reason, fistula isolation is very important to ensure the safety of patents waiting for definite fistula surgeries.

EMERGING TECHNIQUES FOR EAF ISOLATION

EAF requires comprehensive treatments: (1) nutritional support, among which the early total parenteral nutrition is beneficial for intestinal rest and spontaneous fistula closure; (2) somatostatin analogs, which reduce gastrointestinal (GI) secretions and allow fast fistula closure, but do not reduce the mortality. Most of the studies agree that the greatest benefit occurs in the first 10 days of treatment (13, 14); (3) antibiotics, whose application should follow the Surviving Sepsis guidelines, and empiric coverage should not exceed 4 to 7 days (15, 16); (4) maintenance of water and electrolyte balance. Fluid infusion is administered based on a general analysis of fistula's output and body fluid balance; (5) others, such as fibrin glue, endoscopic clips, and fistula plug can be considered the adjuvant therapy for non-operative fistula closure (17–20). In addition, various EAF isolation approaches have been invented for improving the wound protection and maintaining the GI homeostasis, therefore playing increasing therapeutic roles.

NPWT

NPWT has been widely used for TAC in clinical practice. Firstly, the skin necrosis and any other necrotic tissues need to be debrided. Secondly, an obligatory non-adherent polyvinyl alcohol membrane serves as the first layer of NPWT over the intestinal loops and a piece of white sponge as the second. The non-adherent layer can effectively prevent the adhesion between the intestinal loops and the sponge. It is worth noting that the sponge needs to be tailored slightly smaller than the size of abdominal wound to leave enough space for abdominal wall traction. If there are any skin folds, stoma and drainage tubes, the stoma pastes or silicone gels are required to make the entire negative pressure system sealed. Finally, the adhesive drape is placed over the sponge with the margins of intact skin. An external negative pressure is chosen ranging from −100 to −125 mmHg to drain the intestinal fluids according to their output, the number of EAFs, the amount of NPWT, and the process of wound healing (21). The whole equipment for NPWT is described in **Figure 1A**, which has been commercially available from KCI (TX, USA). **Figure 1B** shows the practice of NPWT in our medical center.

Although treated with NPWT, the spontaneous closure of EAF is very rare and depends on the fistula location and output (22, 23). Once the mucosal protrusion of EAF occurs, spontaneous closure becomes impossible, and the only chance for patients is to survive with the intention of further surgery. In this situation, further aggressive approaches can be considered if a satisfied source control has not been achieved. For example, Foley catheter can be placed directly into the intestine lumen and pulled out through holes in every layer of the NPWT dressing (**Figure 1C**), which enables drainage of high-output fistula and achieves a more satisfying result than the NPWT alone (21). Similarly, the silicone fistula adapter (SFA) has been invented by PPM Fistelapater to realize the isolation of fistula opening in combination with NPWT (**Figures 1D,E**) and drains the EAF more efficiently (24).

Fistuloclysis

Management of EAF requires sufficient nutritional and metabolic supports by the means of gradual transition from parenteral nutrition to enteral nutrition. Long-term parenteral nutrition may lead to complications such as the catheter-related bloodstream infections, liver injury, and intestinal dysfunction, while enteral nutrition can improve those conditions. As an enteral nutrition routine, fistuloclysis can be used to infuse enteral nutrients, formula, or proximal GI secretions to the distal limb of fistula in order to improve the nutritional status and maintain fluid/electrolyte homeostasis (25, 26). **Figure 2** shows that this technique was applicable in granulating the open abdomen with EAF in our medical center. It was revealed by Mettu et al. (27) that fistuloclysis could replace the parenteral nutrition and reduce the cost of nutritional support. For these critically ill surgical patients, fistulaclysis allows early enteral nutrition, which improves prognosis through improvements of intestinal barrier functions and immune states (28, 29).

However, fistuloclysis has been less popular in recent years mainly due to technical and aesthetic concerns (30). Some EAFs are not appropriate for fistuloclysis because of their distal locations or failure in the placement of feeding tubes. In addition, this approach is accomplished with risks of the tube dislocation, effluent deterioration, and wound contamination, thus consuming large amounts of nursing work. Through combining with NPWT, it facilitates the control of fistula effluent and fixation of fistuloclysis tube, which makes fistuloclysis safer (31). Collectively, our opinion is to carry out this technique if enteral nutrition is achieved especially when EAF is located in the proximal part of small intestine, and this approach will enhance the physical strength of patients to tolerate definite surgery.

Abbreviations: EAF, enteroatmospheric fistula; NPWT, negative pressure wound therapy; CT, computerized tomography; STL file, stereolithography file; ACS, abdominal compartment syndrome; TAC, temporary abdominal closure; GI, gastrointestinal; FDM, fused deposition model; PLA, polylactic acid; TPU, thermoplastic polyurethane; MRI, magnetic resonance imaging.

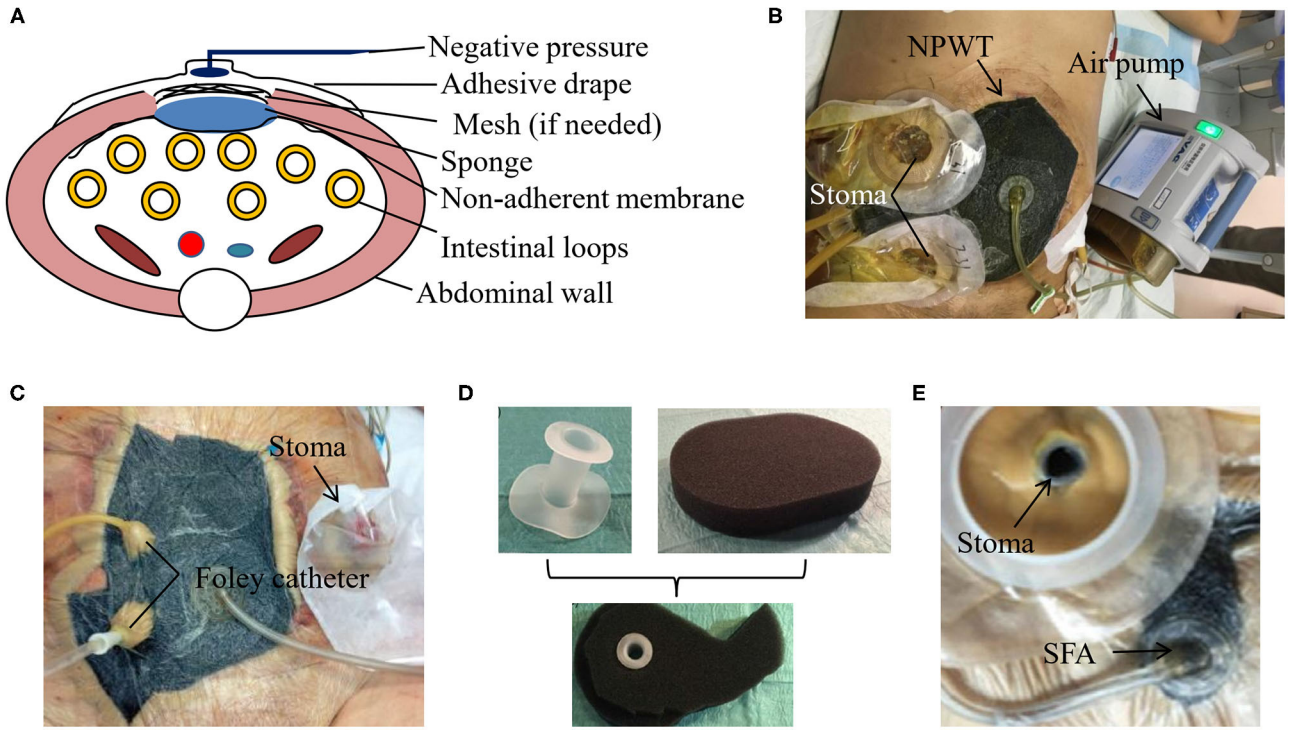

FIGURE 1 | NPWT for EAF isolation. **(A)** The schematic diagram of the vacuum-assisted closure (VAC) device for NPWT. **(B)** The patient with EAF received NPWT in our medical center. The use of picture was approved by the patient. **(C)** Foley catheter can enhanced the drainage of EAF with protruded mucosa. Reproduced with the permission from Bobkiewicz et al. **(D,E)** The real product of the silicone fistula adapter (SFA) and its application in EAF for an efficient drainage. Reproduced with the permission from Wirth et al.

Fistula Patch

Compared with fistuloclysis, intraluminal occlusion of EAF is more advantageous since it supports the physical integrity of GI tract and ensures the pass of digestive contents with less leakage from EAF. Fistula patch is the first-generation device that addresses this issue. As shown in **Figure 3A**, the patch is made of two pieces of silica gels embedded with a polypropylene mesh, combining the materials' elasticity and plasticity. This design enables the rolling of the patch for implantation as well as rapid shape recovery in the intestinal lumen (**Figure 3B**).

Notably, the patch can only be applied to the EAFs with mucosal protrusion and needs to be tailored in accordance with their anatomic characteristics. **Figure 3C** shows a patient treated with the fistula patch, which was fixed above the abdominal wounds using a tube. A study from our medical center revealed that this technique could help restore enteral nutrition and reduce the effluent of EAF (32). However, only around half of patients were suitable for this treatment because of the implanting difficulties and anatomic complexity of EAFs. Moreover, the safety concerns regarding this technique have also been raised particularly in these patients with intestinal edema or anatomic mismatch of the patch to the EAF. This is because under those conditions, the intestinal wall is prone to the physical cutting of the patch edge (**Figure 3D**), leading to GI rupture and bleeding, although these complications are rare.

Fistula Stent

More insights have been put on the fistula stent that can be made tubularly and conforms to the shape of intestinal tract. As shown in **Figure 4**, Rebibo et al. (33) reported a covered self-expanding metal stent (Hanarostent HRC, Life Partners Europe, Bagnolet, France) to close the EAF. This stent was implanted through a terminal ileostomy assisted by a guide wire and the endoscopy. Three patients received this treatment and regained the enteral nutrition. Combined with NPWT, two of them achieved the spontaneous closure of EAF, and then the stent could be removed in the assistance of endoscopy. This study preliminarily indicated the effectiveness of the covered self-expanding metal stent. However, pre-existing ileostomy and complicated implanting process greatly limit the indication of this management for EAF.

Our medical center explored a novel approach that extended the application of fistula stent to patients without ileostomy by using a 3D printing technique (34–37). This technique was based on a fused deposition model (FDM) in which the thermoplastic polyurethane (TPU) filament was melted and reshaped as desired. To obtain an appropriate stent, the first step was to investigate the anatomic parameters of EAF. Three methods can be used to measure the EAF including the finger palpation, x-ray imaging, and computerized tomography (CT) (**Figure 5A**). The finger palpation is the most direct way. By

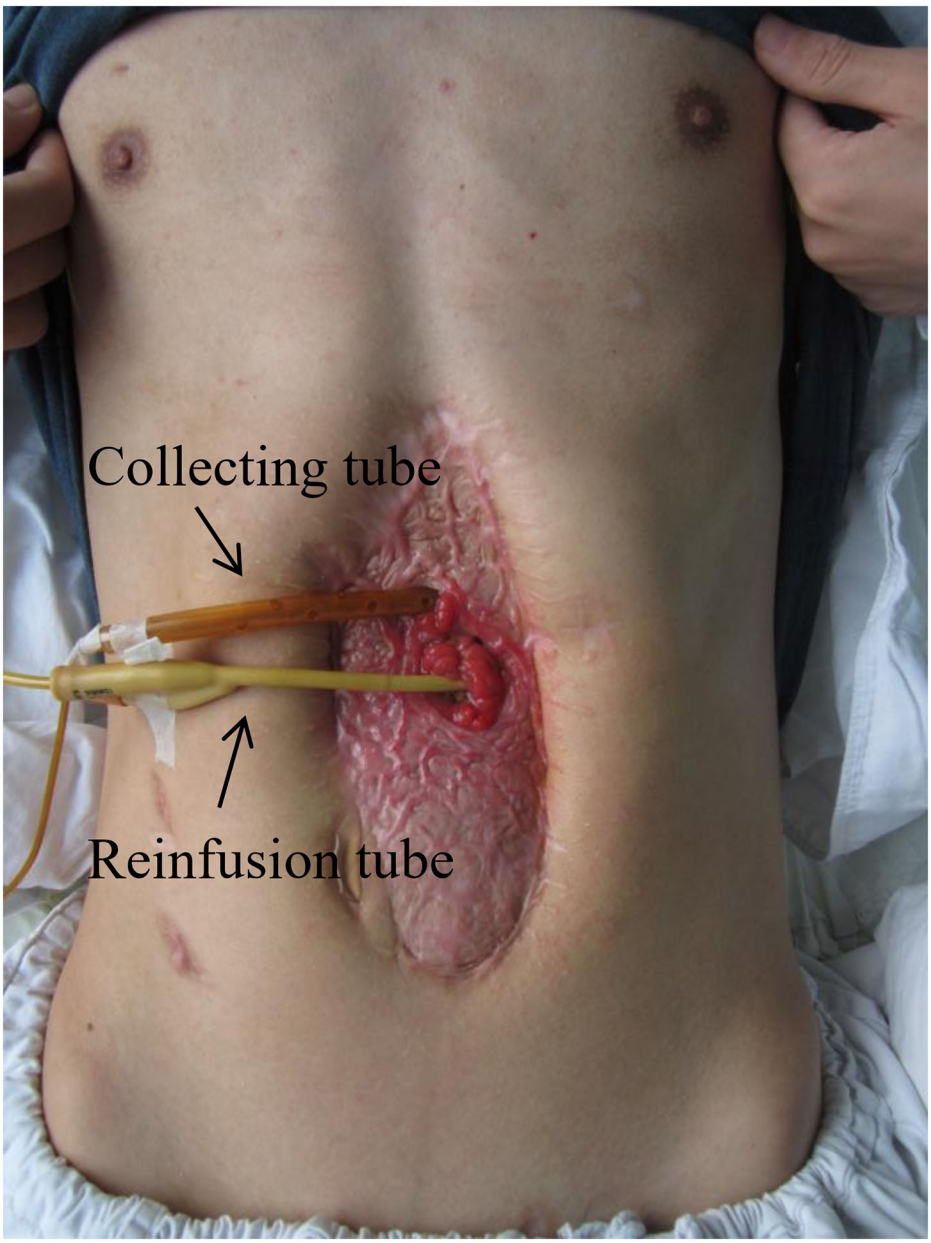

FIGURE 2 | Fistuloclysis for the restoration of enteral nutrition. This patient was treated with open abdomen (grade 4, frozen abdomen) and the effluent was immediately reinfused into distal limb of EAF. The use of picture was approved by the patient.

wearing sterile gloves, fingers can reach into the intestinal lumen though the EAF orifice; however, this does not always work when the orifice is too small or the intestinal lumen is too narrow. Moreover, due to the inaccurate and limited touch, some tiny fistulas are easily omitted. Fistulography by the x-ray imaging can be used to detect these tiny fistulas and achieve a general view toward the GI tract integrity (38). Contrast-mediated high resolution CT is a more advantageous method not only due to its high sensitivity for the fistula (39), but also because the images can be reconstructed in 3D so that we are able to visualize the anatomic parameters of EAF (34). The goal of these detection approaches is to obtain the diameters of proximal and distal limbs (L_1, L_2) and their resulting angle (β) in order to design a suitable stereolithography (STL) file based on the measurements (**Figure 5B**). This STL file can be recognized by an FDM 3D printer to print a fistula stent made of TPU (**Figure 5C**). Because of the elasticity of TPU, the resulting stent can be remodeled during the implantation (**Figure 5D**). **Figure 5E** demonstrates a case who received a 3D printing fistula stent for isolation of the EAF. This treatment allowed the patient to restore the

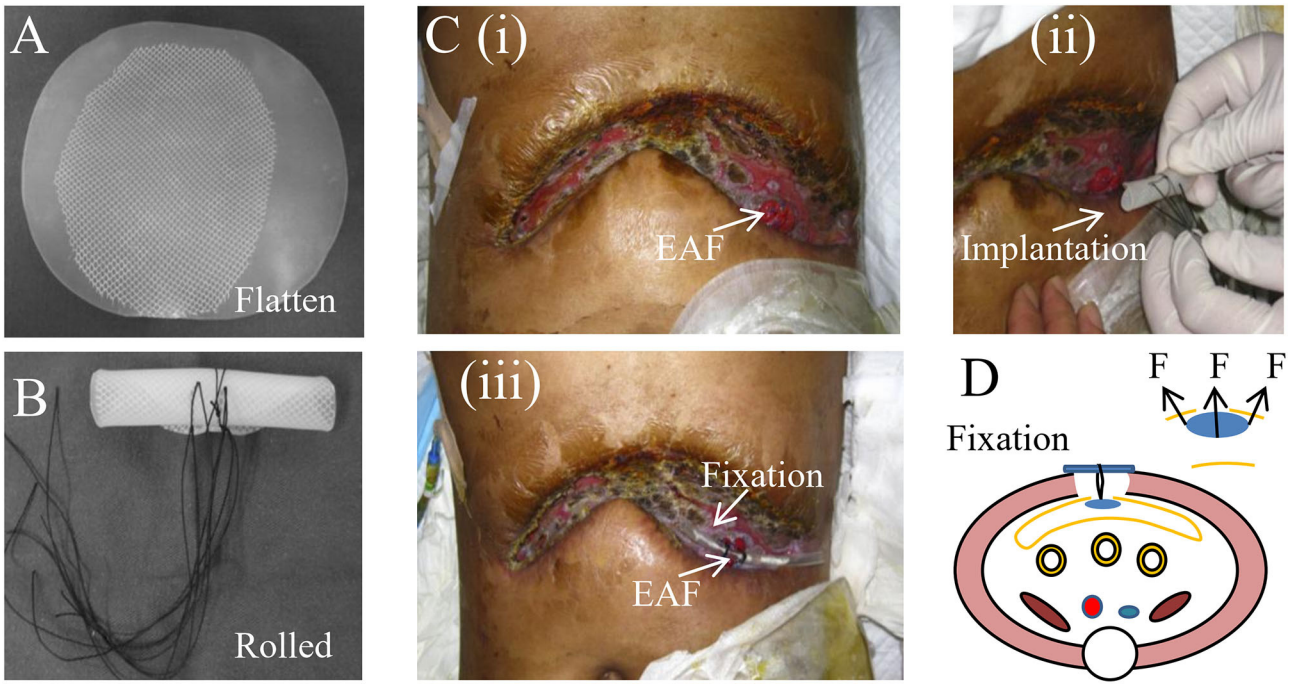

FIGURE 3 | Fistula patch for the occulsion of EAF. **(A)** The appearance of fistula patch. **(B)** The fistula patch needs to be rolled up for implantation. **(C)** The patients with EAF received the treatment of fistula patch that was fixed using a tube. Reproduced with the permission from Wang et al. **(D)** The schematic diagram of the fistula patch application and fixation. It highlights the potential risks for cutting the intestinal wall caused by the patch edge.

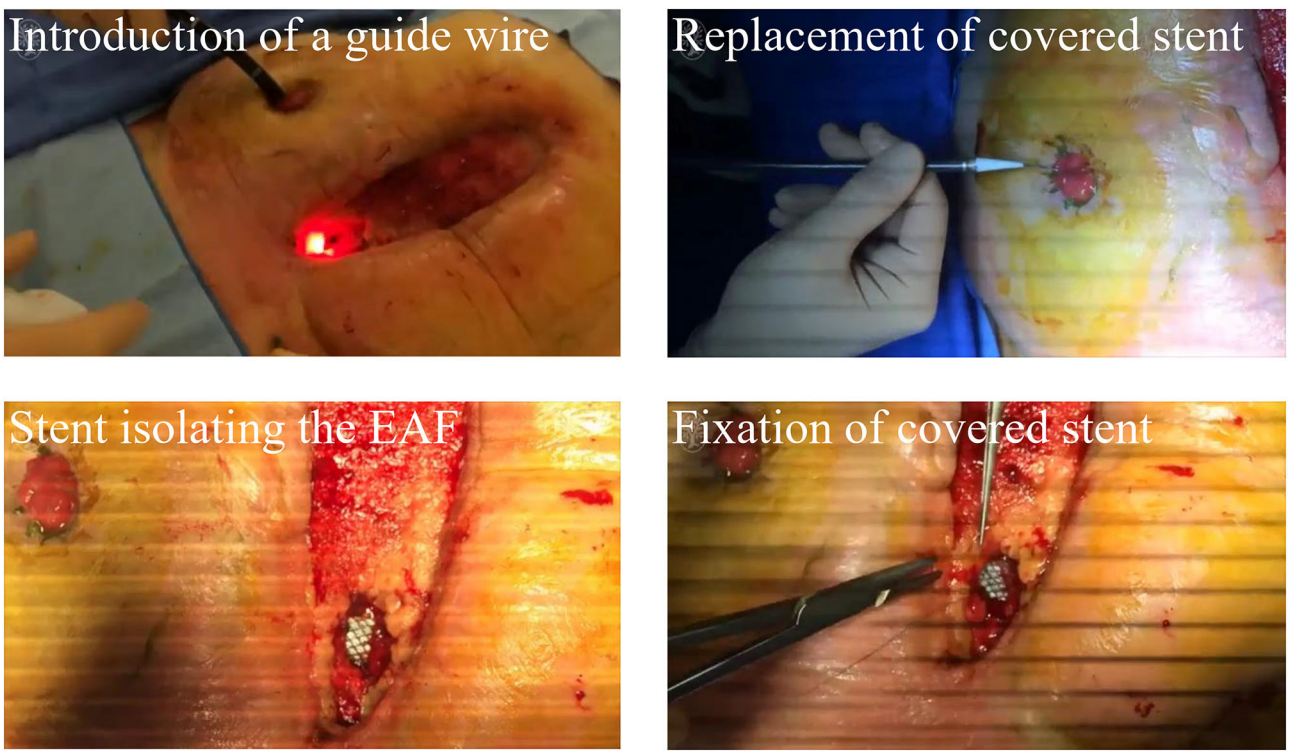

FIGURE 4 | A commercial covered self-expanding metal stent was used to isolate the EAF. Reproduced with the permission from Rebibo et al.

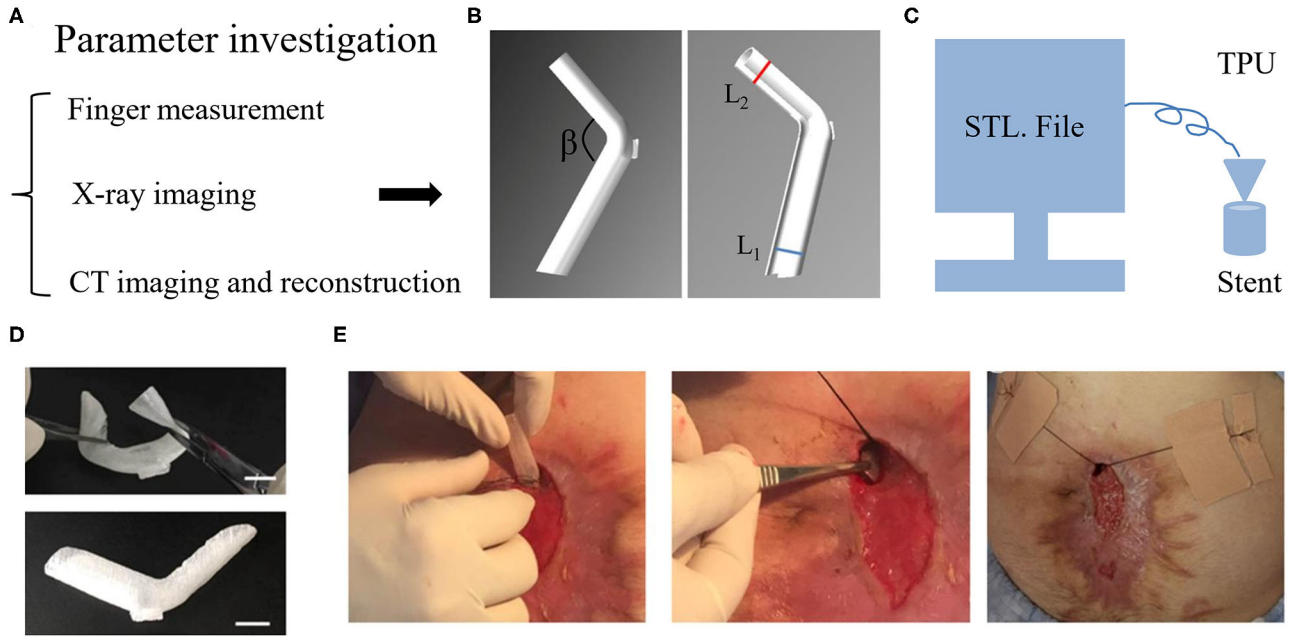

FIGURE 5 | 3D printing stent for the isolation of EAF. **(A)** The methods to measure the anatomic parameters of EAF. **(B)** The STL file of stent designed using Solidwork software according to the measurement of EAF anatomy. **(C)** The schematic diagram of a 3D printer run in the FDM model to print the stent. **(D)** Implantability of the stent due to its shape flexibility. **(E)** The process of the stent implantation and fixation. Reproduced with the permission from Huang et al.

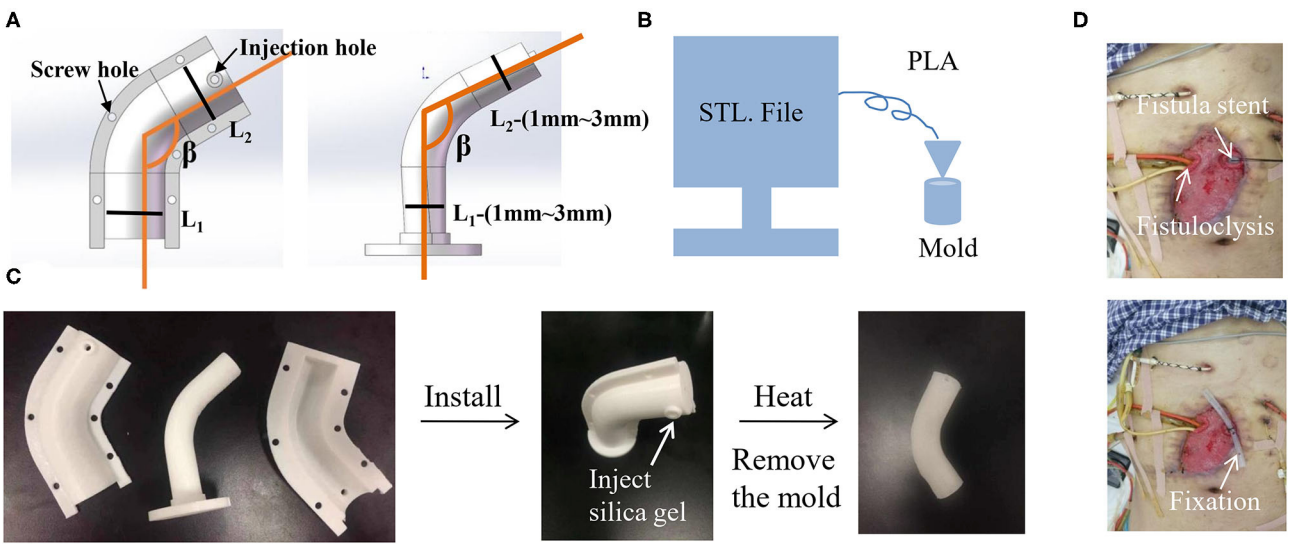

FIGURE 6 | Injection molding stent as a universal approach for the isolation of EAF. **(A)** The STL file of mold designed by Solidwork software according the measurement of EAF anatomy. **(B)** The schematic diagram of an FDM 3D printer printing the mold. **(C)** The real product of the printed mold and the stent that was casted from the mold. **(D)** The application of an injection molding stent in combination with fistuloclysis for the treatment of multiple EAFs. The use of picture was approved by the patient.

enteral nutrition, reduce the effluent, and feel free when doing some exercise for the recovery of physical strength. Notably, the anatomic features of EAF may be altered with the change of intestinal adhesion; therefore, a new stent is needed at this situation to replace the old, particularly in case the effluent greatly increased. Considering the implanting difficulties, the stent is

TABLE 1 | Comparisons of fistula isolation approaches.

	NPWT	Fistuloclysis	Fistula patch	Covered metal stent	3D printing stent	Injection molding stent
Commercially available	Yes	Yes	Yes	Yes	No	No
Average time for device preparation and implantation (hour)	0.5	0.2	0.2	Not known	12-24	1
Contraindications	Not specific	Fistula distally located; distal tract not accessed.	Small fistula orifice	Without intestinal stoma	Small fistula orifice	Small fistula orifice
Potential technical risks	Not specific	Chyme contamination	Mechanical damage to adherent mucosa	Iatrogenic injury (endoscopic perforation)	Iatrogenic injury during implantation	Iatrogenic injury during implantation
Clinical evidence	High	Moderate	Low	Low	Low	Low

only indicated to a relatively large orifice of EAF with mucosal protrusion. Moreover, the complicated manufacturing process limited the promotion of this technology to other medical centers so that the current clinical evidence is low.

As an alternative, injection molding stent was invented and was easily promoted because the molds can be prepared in advance based on different anatomic parameters of EAF with the β ranging from 70° to 180° and the parameters ranging from 1 cm to 3 cm. The extreme case still requires a 3D printing stent or to customize a mold. As shown in **Figure 6A**, the mold consists of two shells and one core. The shell is tailored with the holes at the edge for fixation and the hole in the middle for injection of silica gel, which fills up the space between the shell and core and then is solidified at 100°C for 30 min. The mold is fabricated using a 3D printer in FDM and made of the polylactic acid (PLA) (**Figure 6B**). **Figure 6C** demonstrates the manufacturing process of a stent casted by a mold from the mold installation, silica gel injection, to the mold removal. The silica gel product is featured on its elasticity so that the stent is easily implanted into EAF (**Figure 6D**). This technique consumes less time (merely 1h) to access a personalized stent compared with the 3D printing stent. Because of a similar size to the 3D printing stent, this injection molding stent is also only indicated to a relatively large orifice of EAF with mucosal protrusion. **Table 1** lists the comparisons among all mentioned approaches from technical and clinical perspectives, and the choice is based on the individual conditions of patients.

OUTLOOK FOR EAF MANAGEMENT

Although the progress has been achieved on EAF isolation, the technique still needs to be further optimized. First, due to the limited contrast between intestinal tissues and the surrounding soft tissues, current imaging methods cannot extract the intestinal photos directly so that we have to design the STL file separately using the Solidwork software, which is time-consuming. Magnetic resonance imaging (MRI) technology has shown higher sensitivity in distinguishing GI fistula from soft tissues (40, 41), and is promising to provide a more precise tool for the measurement of EAF anatomy. When combined with artificial intelligence, the ultimate goal is to achieve the STL file of fistula stents directly from the fistula images in a quick and convenient manner (42–45). Moreover, the small size of EAF's orifice hinders the implantation of the fistula stent. To address this issue, elastic and shape-memory biomaterials should be tested for production of the stent (46–48). In addition, the clinical trials based on these techniques are urgently needed for providing more evidence.

CONCLUSION

In this review, we introduced several isolation approaches for the management of EAF after open abdomen including NPWT, fistuloclysis, fistula patch, surgical covered stent, 3D printing stent, and injection molding stent. The choice of these approaches should consider the condition of EAF, general body habitus, and the treatment purpose. The fistula stent is a new solution with promising functions in the maintenance of the GI tract physical integrity. The cooperation between surgeons and engineers is advocated to promote the improvement and application of these techniques.

AUTHOR CONTRIBUTIONS

JR and XW conceived this review. JH organized literatures and wrote this review. HR organized the photographs and the table. YJ participated in the discussion. All authors contributed to the article and approved the submitted version.

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REFERENCES

1. Coccolini F, Montori G, Ceresoli M, Catena F, Moore EE, Ivatury R, et al. The role of open abdomen in non-trauma patient: WSES consensus paper. *World J Emerg Surg.* (2017) 12:39. doi: 10.1186/s13017-017-0146-1
2. Mathes SJ, Steinwald PM, Foster RD, Hoffman WY, Anthony JP. Complex abdominal wall reconstruction: a comparison of flap and mesh closure. *Ann Surg.* (2000) 232:586–96. doi: 10.1097/00000658-200010000-00014
3. Choi JJ, Palaniappa NC, Dallas KB, Rudich TB, Colon MJ, Divino CM. Use of mesh during ventral hernia repair in clean-contaminated and contaminated cases: outcomes of 33,832 cases. *Ann Surg.* (2012) 255:176–80. doi: 10.1097/SLA0b013e31822518e6
4. Huang J, Li Z, Hu Q, Chen G, Ren Y, Wu X, et al. Bioinspired anti-digestive hydrogels selected by a simulated gut microfluidic chip for closing gastrointestinal fistula. *iScience.* (2018) 8:40–8. doi: 10.1016/j.isci.2018.09011
5. Petersson P, Petersson U. Dynamic fascial closure with vacuum-assisted wound closure and mesh-mediated fascial traction (VAWCM) treatment of the open abdomen—an updated systematic review. *Front Surg.* (2020) 7:577104. doi: 10.3389/fsurg.2020577104
6. Coccolini F, Ceresoli M, Kluger Y, Kirkpatrick A, Montori G, Salvetti F, et al. Open abdomen and entero-atmospheric fistulae: an interim analysis from the International Register of Open Abdomen (IROA). *Injury.* (2019) 50:160–6. doi: 10.1016/j.injury.2018.09.040
7. Li Z, Wu C, Liu Z, Li Z, Peng X, Huang J, et al. A polypropylene mesh coated with interpenetrating double network hydrogel for local drug delivery in temporary closure of open abdomen. *RSC Adv.* (2020) 10:1331–40. doi: 10.1039/C9RA10455K
8. Montori G, Allievi N, Coccolini F, Solaini L, Campanati L, Ceresoli M, et al. Negative pressure wound therapy versus modified barker vacuum pack as temporary abdominal closure technique for open abdomen management: a four-year experience. *BMC Surg.* (2017) 17:86. doi: 10.1186/s12893-017-0281-3
9. Rather HA, Thakore R, Singh R, Jhala D, Singh S, Vasita R. Antioxidative study of Cerium Oxide nanoparticle functionalised PCL-Gelatin electrospun fibers for wound healing application. *Bioact Mater.* (2018) 3:201–11. doi: 10.1016/j.bioactmat.2017.09006
10. Guo K, Gong W, Zheng T, Hong Z, Wu X, Ren H, et al. Clinical parameters and outcomes of necrotizing soft tissue infections secondary to gastrointestinal fistulas. *BMC Infect Dis.* (2019) 19:597. doi: 10.1186/s12879-019-4248-0
11. Hodgkinson JD, Oke SM, Warusavitarne J, Hanna GB, Gabe SM, Vaizey CJ. Incisional hernia and enterocutaneous fistula in patients with chronic intestinal failure: prevalence and risk factors in a cohort of patients referred to a tertiary centre. *Colorectal Dis.* (2019) 21:1288–95. doi: 10.1111/codi14735
12. Coccolini F, Roberts D, Ansaloni L, Ivatury R, Gamberini E, Kluger Y, et al. The open abdomen in trauma and non-trauma patients: WSES guidelines. *World J Emerg Surg.* (2018) 13:7. doi: 10.1186/s13017-018-0167-4
13. Gomes-Porras M, Cardenas-Salas J, Alvarez-Escola C. Somatostatin analogs in clinical practice: a review. *Int J Mol Sci.* (2020) 21:1682. doi: 10.3390/ijms21051682
14. Gribovskaja-Rupp I, Melton GB. Enterocutaneous Fistula: proven Strategies and Updates. *Clin Colon Rectal Surg.* (2016) 29:130–7. doi: 10.1055/s-0036-1580732
15. Dellinger RP, Schorr CA, Levy MM. A users' guide to the 2016 Surviving Sepsis Guidelines. *Intensive Care Med.* (2017) 43:299–303. doi: 10.1007/s00134-017-4681-8
16. Vassalos A, Rooney K. Surviving sepsis guidelines 2012. *Crit Care Med.* (2013) 41:e485–6. doi: 10.1097/CCM0b013e31829644e8
17. Wu X, Ren J, Gu G, Wang G, Han G, Zhou B, et al. Autologous platelet rich fibrin glue for sealing of low-output enterocutaneous fistulas: an observational cohort study. *Surgery.* (2014) 155:434–41. doi: 10.1016/j.surg.2013.09001
18. Wu X, Ren J, Yao G, Zhou B, Wang G, Gu G, et al. Biocompatibility, biodegradation, and neovascularization of human single-unit platelet-rich fibrin glue: an *in vivo* analysis. *Chin Med J.* (2014) 127:408–11. doi: 10.3760/cma.j.issn.0366-6999.20130412
19. Ren J, Wu X, Wang G, Chen J, Gu G, Li J. Fistula fiberscope-assisted percutaneous glue sealing for enterocutaneous fistulas: a case report. *Surg Laparosc Endosc Percutan Tech.* (2013) 23:e235–6. doi: 10.1097/SLE0b013e31828f6efa
20. Huang J, Jiang Y, Liu Y, Ren Y, Xu Z, Li Z, et al. Marine-inspired molecular mimicry generates a drug-free, but immunogenic hydrogel adhesive protecting surgical anastomosis. *Bioact Mater.* (2021) 6:770–82. doi: 10.1016/j.bioactmat.2020.09010
21. Bobkiewicz A, Walczak D, Smolinski S, Kasprzyk T, Studniarek A, Borejsza-Wysocki M, et al. Management of enteroatmospheric fistula with negative pressure wound therapy in open abdomen treatment: a multicentre observational study. *Int Wound J.* (2017) 14:255–64. doi: 10.1111/iwj 12597
22. Leang YJ, Bell SW, Carne P, Chin M, Farmer C, Skinner S, et al. Enterocutaneous fistula: analysis of clinical outcomes from a single Victorian tertiary referral centre. *Anz J Surg.* (2018) 88:E30–3. doi: 10.1111/ans13686
23. Visschers RG, Olde DS, Winkens B, Soeters PB, van Gemert WG. Treatment strategies in 135 consecutive patients with enterocutaneous fistulas. *World J Surg.* (2008) 32:445–53. doi: 10.1007/s00268-007-9371-1
24. Wirth U, Renz BW, Andrade D, Schiergens TS, Arbogast H, Andrassy J, et al. Successful treatment of enteroatmospheric fistulas in combination with negative pressure wound therapy: experience on 3 cases and literature review. *Int Wound J.* (2018) 15:722–30. doi: 10.1111/iwj12916
25. Cresci GA, Martindale RG. Metabolic and nutritional management of a patient with multiple enterocutaneous fistulas. *Nutrition.* (1997) 13:446–8, 448–9. doi: 10.1016/S0899-9007(97)00094-4
26. Sharma P, Davidson R, Davidson J, Keane C, Liu C, Ritchie SR, et al. Novel chyme reinfusion device for gastrointestinal fistulas and stomas: feasibility study. *Br J Surg.* (2020) 107:1199–210. doi: 10.1002/bjs11516
27. Mettu SR. Fistuloclysis can successfully replace parenteral feeding in the nutritional support of patients with enterocutaneous fistula. *Br J Surg.* (2004) 91:625–31. doi: 10.1002/bjs.4520
28. Bhat S, Sharma P, Cameron NR, Bissett IP, O'Grady G. Chyme Reinfusion for Small Bowel Double Enterostomies and Enteroatmospheric Fistulas in Adult Patients: a systematic review. *Nutr Clin Pract.* (2020) 35:254–64. doi: 10.1002/ncp10417
29. Ortiz LA, Zhang B, McCarthy MW, Kaafarani H, Fagenholz P, King DR, et al. Treatment of enterocutaneous fistulas, then and now. *Nutr Clin Pract.* (2017) 32:508–15. doi: 10.1177/0884533617701402
30. Polk TM, Schwab CW. Metabolic and nutritional support of the enterocutaneous fistula patient: a three-phase approach. *World J Surg.* (2012) 36:524–33. doi: 10.1007/s00268-011-1315-0
31. Subramaniam MH, Liscum KR, Hirshberg A. The floating stoma: a new technique for controlling exposed fistulae in abdominal trauma. *J Trauma.* (2002) 53:386–8. doi: 10.1097/00005373-200208000-00037
32. Wang G, Ren J, Liu S, Wu X, Gu G, Li J. "Fistula patch". *J Trauma Acute Care.* (2013) 74:1175–7. doi: 10.1097/TA0b013e318282705e
33. Rebibo L, Wacrenier A, Thiebault H, Delcenserie R, Regimbeau JM. Combined endoscopic and surgical covered stent placement: a new tailored treatment for enteroatmospheric fistula in patients with terminal ileostomy. *Endoscopy.* (2017) 49:E35–6. doi: 10.1055/s-0042-121489
34. Huang JJ, Ren JA, Wang GF, ZA Li, Wu XW, Ren HJ, et al. 3D-printed "fistula stent" designed for management of enterocutaneous fistula: an advanced strategy. *World J Gastroenterol.* (2017) 23:7489–94. doi: 10.3748/wjg.v23.i417489
35. Xu ZY, Ren HJ, Huang JJ, ZA Li, Ren JA. Application of a 3D-printed "fistula stent" in plugging enteroatmospheric fistula with open

abdomen: a case report. *World J Gastroenterol.* (2019) 25:1775–82. doi: 10.3748/wjg.v25.i141775
36. Derakhshanfar S, Mbeleck R, Xu K, Zhang X, Zhong W, Xing M. 3D bioprinting for biomedical devices and tissue engineering: a review of recent trends and advances. *Bioact Mater.* (2018) 3:144–56. doi: 10.1016/j.bioactmat.2017.11008
37. Wei L, Wu S, Kuss M, Jiang X, Sun R, Reid P, et al. 3D printing of silk fibroin-based hybrid scaffold treated with platelet rich plasma for bone tissue engineering. *Bioact Mater.* (2019) 4:256–60. doi: 10.1016/j.bioactmat.2019.09001
38. Oksuzoglu G, Arat A, Iret D, Sivri B. Fistulography in a difficult case: using a new, practical, and inexpensive device. *AJR Am J Roentgenol.* (1996) 167:281. doi: 10.2214/ajr.167.18659406
39. Liang C, Lu Y, Zhao B, Du Y, Wang C, Jiang W. Imaging of anal fistulas: comparison of computed tomographic fistulography and magnetic resonance imaging. *Korean J Radiol.* (2014) 15:712–23. doi: 10.3348/kjr.2014.15.6712
40. Gatti M, Allois L, Carisio A, Dianzani C, Garcia MM, Ruggirello I, et al. Magnetic resonance enterography. *Minerva Gastroenterol Dietol.* (2019) 65:319–34. doi: 10.23736/S1121-421X.1902639-4
41. Konan A, Onur MR, Ozmen MN. The contribution of preoperative MRI to the surgical management of anal fistulas. *Diagn Interv Radiol.* (2018) 24:321–7. doi: 10.5152/dir.201818340
42. Wang L, Yang S, Yang S, Zhao C, Tian G, Gao Y, et al. Automatic thyroid nodule recognition and diagnosis in ultrasound imaging with the YOLOv2 neural network. *World J Surg Oncol.* (2019) 17:12. doi: 10.1186/s12957-019-1558-z
43. Su L, Dong Q, Zhang H, Zhou X, Chen Y, Hao X, et al. Clinical application of a three-dimensional imaging technique in infants and young children with complex liver tumors. *Pediatr Surg Int.* (2016) 32:387–95. doi: 10.1007/s00383-016-3864-7
44. Neftci EO. Data and power efficient intelligence with neuromorphic learning machines. *iScience.* (2018) 5:52–68. doi: 10.1016/j.isci.2018.06010
45. Goodhill GJ. Theoretical models of neural development. *iScience.* (2018) 8:183–99. doi: 10.1016/j.isci.2018.09017
46. Wu Y, Wang L, Zhao X, Hou S, Guo B, Ma PX. Self-healing supramolecular bioelastomers with shape memory property as a multifunctional platform for biomedical applications via modular assembly. *Biomaterials.* (2016) 104:18–31. doi: 10.1016/j.biomaterials.2016.07011
47. Lendlein A, Behl M, Hiebl B, Wischke C. Shape-memory polymers as a technology platform for biomedical applications. *Expert Rev Med Devices.* (2010) 7:357–79. doi: 10.1586/erd.108
48. Zhao YQ, Yang JH, Ding X, Ding X, Duan S, Xu FJ. Polycaprolactone/polysaccharide functional composites for low-temperature fused deposition modelling. *Bioact Mater.* (2020) 5:185–91. doi: 10.1016/j.bioactmat.2020.02006

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frontiers in Surgery

ORIGINAL RESEARCH
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Effect of Negative Pressure Therapy on Open Abdomen Treatments. Prospective Randomized Study With Two Commercial Negative Pressure Systems

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Introduction: The use of negative pressure dressings for open abdominal therapy has made a great impact on strategies for open abdominal treatment. Observed intestinal damage and developement of fistula formation raises questions about safety of commonly used systems (AB-Thera). The most common used system uses foils for shielding intestines directly from negative pressure. As an alternative a system with open pore dressing in double layer film was introduced (Suprasorb CNP) and proved to safe in animal studies. We compared the effects of this two systems on patients requiring open abdominal treatment.

Materials and methods: Patients with secondary peritonitis in at least two abdominal quadrants were included in this randomized study. Inclusion criteria were secondary peritonitis (ACS), abdominal compartment syndrome, and abdominal trauma combined with ACS and/or contaminated abdomen. Patients with active bleeding and pancreatitis were not included. We examined Mannheim peritonitis Index (MPI), bloodcount, PCT, amount of fluid collected, and morphological changes on the bowel. Data were collected on day 2, 4, 7, 14, 21, and 28. Primary end point was fascial closure. Examination was terminated in case of death and damage to the abdominal organs. Groups were compared using Mann Whitney *U*-test and chi square test. Trend evaluation was evaluated using an one way repeated measure analysis of variance. *P*-values below 0.05 was considered significat.

Results: Thirty four patients were included between August 2010 and September 2012. There were no significant difference between two groups in MPI, age, and gender. Mean duration of treatment, WBC, CRP, and abdominal closure rate were not significantly different between groups. Suprasorb CNP System collected twice more fluid than AB-Thera and decreased PCT on significantly faster rate than AB-Thera. Four patients died (11%) and four patients developed enteric fistula (11%). Closure rate was achieved in 27 out of 34 Patients (79.5%). Closure rate was not significantly different between groups.

Conclusion: The use of both systems proved to be efficient and safe. The application of well-dosed, moderate negative pressure on contaminated areas of the abdomen seems to have a lot of potential and it is worth directing greater research potential in this direction.

Keywords: open abdomen therapy, abdomen vac therapy, abdomen sepsis, abdominal compartment syndrome, negative pressure on bowel surface, Suprasorb CNP_R, $ABthera_R$

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INTRODUCTION

The use of negative pressure dressings for open abdominal therapy (OAT) was probably first described by Brock 1995 (1) and has influenced the development of strategies for treatment of secondary peritonitis (SP) and abdominal compartment syndrome (ACS). Without any doubt, negative pressure therapy (NPT) systems offer a new dimension in OAT, fulfilling most of the criteria for optimizing success and minimizing risks in OAT (2). Nevertheless, the controversy between open abdomen treatment and "en demand" strategy with the risk of tertiary peritonitis is inherent in the therapy strategies. Opponents of OAT can also rightly point out that there are no guidelines for an exact indication and technical processes. Additionally reports of intestinal damage, fistula formation, can cause uncertainty about the use of OAT treatments with NPT (3–7). The question arises whether the currently widespread systems actually represent the only and correct philosophy or if there is still potential in the further development of the NPT systems. The most widespread system, AB-Thera® (ABThera system, KCI, San Antonio, Texas, USA) (**Figure 1**), and most commercial applications, use soft foils to protect the intestinal bundle, and only sparse openings to keep the negative pressure away from the intestinal surfaces (8). Opposite to these systems, we use a second film system, Suprasorb-CNP® (Suprasorb CNP system, Lohmann & Rauscher, Austria-Germany) (**Figure 1**), which protects the intestinal surfaces through soft material properties, but remains permeable to the negative pressure. In a preclinical animal study we have examined this system to determine whether the effect of negative pressure on the surface of the intestine and on organs causes damage (9). This system works with closely spaced pores in a double-layer film. In our *in vitro* study, this system showed the double drainage effect to the AB-Thera film (10).

In this study, the effects of both systems are compared. In addition, the sum of both systems should show how effectively NPT therapy works in a controlled study conducted by surgeons with special experience in open abdomen treatment, on patients of different degrees of severity.

MATERIALS AND METHODS

Thirty-four patients were included during 2.5 years in an "Intention to treat" protocol. Patients were randomly assigned to experimental groups using the web-based randomizer (11). The inclusion was carried out without any influence from the treating surgeon by calling up the selection decision on the web-based randomizer. The study followed the rules approved by the ethics committee of the Medical University of Graz, Austria (No.: 21-198, 08/09).

The AB-Thera® system, referred to as VAC-system, consisted of polyurethane-foam (PUF) in star form, welded onto a fenestrated plastic film (**Figure 1**). This was inserted in the abdomen covering the greater omentum and the whole intestine up to the liver and down into the pelvic cavity. The 1.5 cm

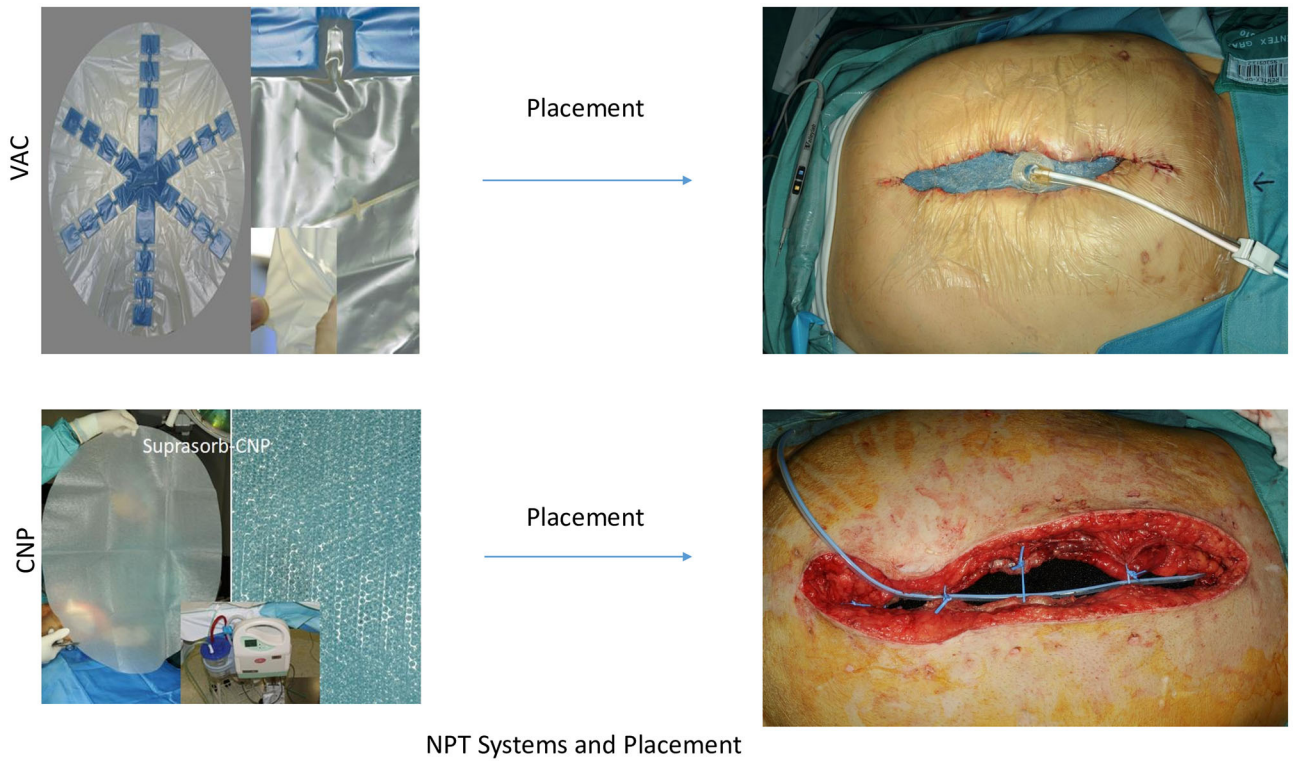

FIGURE 1 | AB-Thera® NP-Dressing, Suprasorb-CNP® Dressing.

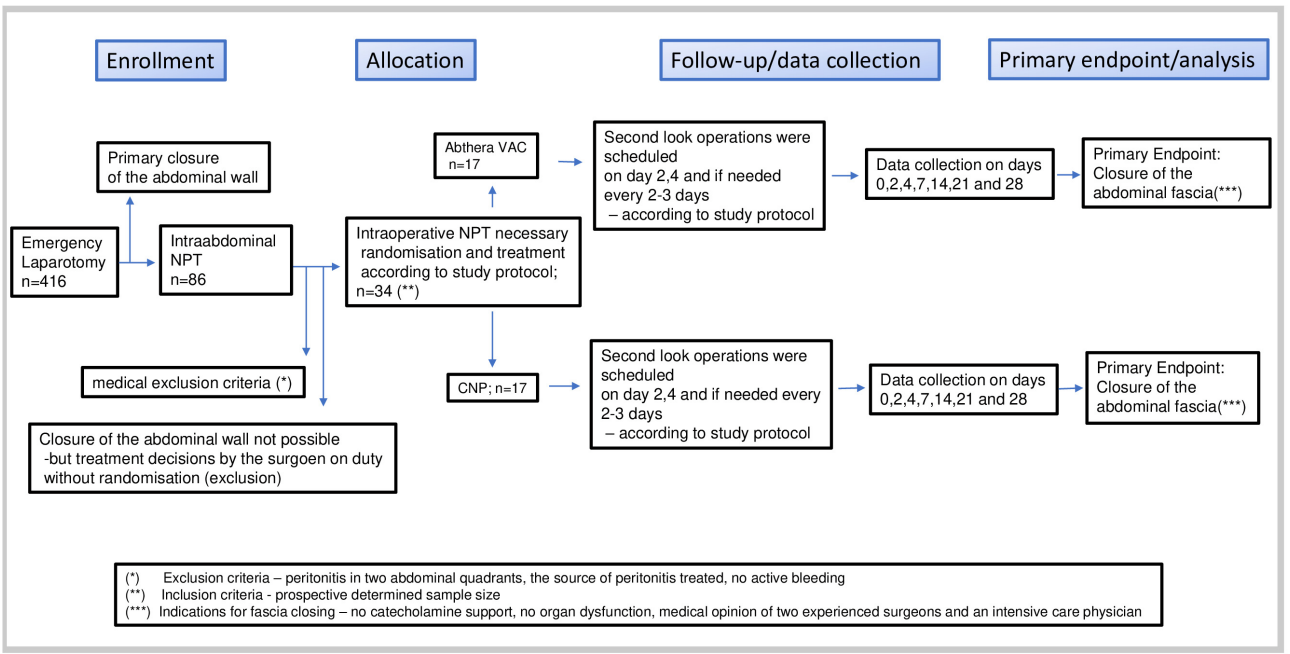

FIGURE 2 | Study flow diagram according to CONSORT NPT.

pre-shaped PUF-oval was placed over this protecting contact layer and positioned 3–4 cm below the edges of the inner abdominal wall. There were 3–4 vessel loops® (Vessel loops, Devan, Covidien, USA) used as single stitches to approximate the muscle-fascia layers as a kind of dynamic retention suture (12). The subcutaneous space was filled with a second layer of 1.5 cm pre-shaped PUF-oval, attached to the skin's edges with staples. The wound was closed with the system's adhesive drape. Using a fixed suction line and suction pump, a negative pressure of −125 mmHg was maintained in all cases in accordance with the company's recommendations (**Figure 1**).

The Suprasorb-CNP® system, referred to as S-CNP-system (**Figure 1**) used a membrane as described above, shielding the intestine, liver surface and pelvic cavity (**Supplementary Material**, L&R product description). The film was covered with 1.5 cm PUF and 3–4 dynamic sutures were placed exactly as forementioned in the VAC system. In this system, however, a perforated silicon drainage tube was placed in this plane and connected with the suction pump, served as the suction line (**Figure 1**). After filling the subcutaneous space with Kerlix®-gauze (Kerlix-Gauze, Covidien, USA), the skin around the wound was covered with a few layers of Kerlix®-gauze and then closed with the adhesive drape. A negative pressure of −60 mmHg (−50 to −80 mmHg) was maintained, according to the cited reference animal study (9).

Inclusion Criteria

Flow diagram (**Figure 2**).

- Patients with secondary peritonitis in at least two abdominal quadrants were included, when the cause of the peritonitis (source) had been found and treated. The decision for open abdominal treatment was made by the surgeon on duty. Criteria for the decision were defined as follows:
- Patients who had exhibited peritonitis for more than 24 h and in whom a second look was planned or for whom the abdomen could not be closed for other reasons;
- Patients presenting with ACS for whom the indication for open abdominal treatment after failure of conservative treatment was made, when they had been otherwise stabilized and no active bleeding was present;
- Patients after abdominal trauma combined with ACS and/or contaminated abdomen due to enteral perforation, when they had been stabilized, and no active bleeding was present.

Exclusion Criteria

- Patients with pancreatitis as the source of peritonitis
- Patients with active abdominal bleeding
- Pregnancy
- Patients under 18 years of age.

Whenever a patient developed an obvious entero-atmospheric fistula, the observation was terminated and subsequent treatment was given outside this study. If enteric opening was observed we repaired it with sutures as usual, and gave a "c" according to the amended OA classification (13), as described below in the secondary parameters. If the opening persisted after the 2nd attempt at repair, it was then categorized as fistula and marked with "4," according to same classification (13). Those patients were then excluded from further observations in this study.

Study Design

The Mannheim Peritonitis Index (MPI) (14–18) was determined for every patient at the time of inclusion. During and

after the operation, photographic records were made on the following objects:

- OP-site before and after treating the source of peritonitis
- The development during NPT and the condition of dressings after application and before removal.

Changes of dressings with abdominal lavage were planned in the operating room on days 2, 4, and every 2–3 days thereafter.

Data collections were performed on days 0, 2, 4, 7, 14, 21, and 28 in Examinations 1–7 (E1–E7).

Primary End Point

Primary end point was defined as closure of the muscle-fascia- abdominal wall before or on day 28. The examination of all patients for this study was terminated on day 28. The follow-up regarding the death was continued for the entire inpatient process.

Secondary Examination Parameters

1. Age, gender and BMI distribution for both groups.
2. MPI at the time of inclusion of the patient. According to published data of predicted mortality and MPI values, a cut-off point was set to a value of 25 MPI points to show the distribution of low and high risk patients of both groups (14, 17). To facilitate the comparison of the distribution, MPI classification was divided into 4 groups according to the severity of peritonitis and concomitant parameters.
3. Medical history and diagnosis relevant for inclusion: E1
4. Blood cell count and chemistry: Leucocytes, C-reactive protein (CRP), Pro-calcitonin (PCT), at every examination.
5. Amount of fluids collected per 24 h via the NPT System: E2–end.
6. Damage to the abdominal organs and tissue caused by the NPT system: E2–end.
7. Open abdomen classification (13): E1–End (Abdominal closure, premature termination).

Criteria for abdominal closure:

- Patients' clinical state had to improve to the extent that they were free of catecholamine support and no longer had any major organ dysfunction requiring external support (ventilation, hemofiltration).
- The inflammatory parameters tend to normalize.
- Two experienced surgeons with the involvement of the responsible intensive care physician decided whether the abdomen was ready for closure.

Statistical Analysis

We did a pilot study including 17 patients per group based on the following sample size considerations. A sample size of 17 in each group will have 80% power to detect a difference in means of 7 (the difference between a Group 1 mean, $\mu 1$, of 14 and a Group 2 mean, μ_2, of 7) assuming that the common standard deviation is 7 using a two group *t*-test with a 5% two-sided significance level.

The data obtained for patients were mean, median, standard deviation (stand.dev.), minimum (min), and maximum (max) for continuous variables and absolute and relative frequency for categorical data. The differences between the two groups were analyzed using the Mann-Whitney *U*-test and the chi-square test as appropriate. To compare trends in the inflammation parameters, a one-way repeated measure analysis of variance was used. We performed a linear mixed model analysis for the rank-transformed PCT values using patient as random effect and group (S-CNP or VAC) as well as a linear trend over time as fixed effects. A *p*-value below 0.05 was considered significant. The software package SPSS 20.0.0 was used for statistical analysis.

RESULTS

Thirty-four patients were included, 17 in each group.

Overall there were 22 male and 12 female patients with a median age of 59.5 years (range: 23–79).

The distribution of age, gender, MPI, MPI range, and BMI for both groups is shown in **Table 1**.

The causes of peritonitis and indications for open abdominal treatment are listed in **Table 2**. Lower intestine defects were more frequent in the S-CNP group (8 compared to 5) whereas upper intestine defects were equally frequent in both groups.

The MPI values showed in **Table 1C**. were only slightly different, the difference was not statistically significant.

The distributions of MPI values below and above 25 (**Table 1D**) were equal for both groups. Values higher than 30 occurred more often in the S-CNP group (7 vs. 5, respectively). The difference was not significant.

The values of BMI are displayed in **Table 1E**. The difference between the groups was significant. Two severely obese patients were found with a BMI of 48 in the VAC group, while an underweight patient with a BMI of only 17 was found in the S-CNP group. The BMI was involved to observe the influence on fistula formation and mortality (**Tables 3**, **4**).

The mean duration of treatment (**Table 5A**) was found to be 6.6 days with VAC and 8.9 days with S-CNP. Although the maximum treatment duration was longer for S-CNP than VAC (25 and 15 days, respectively). The difference between the two groups was not significant.

Fluid collections during 24 h before examinations are shown in **Table 5B**. With the S-CNP treatment, about twice the amount of fluids was delivered than with the VAC system. The difference was statistically significant ($p = 0.004$).

All descriptive statistics for Leucocytes and CRP can be found summarized in the **Supplementary Table 1**.

The values of leukocytes and CRP showed a continuous downward trend in both systems. There were also increases in both groups. At one measuring point, E3, a significantly lower value could be recorded for CRP in the VAC system, but this was not confirmed at the following measuring points. Overall, no specifically useful course could be found for leukocytes and CRP.

Descriptive statistics for PCT values are summarized in the addended **Table 2**.

In the PCT values, both groups showed a linear decrease in the values at the successive measuring points. This showed a significance of <0.001 for both. The differences in the values between the groups were clear, the PCT values for VAC were

TABLE 1 | A: Age, B: Gender, C: MPI, D: MPI range, and E: BMI distribution for both groups.

	A: Age			B: Gender		C: MPI			D: MPI Range			E: BMI		
	Mean	**Min/Max**	**Stand.dev.**	**Male**	**Female**	**Mean**	**Min/Max**	**Stand.dev.**	**0–25**	**25–30**	**>30**	**Mean**	**Min/Max**	**Stand.dev.**
VAC	57.1	23/76	17.4	12	5	25	12/36	8.1	7	5	5	31	196/484	7.66
		Sign.:	$p = 0.45$	Sign.:	$p = 0.721$		Sign.:	0.241					Sign.:	0.031
S-CNP	52.8	23/79	15.4	10	7	29	12/43	9	7	3	7	25	176/355	4.335

TABLE 2 | Diagnoses and sources of peritonitis.

Diagnoses	**VAC**	**S-CNP**	**n-total**
Abdominal trauma with rupture and/or necrosis in the colo-rectal area, traumatic gastric perforation		3	3
Spontaneous and post-operative liver abscess	2		2
Perforated appendicitis with peritonitis	4	1	5
Perforation, anastomotic rupture in the colon, sigmoid colon, and rectum.	5	8	13
Gastro- duodenal ulcer perforation	2	1	3
Small bowel perforation, anastomosis rupture, uro-conduit necrosis.	3	4	7
Abdominal compartment syndrome	1		1
n	17	17	34

TABLE 3 | Patients who diet during study observation or hospital stay after study termination.

	Pt.No./Age	**MPI**	**BMI**	**Days E1 to closure or termination**	**Days E1 to +**	**Diagnosis comments**
	5/50	36	19.6	1	1	Liver abscess, Leucemia, Sepsis, MOF
VAC	10/68	32	24.2	4	173	Duodenal fistula, Parkinson's disease
	17/77	30	33.1	15	43	Bladder cancer, Gangrene of the small bowel
S-CNP	29/79	37	27.5	10	13	Late treatment of tubo-ovarian abscess, MOF

Comparative parameters (Age, MPI, BMI). Days from therapy onset to termination and to death, commented main, and accompanying diagnoses.

TABLE 4 | Patients developing enteric fistulae.

Nr	**Study duration- d**	**MPI**	**BMI**	**Location of fistula**	**NP-system**
1	12	12	34.2	Small bowel	VAC
10	4	32	24.2	Duodenum	VAC
12	5	34	48.4	Ileo-transversostomy	VAC
14	5	29	33.1	Small bowel	VAC

Days from therapy onset to termination due to fistula formation, MPI- levels, BMI, and location of fistula formation. All observations were in the VAC group.

significantly higher at all measuring points than those for S-CNP, $p = 0.034$.

A summary of the "Amended open abdomen classifications" (13) (OAC grades) of all patients at E1–End is shown in **Figure 3**. The dominant green for S-CNP indicates the tendency for decreasing OAC-grades, the dominant gray and red for CNP the tendency for constant and increasing OAC-grades.

The difference of tendencies of OA grades for both system groups in **Table 7**. was found to be significant.

Early termination of study treatments:

Four patients were excluded from further study participation when they developed enteric fistulae. Details are listed in **Table 4**.

A total of 4 patients in this study died (**Table 3**). One patient, a 59 years old female, died on the 1st post-operative day of fulminant sepsis due to liver abscess in a myeloid leukemia disease with the appearance of acute multi-organ failure. Two patients died after abdominal consolidation and a closed abdominal wall in the combination of their multiple morbidity and the additional burden of their septic abdominal disease. One patient died on the 173rd post-operative day after initial sewing of a duodenal perforation. The study observation had to be ended on the 4th day after the 2nd NPT dressing change because of fistula formation of the over-sewing. The subsequent treatment outside of the study showed no success and the patient very slowly

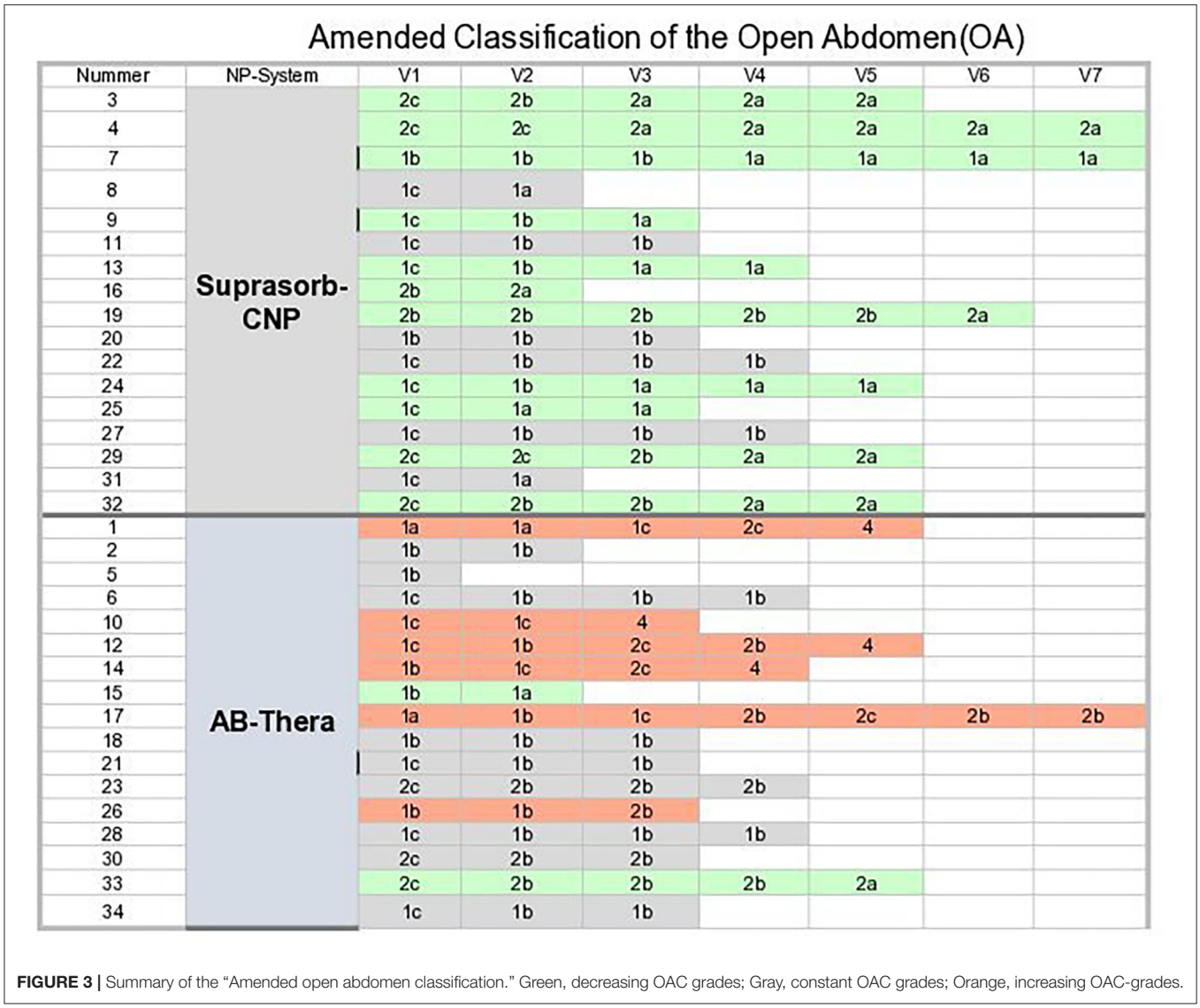

FIGURE 3 | Summary of the "Amended open abdomen classification." Green, decreasing OAC grades; Gray, constant OAC grades; Orange, increasing OAC-grades.

TABLE 5 | A: Duration of treatments (E1—closure or termination), B: Fluid samples collected per 24 h.

	A: Duration of treatments/days			B: Total fluid volume/ml		
	Mean	**Min/max**	**Stand.dev.**	**Mean**	**Min/max**	**Stand.dev.**
VAC	6.6	1/15	3.7	1981.3	220/6,900	1669.7
		Sign.: 0.532			Sign.: 0.004	
S-CNP	8.9	2/25	6.9	3779.4	850/10,700	2250.1

developed a multi-organ failure. All 4 patients were found with MPI >30.

The overall mortality rate was found to be 11.76% (4 out of 34), 1 before and 3 after abdominal wall closure, 3 in VAC group, 1 in the S-CNP group. All of them were part of the MPI >29 group therefore the mortality rate in this specific group was 26.6%.

The primary end point, the closure of the muscle-fascial abdominal wall (**Table 8**), was achieved in 27 out of 34 patients (79.54%), after a mean of 7 days of treatment. Treatments ended with definitive closure of the abdominal wall in 70.6% of the VAC group and 88.2% (n.s.) of the S-CNP group. In 2 patients, due to trauma-related necrosis of the rectus muscles, the fascia could only be closed by bridging with prosthetic material. Both of them were in the S-CNP group and they were not included into the abdominal wall closed group.

There was no significant relationship between MPI, days of treatment and abdominal closure.

TABLE 6 | Mixed model analysis for the rank-transformed PCT values using patient as random effect and group (S-CNP or VAC) as well as a linear trend over time as fixed effects.

	Mean rank (95% CI)	*p*-value
Intercept	71.1 (57.3, 84.8)	<0.001
VAC/S-CNP group	20.0 (2.36, 37.7)	0.034
Visit	−10.8 (−13.3, −8.3)	<0.001

TABLE 7 | Percentage of constant, increasing and decreasing amended open abdomen classification grades for both groups.

	Decreasing %	Constant %	Increasing %
VAC	25	44	31
	$p = 0.008$		
S-CNP	71	29	0

TABLE 8 | Muscle facia closure rate, statistics.

	n	Days E1—closure Mean, min/max	%
VAC	12	6.6, 2/15	70.6
		$p = 0.396$	
S-CNP	15	7.5, 2/25	88.2

Closure rate combined (VAC+S-CNP) was 79.4%.

DISCUSSION

In this study, 33 of the consecutive patients were included with secondary peritonitis and 1 patient with abdominal compartment (**Table 2**). Hence, this can be viewed as a peritonitis study. The severity according to the MPI was slightly higher in the S-CNP group (n.s.), but in both groups it was clearly in the range of higher severity, MPI median 28 and 29 (**Tables 1C,D**). The mortality in this range of MPI grades is indicated as about 44% (17). The selective mortality in this group MPI >29 in this study is 26.6% and thus a clear signal for the benefits of NPT treatment in this indication group. In the MPI <25 group, 17% mortality is listed (17) while in the present study this group shows no mortality. The distribution between the systems for this MPI grades is equal, 7(VAC) and 7 (S-CNP) (**Table 1**).

The results are of course also to be assessed with regard to the performance of intensive care medicine and its progress since 1994.

Inflammation parameters are known to have an accompanying significance as a decision-making aid in the treatment of septic patients. Three common parameters used in the routine of intensive treatment: white blood cell count, CRP, and PCT were tested for their usefulness in NPT. PCT has been described as the most accurate and specific parameter (19–23). Our study confirmed PCT as the best predictive parameter.

The PCT values of both systems showed a significant linear decline, a fairly clear vote for the use of NPT in septic abdomen. However, the difference between the two systems was very clear here: the PCT values of S-CNP were significantly lower overall than with the VAC system (**Table 6**, **Supplementary Table 2**). The interpretation of the possible importance is discussed later in the overview.

The data for the other two inflammation parameters, leukocytes and CRP, were of no use for a specific follow-up of the course of the disease under NPT. No knowledge could be gained by comparing the two systems.

Fluid management, a fundamental requirement of OAT (24), can be described as uncomplicated in both systems and as satisfactory from a patient care point of view. However, the evacuated amount of fluids was significantly higher with S-CNP than with VAC (**Table 5B**), practically to the same extent as was observed in an *in vitro* study (10). Since the rapid evacuation of infectious material is one of the basic requirements for septic abdominal treatment (25, 26), this can be seen as a clear advantage between the two systems.

To objectify and describe the condition of septic abdomen treatment, it is necessary to translate visual perceptions into comparable data. Even if the assessment was carried out by 2 surgeons on the basis of photos presented, the study could not be blinded. This must surely be seen as a weak point in the methodology. In this study, the "amended" score system by Björck et al. (13) was used for classification. The better clarification between "septic abdomen" and enteric leakage in the amended version of the OA classification compared with the original version (13, 27) on one side, there leaves still an area open where an enteric opening to a fistula manifests. A solution for this study was found by setting the definition of a fistula after two unsuccessful attempts at closure.

Figure 3 shows the results after the OAC grading, illustrated by a colored background. In the percentage representation (**Table 7**) the proportion of descending OAC grades is lower for the VAC group than in the S-CNP group; the difference is statistically significant. The proportion of constant OAC grades is higher in the VAC group than in the s-CNP group. The high proportion of ascending OAC grades in the VAC group is mainly due to the fact, that all 4 fistulas that occured were in the VAC group (**Table 4**). Apart from this, together with the significantly higher evacuated amounts of liquid and the observation of significant lower PCT values, the careful conclusion can be drawn that a reduced amount of negative pressure on the contaminated surfaces, including the intestinal surfaces, can be of therapeutic benefit compared to the shielding.

Even if all fistula formations are recorded in the VAC group, the chance factor cannot be ruled out given the small number of cases. An additional factor could also be 3 out of 4 overweight patients in this group, with 1 patient having a BMI of 48 (**Table 4**). Conversely, this study does not support the often anticipated fear that negative pressure on the intestinal surface is the reason for fistula formation (6). The total fistula rate of 11.7% is in the good normal range for abdominal sepsis, 5–20% as learned from the literature (3, 6, 7, 28).

The total abdominal wall closure rate of almost 80% (**Table 8**) is a very high value when measured against rates without the use of an NPT system of 12–24% (29, 30). The average closure rate with NPT systems was found about 70% (3–5, 7). The factors of the consistent additional use of a dynamic fascia anti-retraction system (12) and the work of a continuously competent team still seem to have this potential for improvement. The comparison of the closure rates of both systems of 70.6 (VAC) and 88.2 (S-CNP) is not significant. In both patients in the S-CNP group, where no primary closure could take place, the reason was the necrosis of the rectus muscles due to the underlying abdominal trauma and the abdominal wall could only be closed by bridging with the help of mesh prosthesis. The speculative assumption of these two patients as the primary closure would lead to an occlusion rate of 100% in this group. This should be considered especially under the aspect that in this S-CNP group only a negative pressure of maximum −80 mmHg was used. The negative pressure does not seem to play a major role as an anti-retraction factor and there is still potential for conventional strategies in this area.

The results of this study provide potential evidence that NPT may be useful in OAT. Due to the low number of cases, the data cannot expect any definitive statements. However, the partly significant results indicate that the negative pressure in the abdomen does not end when the wound of the abdominal cavity is treated while the intestine is protected from noteworthy negative pressure effects. The application of well-dosed, moderate negative pressure on contaminated areas of the abdomen shows a lot of potential and it is worth of further research.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by ethics committee of the Medical University of Graz, Austria (No.: 21-198, 08/09). The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

AUTHOR'S NOTE

The study showed that the negative pressure applied to the surface of the intestine has a stronger effect in infected areas than shielding them from the negative pressure. It was important for the author to determine whether this led to the widespread myth of accumulated fistula formation. Since this has not been observed, he would like to understand this as a step away from this myth and urge all interested open abdomen researchers to take a step in this new direction.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fsurg.2020.596056/full#supplementary-material

REFERENCES

1. Brock WB, Barker DE, Burns RP. Temporary closure of open abdominal wounds: the vacuum pack. *Am Surg.* (1995) 61:30–5.
2. Kaplan M, Banwell P, Orgill D, Ivatury R, Demetriades D, Moore FA, et al. Guidelines for the management of the open abdomen. *Wounds.* (2005) 17:1–24.
3. Bee TK, Croce MA, Magnotti LJ, Zarzaur BL, Maish GO, Minard G, et al. Temporary abdominal closure techniques: a prospective randomized trial comparing polyglactin 910 mesh and vacuum-assisted closure. *J. Trauma.* (2008) 65:337–42. doi: 10.1097/TA.0b013e31817fa451
4. Perez D, Wildi S, Demartines N, Bramkamp M, Koehler C, Clavien PA. Prospective evaluation of vacuum-assisted closure in abdominal compartment syndrome and severe abdominal sepsis. *J Am Coll Surg.* (2007) 205:586–92. doi: 10.1016/j.jamcollsurg.2007.05.015
5. Barker DE, Green JM, Maxwell RA, Smith PW, Mejia VA, Dart BW, et al. Experience with vacuum-pack temporary abdominal wound closure in 258 trauma and general and vascular surgical patients. *J Am Coll Surg.* (2007) 204:784–92. doi: 10.1016/j.jamcollsurg.2006.12.039
6. Rao M, Burke D, Finan PJ, Sagar PM. The use of vacuum-assisted closure of abdominal wounds: a word of caution. *Colorect Dis.* (2007) 9:266–8. doi: 10.1111/j.1463-1318.2006.01154.x
7. Shaikh IA, Ballard-Wilson A, Yalamarthi S, Amin AI. Use of topical negative pressure 'TNP' in assisted abdominal closure does not lead to high incidence of enteric fistulae. *Colorectal Dis.* (2009) 12:931–4. doi: 10.1111/j.1463-1318.2009.01929.x
8. Bjarnason T, Montgomery A, Hlebowicz J, Lindstedt S, Peterson 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. doi: 10.1007/s00268-010-0937-y
9. Auer T, Wiederstein-Grasser I, Sauseng S, Delcev P, Preisegger KH. The effect of negative pressure in the abdominal cavity with suprasorb CNP on abdominal organs-an experimental study. *Front Surg.* (2020) 7:584926. doi: 10.3389/fsurg.2020.584926
10. Puchinger M, Bergenz D, Auer T. *In vitro* model to proof the efficacy of 2 foil drainage systems for abdominal pressure therapy. *Wound Med.* (2014) 6:18–21. doi: 10.1016/j.wndm.2014.09.001
11. Web-based patient randomization service for multi-center trials. *Institute for Medical Informatics, Statistics and Documentation, Medical University of*

Graz, Austria. Available online at: www.randomizer.at (accessed September 15, 2012).
12. Kafka-Ritsch R, Zitt M, Schorn N, Stroemmer S, Schneeberger S, Pratschke J, 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. doi: 10.1007/s00268-012-1586-0
13. Björck M, Kirkpatrick AW, Cheatham M, Kaplan M, Leppäniemi A, De Waele JJ. Amended classification of the open abdomen. *SJS.* (2016) 105:5–10. doi: 10.1177/1457496916631853
14. Linder MM, Wacha H, Feldmann U, Wesch G, Streifensand RA, Gundlach E. The Mannheim peritonitis index. An instrument for the intraoperative prognosis of peritonitis. *Chirurg.* (1987) 58:84–92.
15. Rogy M, Függer R, Schemper M, Koss G, Schulz F. The value of 2 distinct prognosis scores in patients with peritonitis. The Mannheim peritonitis index versus the APACHE score. *Chirurg.* (1990) 61:297–300.
16. Demmel N, Muth G, Maag K, Osterholzer G. Prognostic scores in peritonitis: the Mannheim peritonitis index or APACHE II? *Langenbecks Arch Chir.* (1994) 379:347–52. doi: 10.1007/BF00191581
17. Billing A, Frohlich D, Schildbery FW. Peritonitis study group. Prediction of outcome using the Mannheim peritonitis index in 2003 patients. *Br J Surg.* (1994) 81:209–13. doi: 10.1002/bjs.1800810217
18. Bosscha K, Reijnders K, Hulstaert PF, Algra A, van der Werken C. Prognostic scoring systems to predict outcome in peritonitis and intra-abdominal sepsis. *Br J Surg.* (1997) 84:1532–4. doi: 10.1111/j.1365-2168.1997.02809.x
19. Rau B, Kruger CM, Schilling MK. Procalcitonin: improved biochemical severity stratification and postoperative monitoring in severe abdominal inflammation and sepsis. *Langenbecks Arch Surg.* (2004) 389:134–44. doi: 10.1007/s00423-004-0463-1
20. Meisner M, Tscaikowsky K, Palmaers T, Schmidt J. Comparison of procalcitonin (PCT) and C-reactive protein (CRP) plasma concentration at different SOFA scores during the course of sepsis and MODS. *Crit Care Med.* (1999) 3:45–50.
21. Clec'h C, Ferriere F, Karoubi P, Fosse JP, Cupa M, Hoang P, et al. Diagnostic and prognostic value of procalcitonin in patient with septic shock. *Crit Care Med.* (2004) 80:1166–9. doi: 10.1097/01.CCM.0000126263.00551.06
22. Oczenski W, Fitzgerald RD, Schwarz S. Procalcitonin: a new parameter for the diagnosis of bacterial infection in the perioperative period. *Eur J Anaesthesiol.* (1998) 15:202–9.
23. Ugarte H, Silva E, Mercan D, De Mendonça A, Vincent JL. Procalcitonin used as a marker of infection in the intensive care unit. *Crit Care Med.* (1999) 27:498–504. doi: 10.1097/00003246-199903000-00024
24. National Institute for Health and Clinical ExcellenceISBN 978-1-84936-118-7 MidCity Place, 71 High Holborn, London WC1V 6NA. Available online at: www.nice.org.uk (accessed August 25, 2020). N2035 1P 8.5k Dec 09 Negative pressure wound therapy for the open abdomen.
25. Bosscha K, Van Vroonhoven T, Van der Werken CH. Surgical management of severe secondary peritonitis. *Br J Surg.* (1999) 86:1371–7. doi: 10.1046/j.1365-2168.1999.01258.x
26. Rotstein OD, Meakins JL. Diagnostic and therapeutic challenges of intraabdominal infections. *World J Surg.* (1990) 14:159–66. doi: 10.1007/BF01664868
27. Björck M, Bruhin A, Cheatham M, Hinck D, Kaplan M, Manca G, et al. Classification-important step to improve management of patients with an open abdomen. *World J Surg.* (2009) 33:1154–7. doi: 10.1007/s00268-009-9996-3
28. Adkins A, Robbins J, Villalba M. Open abdomen management of intra-abdominal sepsis. *Am Surg.* (2004) 70:137–40.
29. Bosscha K, Hulstaert PF, Visser MR, van Vroonhoven TJ, van der Werken C. Open management oft the abdomen and planned reoperations in severe bacterial peritonitis. *Eur J Surg.* (2000) 166:44–9. doi: 10.1080/110241500750009690
30. Duff JH, Moffat J. Abdominal sepsis managed by leaving abdomen open. *Surgery.* (1981) 90:774–8.

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Early Initiation of a Standardized Open Abdomen Treatment With Vacuum Assisted Mesh-Mediated Fascial Traction Achieves Best Results

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Background: The open abdomen (OA) is an important approach for managing intra-abdominal catastrophes and continues to be the standard of care. Complete fascial closure is an essential treatment objective and can be achieved by the use of different dynamic closure techniques. Both surgical technique and—decision making are essential for optimal patient outcome in terms of fascial closure. The aim of this study was to analyse patients' outcome after the use of mesh-mediated fascial traction (MMFT) associated with negative pressure wound therapy (NPWT) and identify important factors that negatively influenced final fascial closure.

Methods: A single center ambispective analysis was performed including all patients treated for an open abdomen in a tertiary referral center from 3/2011 till 2/2020. All patients with a minimum survival >24 h after initiation of treatment were analyzed. The data concerning patient management was collected and entered into the Open Abdomen Route of the European Hernia Society (EHS). Patient basic characteristics considering OA indication, primary fascial closure, as well as important features in surgical technique including time after index procedure to start mesh mediated fascial traction, surgical closure techniques and patients' long-term outcomes were analyzed.

Results: Data were obtained from 152 patients who underwent open abdomen therapy (OAT) in a single center study. Indications for OAT as per-protocol analysis were sepsis (33.3%), abdominal compartment syndrome (31.6%), followed by peritonitis (24.2%), abdominal trauma (8.3%) and burst abdomen (2.4%). Overall fascial closure rate was 80% as in the per-protocol analysis. When patients that started OA management with MMFT and NPWT from the initial surgery a significantly better fascial closure rate was achieved compared to patients that started 3 or more days later ($p < 0.001$). An incisional hernia developed in 35.8% of patients alive with a median follow-up of 49 months (range 6–96 months).

Conclusion: Our main findings emphasize the importance of a standardized treatment plan, initiated early on during management of the OA. The use of vacuum assisted

closure in combination with MMFT showed high rates of fascial closure. Absence of initial intraperitoneal NPWT as well as delayed start of MMFT were risk factors for non-fascial closure. Initiation of OA with VACM should not be unnecessary delayed.

Keywords: open abdomen, dynamic closure, negative pressure therapy, fascial closure, abdominal compartment syndrome, mesh mediated fascial traction

INTRODUCTION

Open abdomen (OA) is a well-known clinical entity. It leaves a laparotomy incision without closure and is to be distinguished from "burst abdomen", which is an unintended fascial dehiscence after primary closure of a laparotomy incision. Its objective is to temporarily close the abdomen in a tension-free manner and to allow second-look operations. This surgical strategy is now used for managing different pathologies, e.g., intra-abdominal hypertension, sepsis, trauma or staged abdominal wall repair (1). Although this procedure is potentially life-saving, it is also associated with a number of complications and with a high mortality (2, 3). In order to reduce both the complications associated with open abdomen and to improve fascial closure rates, the preferred method of approach now focusses on early closure of the abdomen, preferably within the first 10–14 days (4). There have been several ways of temporary abdominal wall closure (TAC) which help closing the fascia. However, little is known about reasons for non-fascial closure at the end of open abdomen treatment (1, 5). Early planning and an upfront surgical strategy are key-elements. In relation to the overall outcome of an open abdomen treatment, the classification scheme reported and amended by Björk et al. correlates with prognosis and is very helpful in determining both fascial closure rate as well as overall morbidity and mortality (6, 7). An important distinction should be made between the so-called static and dynamic closing techniques. The combination of negative-pressure wound therapy (NPWT) and mesh-mediated fascial traction (MMFT) or NPWT and dynamic fascial sutures (DFS) is associated with highest fascial closure rates (8–10). The purpose is to establish edema reduction in combination with fascial reapproximation (11–13).

Currently, vacuum assisted closure (VAC) in combination with MMFT (VACM) represents the current gold standard with fascial closure rates of up to 90% and is acknowledged to be superior to other techniques lacking mechanical fascial traction (14–17). Recently, the European Hernia Society (EHS) published clinical guidelines on the management of the open abdomen and clearly recommended dynamic closure techniques, with 75.9 vs. 33.9% fascial closure rate compared to the results of static closure techniques (18). The aim of this analysis is to evaluate patient outcome after VACM and to determine crucial factors for optimal treatment, regarding both timing and surgical technique.

MATERIALS AND METHODS

Study Population and Study Design

From 3/2011 till 2/2020, all patients treated with intraperitoneal NPWT at our tertiary referral hospital were both retrospectively and prospectively entered into the Open Abdomen Route of the European Registry of Abdominal Wall Hernias (EuraHS—www.eurahs.eu) (19, 20). As the Open abdomen Route only became available in 2015 all data that was already gathered before was retrospectively entered in EuraHS. Approval of the Medical Ethics Committee was obtained prior to this study.

All files of patients whom underwent VACM at our hospital in this period were retrospectively analyzed. Patients with NPWT without MMFT and patients with only use of MMFT were excluded. Patients who died within 24 h after initiation of open abdomen treatment were also excluded. Variables on every patient and course of treatment were registered including underlying conditions and comorbidities, open abdomen management, clinical course, and clinical follow-up assessments.

VACM Protocol

A standardized protocol was used in all cases as previously described by Petersson et al. (21). At time of initial surgery an intraperitoneal NPWT device was placed when no new anastomosis, bile leak or active bleeding was present. This abdominal dressing (ABThera™ Open Abdomen Negative Pressure Therapy System, KCI, San Antonio, TX) consists of an elliptical shaped perforated polyurethane foam encapsulated in a visceral protective layer, designed to be wrapped around the viscera. It's mandatory for the device to be placed deep in the paracolic gutters and Douglas space, in order to evacuate as much liquid as possible and to avoid formation of adhesions.

In other cases a plain plastic sheet was used as a visceral protective layer. On top of the visceral protective layer a heavyweight mesh is sewn in with a continuous non-resorbable monofilament 2/0 suture at the fascial edges. Strong traction on this mesh is then applied. The mesh is then covered by a macroporous oval shaped foam dressing and protected by an adhesive sheet with attachment of the suction pad and connected to a canister. Suction was applied at −125 mm Hg (**Figure 1**).

Outcome Variables

Our primary outcome was delayed primary fascial closure, i.e., the fascial edges completely sutured together with no remaining fascial defect.

Patient Characteristics

The Open Abdomen Route covers many variables on every patient and course of treatment and is divided into various categories providing information on the patient, underlying conditions and comorbidities, open abdomen management, clinical course, and clinical follow-up assessments.

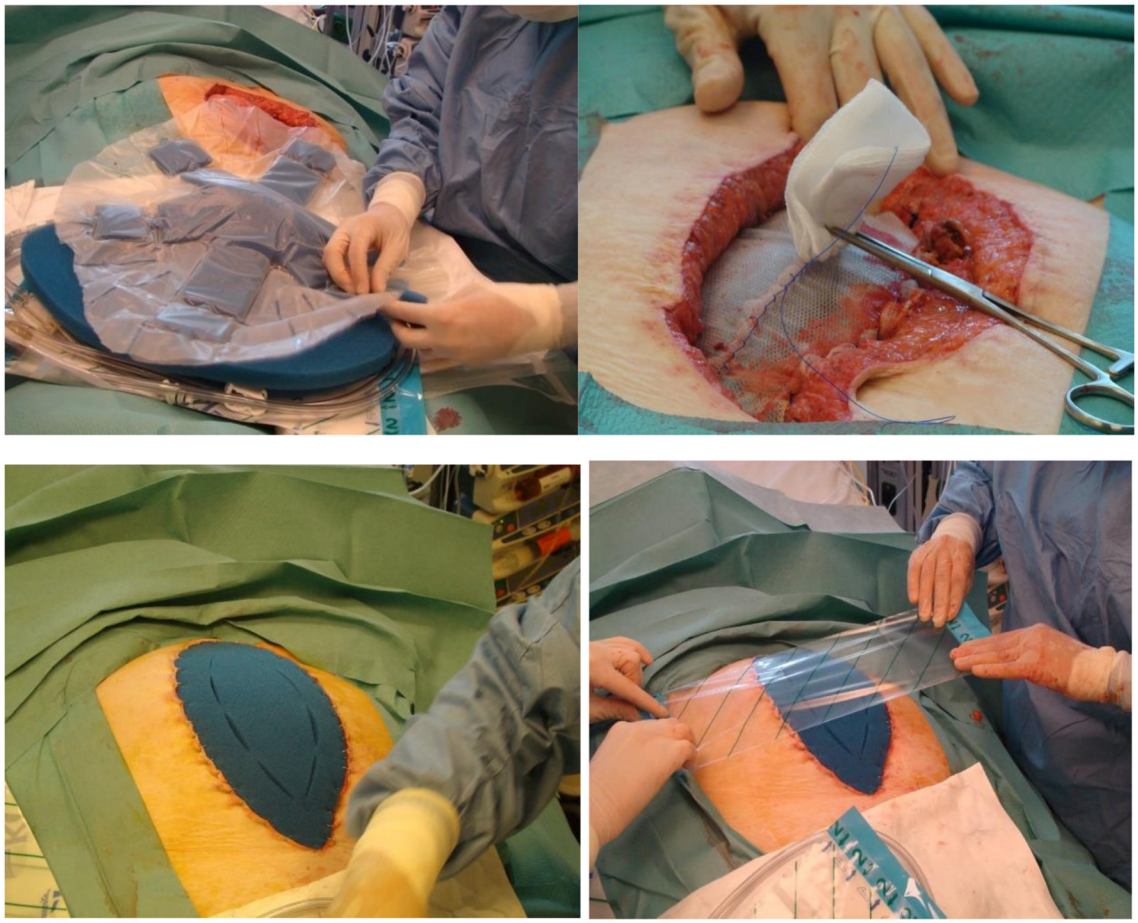

FIGURE 1 | Technique of vacuum assisted mesh mediated fascial traction.

Sex, Body Mass Index (BMI), age at time of surgery, indication for OA therapy, time between initial surgery and start of VACM, duration of VACM, complications and patient mortality were variables chosen for analysis based on their clinical relevance in regard to open abdomen management. Classification of the open abdomen was based on Björck's classification published in 2009 (7).

Follow-up was performed by chart-review at the time of analysis and in case patients were still alive a clinical examination was performed to evaluate incisional hernia formation.

Statistical Analysis

A descriptive analysis was performed on the different targets of the VACM protocol and patient-related factors. Statistical analysis was performed using SPSS (version 25.0) software. Normally distributed variables were presented as means ± standard deviations. Non-normally distributed variables were presented as medians and 95% confidence intervals (CIs). Depending on the distribution and the level of measurement, univariate analyses were performed using Fisher's exact test, chi-squared test or Mann-Whitney U test. The significance threshold was set at $p = 0.05$.

RESULTS

Patient Characteristics of the Complete Study Cohort

Between 08/03/2011 and 20/02/2020 152 patients underwent an open abdomen treatment using VACM. Thirty-two patients were excluded for final analysis of the primary endpoint because they died before final closure of the abdomen or within 24 h after closing the abdomen (9).

The mean age of the patients was 58 years. Sixty-eight percent were male. The mean BMI was 26.0 at the initiation of open abdomen management. Overall hospital mortality was 21% (32 of 152 patients). Baseline characteristics and risk factors regarding abdominal wall closure and wound healing are depicted in **Table 1**.

Patients Completing the Open Abdomen Treatment

Indications were noted as sepsis in 40 patients (33.3%), abdominal compartment syndrome in 38 (31.6%), peritonitis in 29 (24.2%), trauma in 10 (8.3%), and burst abdomen in three patients (2.5%).

TABLE 1 | Patients characteristics.

Number of patients	152
Age (years)	57.53 ± 16.3
Gender (female/male)	82 (68.3%)/38 (31.7%)
Body mass index (BMI)	26.15 ± 5.9
Malignancy	18 (15%)
Diabetes	19 (15.8%)
Cardiopulmonary disease	32 (26.7%)
Immunosuppression	7 (5.8%)
Mannheim Peritonitis Index (MPI)	20 ± 6
Injury Severity Score (ISS)	23 ± 20
In-hospital mortality	32/152 (21.1%)
Type of per protocol incision (midline/transverse/combined, $n = 120$)	99 (82.5%)/16 (13.3%)/5 (4.1%)
Björck's classification at the initiation of OAT	Grade 1A–clean OA (65.8%)
	Grade 1B–contaminated OA (34.2%)
	Grade 2A–clean OA developing adherence (0%)
	Grade 2B–contaminated OA developing adherence (0%)
	Grade 3–OA complicated by fistula (0%)
	Grade 4–frozen OA (0%)
Björck's classification at the completion of OAT	Grade 1A–clean OA (83.7%)
	Grade 1B–contaminated OA (16.3%)
	Grade 2A–clean OA with adherence (0%)
	Grade 2B–contaminated OA with adherence (0%)
	Grade 3–fistula (0%)
	Grade 4–frozen abdomen (0%)

In the per-protocol analysis a midline incision was used in 99 patients (82.5%). In 16 patients there was a transverse incision (13.3%) and in 5 a combined incision (4.1%) was used.

The average duration of the OAT was 13 days (range 1–93 days). The abdomen of 11 patients (9%) was closed within the next operation. Most patients (24%) needed 1 change of the temporary closure. It was evenly distributed for 2, 3, 4, and 5–10 changes of the closure, namely 15%. Only four patients needed more than 11 operations to close the abdomen (**Figure 2**). Considering the different indications for OA therapy trauma patients had the shortest mean closure time (2.6 days), 7.2 days for burst abdomen, 12.4 days for peritonitis patients, and 15.1 days for the patients with sepsis.

The overall fascial closure rate in the per-protocol analysis after VACM in our study population, being our primary endpoint, was 80% (96 of 120 patients), which excluded patients who had died during OA treatment. In the intention-to-treat analysis (including patients that died during treatment) the fascial closure rate was 63.2% (96 of 152 patients). An anatomical closure (fascial closure + subcutaneous and skin closure) was immediately performed in 90 patients (75%). In 6 (5%) the fascia was sutured, but the superficial layers were closed using NPWT. Only one patient needed a bilateral component separation to close the anterior fascia.

The group of patients that needed a short period of OA management and only 1-2 NPWT changes reached fascial closure in 80% of cases, while the groups that needed 7–21 days of OA management did show a closure rate of 78% (**Table 2**).

Considering the classification of OA according to Björk, most patients in our series had a Grade 1A or 1B. We did not observe any patients with frozen abdomen as all patients had their initial surgery as well as the decision for OA treatment in our hospital. During every change of the NPWT, both the abdomen and the viscera are flushed and gently mobilized, especially at the level of the abdominal wall. As this happens 2× a week, frozen abdomen is not an issue. If final fascial closure is not feasible, at the last change and closure of the abdomen, we replaced the non-absorbable mesh by a absorbable mesh and skin closure. This did not cause any fistulae.

Analysis of Non-fascial Closure

When analyzing the determining factors for non-closure of the fascia, 19 out of 24 patients that could not be closed, started their initial VACM 3 or more days after the index procedure with leaving the abdomen open (79.2%). Reasons for not starting VACM at initial surgery were risk for postoperative bleeding ($n = 14$), fear for anastomotic leakage $n = 4$ and risk for biliary fistula ($n = 1$). In those cases a type of Bogota bag was installed without NPWT nor mesh placement. Only four out of 24 got their fascia edges closed despite starting late (20.8%). Out of the patients that were not closable after OA management, there was a significant difference between patients started their VACM immediately at the time of initial surgery (5/96, 5.2%) vs. patients with a late start of their VACM (19/24, 79.2%; $p < 0001$). Mortality 12 months after closure was 4.2% (1/24 patients) vs. 3.1% (3/96 patients; $p = 1.0$). Median length of hospital stay of the analyzed 120 patients was 54 days (range: 4–275 days).

Development of Incisional Hernia During Follow Up

Considering the follow-up of this specific cohort of patients, an incisional hernia developed in 35.8% of patients considering the per-protocol analysis; all patients in which fascial closure could not be achieved ($n = 24$) developed an incisional hernia, of which only seven had a mesh repair. The other 17 did not want their hernia defect repaired (70.8%). Out of the 90 patients with fascial closure, 19 developed an incisional hernia as well (21.1%), and 15 had an abdominal wall repair with retromuscular mesh (78.9%). The median follow-up period of 49 months (range 6–96 months).

DISCUSSION

The present study analyzed a large patient cohort with OA for several indications. When treating this type of patients with necessity for an open abdomen management, time strategy is of utmost importance, as closure of the abdominal wall,

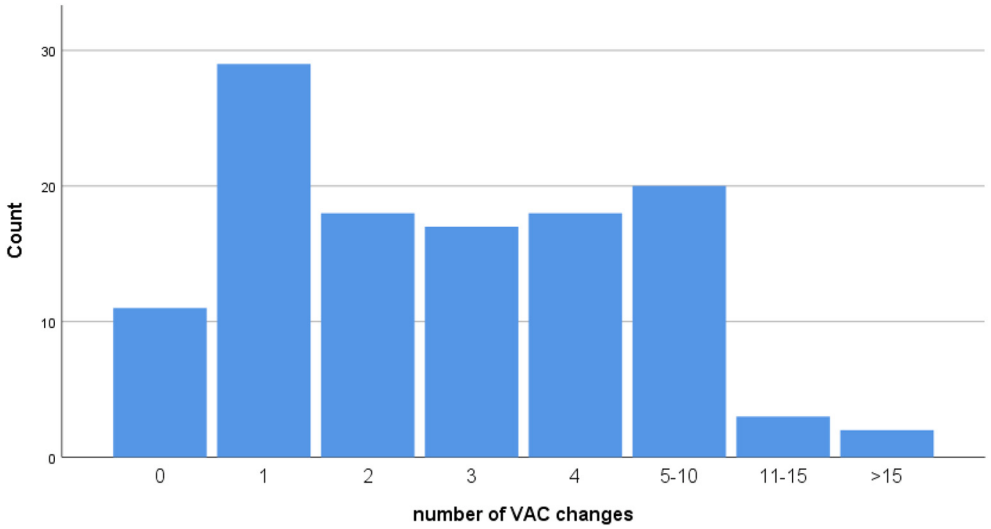

FIGURE 2 | Number of VAC changes classified according to EuraHS.

TABLE 2 | Treatment characteristics.

	Number of patients	%	*p*-value
Complete fascial closure (per-protocol analysis)	96/120	80	
Complete fascial closure (intention-to-treat analysis)	96/152	63.2	
Fascial closure rates according to OA indication			0.01
Trauma	9/10	90.0	
Peritonitis	24/29	82.8	
Abdominal compartment syndrome	31/38	81.6	
Burst abdomen	1/3	33.3	
Sepsis	31/40	77.5	
Duration of OAT		Fascial closure (%)	0.62
<7 days (1–2 reoperations)	50	80	
7–21 days (3–6 reoperations)	47	78	
>21 days (7 or more reoperations)	23	78	

i.e., fascial closure, should be aimed within 10–14 days. Initial therapy during the first 24–48 h should not only be focused on adequate edema- and excessive fluid removal as well as on hemodynamic stabilization. Surgeons should be thinking about how to handle the abdominal wall, to evaluate its compliance and finally how to obtain fascial closure. It is well-know that a non-closed abdominal cavity poses an increased risk for complications, not in the least entero-atmospheric fistulae. Closure is mandatory at the earliest possibility (22).

The EHS clinical expertise guidelines strongly recommended the use of dynamic closure techniques over other (static) techniques to achieve best fascial closure rates and low morbidity and mortality (18).

Our main findings in this analysis emphasize the importance of a structured treatment plan, initiated early on during management of the OA since the use of VACM showed high rates of fascial closure. The absence of initial intra-abdominal NPWT as well as a delayed start of MMFT, or the combination of both, were associated with a high risk of non-fascial closure. Cirocchi et al. also found better outcomes with NPWT when compared to techniques without NPWT (1). The difference in fascial closure rates was not significant and emphasizes the fact that NPWT alone may not be able to sufficiently prevent fascial lateralization during OA treatment (23). In some reports we see fascial closure rates drop to 60% or even to 30% in postponed NPWT/MMFT (24, 25). A recent review specifically focused on dynamic closure techniques only. The combination of NPWT and progressive fascial traction to the midline gives an overall closure rate between 72 and 93% (26). Main reasons for not to immediately initiate VACM in our study were bleeding/oozing at first laparotomy, bile leakage after severe liver trauma or a concomitant bowel anastomosis during the initial surgery. Traction was also not always applied from the start of OA as for some patients quick closure was initially expected. As these patients had significantly less fascial closure achieved than patients with immediate start of MMFT and NPWT, a clear message would be to better use a mesh too many than diminishing the chances for complete fascial closure. Surgeon's experience does not play an important role in this decision making, as both the initial surgery and the decision for OA management were always performed by a senior surgeon, familiar with the mesh mediated fascial traction technique.

Another point of attention using the MMFT technique is the use of a permanent heavy weight, small pore mesh for traction. We believe this is essential in these indications in which heavy traction should be applied on the fascial edges. Large pore meshes are not suitable for this purpose as they are too elastic and will be torn during the process.

The distribution of our patient population and the indications for OA management reflect those commonly found in the literature: the most frequently reported indications for OA were peritonitis or sepsis, followed by ACS, and trauma. The differences in mortality rates most likely reflect differences in patient population and only to a lesser extent imply a direct effect of the applied dynamic closure technique. In our study, in-hospital mortality of 21% was in line with the literature for OA, which varies between 10 and 45% (16, 27, 28).

There was a difference in fascial closure rates between the various indications for OA treatment in our series and the highest rates were observed for trauma patients (90%), which can be explained by a combination of the need for a short treatment period and less systemically ill patients, as shown by Montori et al. (29). In case fascial closure might take longer, there has been published sparse data on the use of Botulinum Toxin A (BTA) in OA management by Zielinski and colleagues in 18 patients (30). This toxin functions by blocking the release of acetylcholine and pain modulators (calcitonin gene–related peptide and substance P) from the pre-synaptic cholinergic nerve terminal, resulting in flaccid paralysis and pain modulation. If this paralysis may diminish lower midline abdominal wall tension, the rate of primary fascial closure might increase. However, at the time of life-saving surgical procedures or trauma, it is neither indicated nor possible to obtain informed consent from patients. Alternatively, the procedure for injection of BTA can be performed during a return trip to the OR. The clinical effect of this paralysis can be demonstrated as early as day 3 after intramuscular injection with maximum effect reached at 2 weeks (31). In the series of Zielinski et al. the primary fascial closure rate was 83% with a partial fascial closure rate of 6% and a planned ventral hernia rate of 11%, but no comparative analysis was performed with patients without BTA injections. There were no complications related to BTX (29). Surprisingly, no other reports have been published using this approach since.

Despite all efforts to finally obtain full fascial closure in OA patients, the longterm follow-up of these patients in terms of incisional hernia rate is scarce, and rather worrisome (21, 32, 33). The incidence of incisional hernias ranged from 21% at 21 months to 54% after 5 years of follow-up. The repair rate in these series differed and was 33 and 42%, respectively. In our series the incisional hernia rate was, as can be expected, 100% for patients in which fascial closure could not be obtained, but it is rather remarkable that only seven out of these 24 patients requested a hernia repair (29.2%).

Bjarnason and co-workers reported their 1-year follow-up after MMFT in combination with NPWT and described 66% of incisional hernias in these patients using CT evaluation (34). Despite the fact that more patients can be closed after OAT using fascial traction in combination with NPWT, the focus for these patients should now more and more be on how to prevent incisional hernias developing after final fascial closure in this severely ill patient population. Petersson et al. recently published a small series in which an onlay mesh was applied early during treatment by suturing to the fascia in two rows with a 3- to 4-cm overlap from the midline incision, used for traction and kept for reinforced permanent closure. A total of 11 patients were treated with a fascial closure rate of 100% and a 30 days mortality of 0%. Only two out of nine patients developed a hernia. Neither of the hernias were symptomatic nor clinically detectable. Therefore, this reinforced fascial closure might help toward a decreased long-term incisional hernia rate (35).

Our study has several limitations: in the absence of sufficiently large numbers of patients, a multivariate analysis has not been performed to assess the effects of different factors on fascial closure rates. Secondly, despite the fact that it is an ambispective dataset, this single center analysis involves OA patients with different etiologies. This leads to a heterogeneous mixture of parameters and without multivariate analysis the influence on fascial closure rate is difficult to estimate.

In conclusion, the analysis of this large cohort of open abdomen patients confirmed that VACM is an effective and safe technique and achieves good results regarding delayed fascial closure. It is important to realize that several factors are key in achieving best outcomes and are related to early surgical decision making: 1. Fast start of intra-abdominal NPWT and 2. implementing fascial traction as soon as possible.

As comparative data considering the different techniques of dynamic closure are still lacking, NPWT should be used in combination with dynamic closure techniques and devices to obtain better insight in how to best treat these cohorts of patients in the future.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethical Committee of Ghent University Hospital. Written informed consent for participation were not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

FB was involved in design of the study, data analysis, and writing of the manuscript. AV was involved in design of the study and critical review of the manuscript. SC was involved in critical review of the manuscript. KJ and KS was involved in data gathering and critical review of the manuscript. SL was involved in data gathering, data analysis, and critical review of the manuscript. All authors contributed to the article and approved the submitted version.

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REFERENCES

1. Cirocchi R, Birindelli A, Biffl WL, Mutafchiyski V, Popivanov G, Chiara O, et al. What is the effectiveness of the negative pressure wound therapy (NPWT) in patients treated with open abdomen technique? A systematic review and meta-analysis. *J Trauma Acute Care.* (2016) 81:575–84. doi: 10.1097/TA.0000000000001126
2. Lambertz A, Mihatsch C, Röth A, Kalverkamp S, Eickhoff R, Neumann UP, Klink CD, Junge K. Fascial closure after open abdomen: Initial indication and early revisions are decisive factors - A retrospective cohort study. *Int J Surg.* (2015) 13:12–16. doi: 10.1016/j.ijsu.2014.11.025
3. Sartelli M, Abu-Zidan FM, Ansaloni L, Bala M, Beltrán MA, Biffl WL, et al. The role of the open abdomen procedure in managing severe abdominal sepsis: WSES position paper. *World J. Emerg. Surg.* (2015) 12:35. doi: 10.1186/s13017-015-0032-7
4. Berrevoet F. Prevention of incisional hernias after open abdomen treatment. *Front. Surg.* (2018) 26:11. doi: 10.3389/fsurg.2018.00011
5. Karhof S, Haverkort M, Simmermacher R, Hietbrink F, Leenen L, van Wessem K. Underlying disease determines the risk of an open abdomen treatment, final closure, however, is determined by the surgical abdominal history. *Eur J Trauma Emerg Surg.* (2019) doi: 10.1007/s00068-019-01205-2. [Epub ahead of print].
6. Björck M, Kirkpatrick AW, Cheatham M, Kaplan M, Leppäniemi A, De Waele JJ. Amended classification of the open abdomen. *Scand J Surg.* (2016) 105:5–10. doi: 10.1177/1457496916631853
7. Björck M, Bruhin A, Cheatham M, Hinck D, Kaplan M, Manca G, Wild T, Windsor A. Classification - important step to improve management of patients with an open abdomen. *World J Surg.* (2009) 33:1154–7. doi: 10.1007/s00268-009-9996-3
8. Acosta S, Bjorck M, Petersson U. Vacuum-assisted wound closure and mesh-mediated fascial traction for open abdomen therapy - a systematic review. *Anaesthesiol Intensive Ther.* (2017) 49:139–45. doi: 10.5603/AIT.a2017.0023
9. Willms A, Gusgen C, Schaaf S, Bieler D, von Websky M, Schwab R. Management of the open abdomen using vacuum-assisted wound closure and mesh-mediated fascial traction. *Langenbecks Arch Surg.* (2015) 400:91–9. doi: 10.1007/s00423-014-1240-4
10. Hofmann AT, Gruber-Blum S, Lechner M, Petter-Puchner A, Glaser K, Fortelny R. Delayed closure of open abdomen in septic patients treated with negative pressure wound therapy and dynamic fascial suture: the long-term follow-up study. *Surg Endosc.* (2017) 31:4717–24. doi: 10.1007/s00464-017-5547-4
11. Tolonen M, Mentula P, Sallinen V, Rasilainen S, Bäcklund M, Leppäniemi A. Open abdomen with vacuum-assisted wound closure and mesh-mediated fascial traction in patients with complicated diffuse secondary peritonitis: a single-center 8 year experience. *J Trauma Acute Care Surg.* (2017) 82:1100–5. doi: 10.1097/TA.0000000000001452
12. Wang Y, Alnumay A, Paradis T, Beckett A, Fata P, Khwaja K, et al. Management of open abdomen after trauma laparotomy: a comparative analysis of dynamic fascial traction and negative pressure wound therapy systems. *World J Surg.* (2019) 43:3044–50. doi: 10.1007/s00268-019-05166-w
13. Fortelny RH, Hofmann A, Gruber-Blum S, Petter-Puchner AH, Glaser KS. Delayed closure of open abdomen in septic patients is facilitated by combined negative pressure wound therapy and dynamic fascial suture. *Surg Endosc.* (2014) 28:735–40. doi: 10.1007/s00464-013-3251-6
14. Coccolini F, Roberts D, Ansaloni L, Ivatury R, Gamberini E, Kluger Y, et al. The open abdomen in trauma and non-trauma patients: WSES guidelines. *World J Emerg Surg.* (2018) 13:7.
15. Cristaudo A, Jennings S, Gunnarsson R, DeCosta A. Complications and mortality associated with temporary abdominal closure techniques: a systematic review and meta-analysis. *Am Surg.* (2017) 83:191–216. doi: 10.1177/000313481708300220
16. Salamone G, Licari L, Guercio G, Comelli A, Mangiapane M, Falco N, et al. Vacuum-assisted wound closure with mesh-mediated fascial traction achieves better outcomes than vacuum-assisted wound closure alone: a comparative study. *World J Surg.* (2018) 42:1679–86. doi: 10.1007/s00268-017-4354-3
17. Bruhin A, Ferreira F, Chariker M, Smith J, Runkel N. Systematic review and evidence based recommendations for the use of negative pressure wound therapy in the open abdomen. *Int J Surg.* (2014) 12:1105–14. doi: 10.1016/j.ijsu.2014.08.396
18. Lopez-Cano M, Garcia-Alamino JM, Antoniou SA, Bennet D, Dietz UA, Ferreira F, et al. EHS clinical guidelines on the management of the abdominal wall in the context of the open or burst abdomen. *Hernia.* (2018) 22:921–39. doi: 10.1007/s10029-018-1818-9
19. Muysoms F, Campanelli G, Champault GG, DeBeaux AC, Dietz UA, Jeekel J, et al. EuraHS: the development of an international online platform for registration and outcome measurement of ventral abdominal wall hernia repair. *Hernia.* (2012) 16:239–50. doi: 10.1007/s10029-012-0912-7
20. Willms A, Muysoms F, Gusgen C, Schwab R, Lock J, Schaaf S, et al. The Open Abdomen Route by EuraHS: introduction of the data set and initial results of procedures and procedure-related complications. *Hernia.* (2017) 21:279–89. doi: 10.1007/s10029-017-1572-4
21. Petersson U, Acosta S, Björck 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. doi: 10.1007/s00268-007-9222-0
22. Coccolini F, Roberts D, Ansaloni L, Ivatury R, Gamberini E, Kluger Y, et al. The open abdomen in trauma and non-trauma patients: WSES guidelines. *World J Emerg Surg.* (2018) 13:7.
23. 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. doi: 10.1007/s00268-008-9762-y
24. 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. doi: 10.1007/s00268-008-9867-3
25. Caro A, Olona C, Jimenez A, Vadillo J, Feliu F, Vicente V. Treatment of the open abdomen with topical negative pressure therapy: a retrospective study of 46 cases. *Int Wound J.* (2011) 8:274–9. doi: 10.1111/j.1742-481X.2011.00782.x
26. Poortmans N, Berrevoet F. Dynamic closure techniques for treatment of an open abdomen: an update. *Hernia.* (2020) 24:325–331. doi: 10.1007/s10029-020-02130-9
27. 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. doi: 10.1002/bjs.8914
28. Pliakos I, Papavramidis TS, Michalopoulos N, Deligiannidis N, Kesisoglou I, Sapalidis K, et al. The value of vacuum-assisted closure in septic patients treated with laparostomy. *Am Surg.* (2012) 78:957–61. doi: 10.1177/000313481207800935
29. Montori G, Allievi N, Coccolini F, Solaini L, Campanati L, Ceresoli M, et al. Negative Pressure Wound Therapy versus modified Barker Vacuum Pack as temporary abdominal closure technique for Open Abdomen management: a four-year experience. *BMC Surg.* (2017) 17:86. doi: 10.1186/s12893-017-0281-3
30. Zielinski MD, Goussous N, Schiller HJ, Jenkins D. Chemical components separation with botulinum toxin A: a novel technique to improve primary fascial closure rates of the open abdomen. *Hernia.* (2013) 17:101–7. doi: 10.1007/s10029-012-0995-1
31. Manual of Botulinum Toxin Therapy. In: Truong D, Dressler D, Hallett M, editors. *Chapter 3. Pharmacology of Botulinum Toxin Drugs*. Cambridge: Cambridge University Press (2009). p. 12–5.
32. Bjørsum-Meyer T, Skarbye M, Jensen KH. Vacuum with mesh is a feasible temporary closure device after fascial dehiscence. *Dan Med J.* (2013) 60:A4719.
33. Willms A, Schaaf S, Schwab R, Richardsen I, Bieler D, Wagner B, et al. Abdominal wall integrity after open abdomen: long-term results of vacuum-assisted wound closure and mesh-mediated fascial traction (VAWCM). *Hernia.* (2016) 20:849–58. doi: 10.1007/s10029-016-1534-2
34. Bjarnason T, Montgomery A, Ekberg O, Acosta S, Svensson M, Wanhainen A, et al. One-year follow-up after open abdomen therapy with vacuum-assisted wound closure and mesh-mediated fascial traction. *World J Surg.* (2011) 37:2031–8. doi: 10.1007/s00268-013-2082-x
35. Petersson P, Montgomery A, Petersson U. Vacuum-assisted wound closure and permanent onlay mesh-mediated fascial traction: a novel technique for

the prevention of incisional hernia after open abdomen therapy including results from a retrospective case series. *Scand J Surg.* (2019) 108:216–26. doi: 10.1177/1457496918818979

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ORIGINAL RESEARCH
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The Effect of Negative Pressure in the Abdominal Cavity With Suprasorb CNP on Abdominal Organs—An Experimental Study

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Since the introduction of negative pressure therapy of the abdomen, care has been taken to protect the intestine from the effects of negative pressure in order to avoid impairments of abdominal organs. As an alternative to the widespread AB-Thera^{R} system (KCI, San Antonio, Texas, USA), the different concept of Suprasorb CNP^{R} (Lohmann & Rauscher, Austria-Germany) was introduced by the producer with the premise of achieving a better therapeutic effect. Due to numerous pores of the film, the effects of the negative pressure are brought to the surface of the intestinal organs and these effects were tested on seven experimental animals. Particular attention was paid to the small intestine, colon, liver, and pancreas. Over 8 h continuously, three animals were tested with −80 mmHg, 4 with −60 mmHg. The results showed no macroscopic pathological changes. The histological results showed borderline changes in the small intestine and colon with −80 mmHg application, minimal or none with −60 mmHg. The liver and pancreas were found free of pathological changes. For use on human organs, the intra-abdominal application of −60 mmHg for the Suprasorb CNP system is proposed as the standard.

Keywords: negative pressure, open abdominal therapy, Suprasorb CNP^{R}, porcine model, fistula

INTRODUCTION

The use of negative pressure (NP) dressings for open abdominal therapy has undoubtedly advanced the treatment of secondary peritonitis and abdominal compartment syndrome (1–4). Concerns were expressed since the introduction of NP-driven intra-abdominal dressings; these treatments could be the inherent source of intestinal impairments (5–8).

AB-Thera-V.A.C.^{R} (KCI, San Antonio, USA) is a widely used commercial system. The system uses a double-layer foil with polyurethane foam welded between. Both foils are perforated with slits to transport the fluids out of the abdomen and protect the intestine simultaneously with the nonadhesive foil on the surface. A further protective effect was thought with the fact that very low NP (−2 to −10 mmHG) of the applied −50 to −150 mmHg affects the intestine surface (9, 10). An alternative abdominal NP system was presented with the Suprasorb-CNP^{R} system (Lohmann & Rauscher, Austria-Germany). In contrast, this system uses a multiple-perforated double-layer foil

(**Figure 1**) in direct contact with the intestinal organs with the intent to clean out the contaminated intestinal surface from both fluids and inflammatory material, as anticipated by the producer.

This large animal study was designed to elucidate the effect of full NP application on different intestinal organ structures using the Suprasorb-CNP^{R} system.

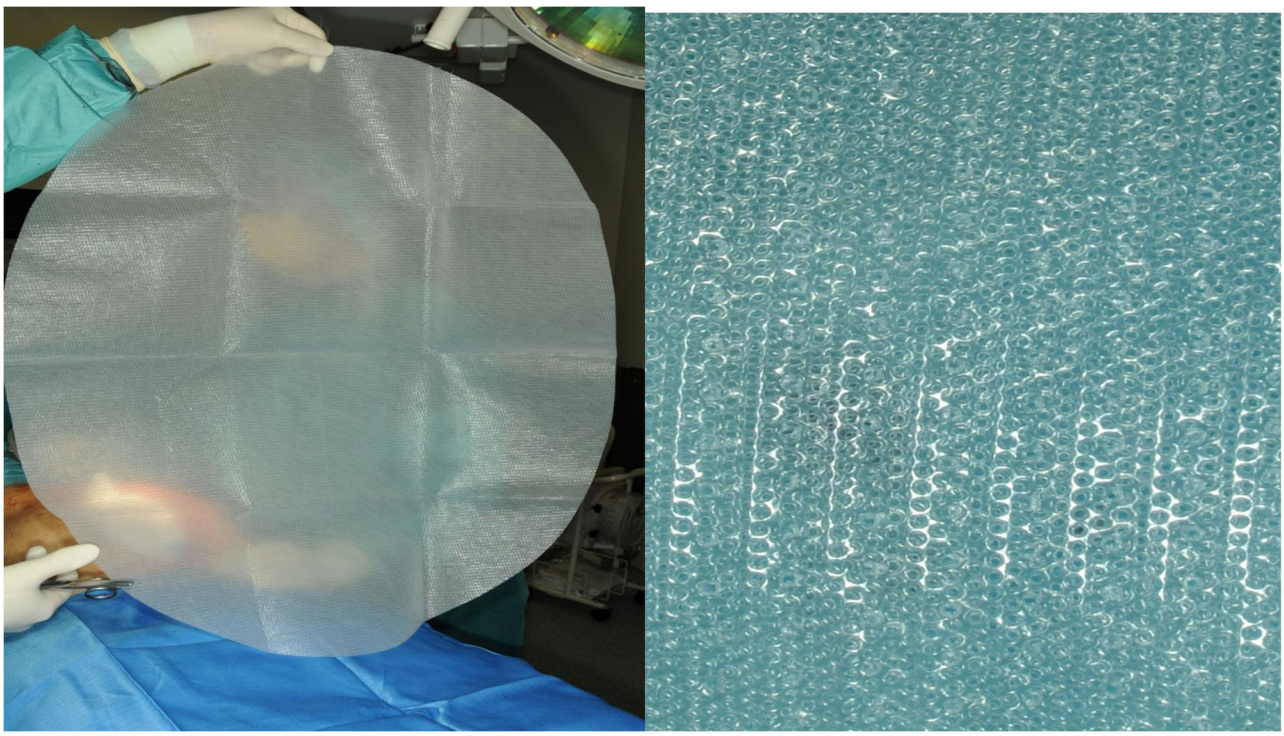

FIGURE 1 | Suprasorb CNP film.

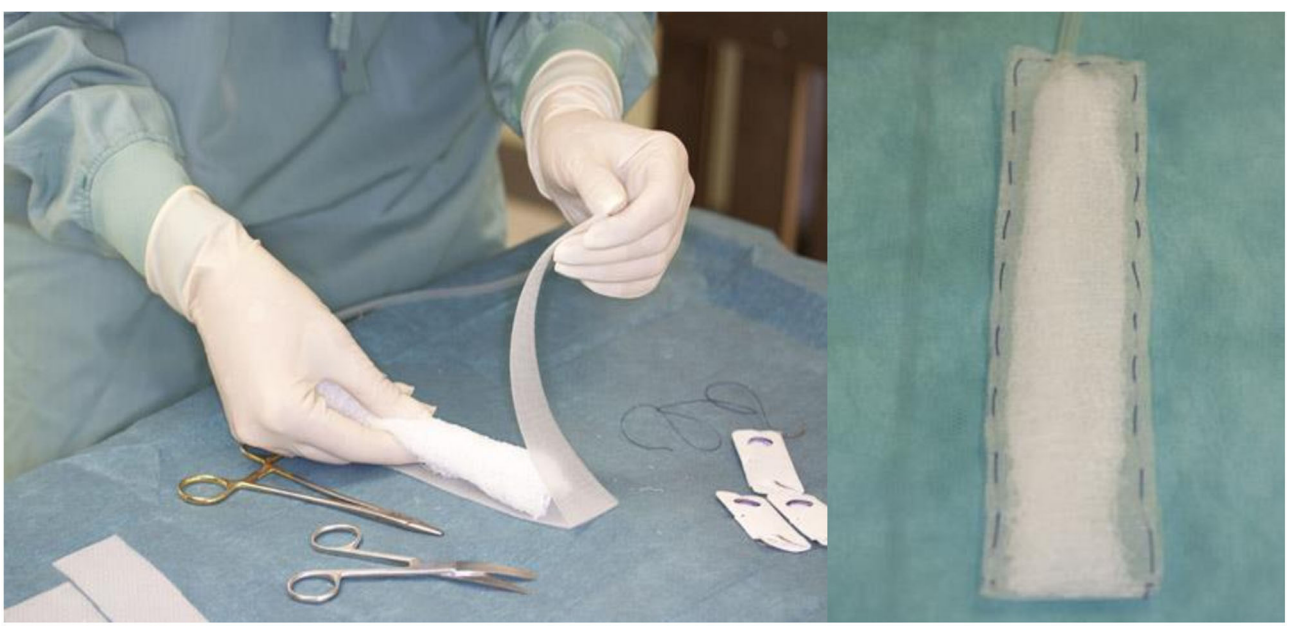

FIGURE 2 | Production of the suction pads.

MATERIALS AND METHODS

By Approval of the Austrian Ministry, according to the animal testing law (BGBI.Nr.501/1988 i.d.g.F.), seven domestic pigs (30–35 kg) were operated under general anesthesia. The general anesthesia was performed by an experienced specialist in animal anesthesia and the help of two animal keepers, for all animals for the entire duration. The abdominal cavity was opened with median laparotomy. Surgical procedures such as cholecystectomy, a small bowel stapler side–side anastomosis, a longitudinal colon diathermy incision, closed with a single-stitch suture line, and exploration of the pancreas surface were

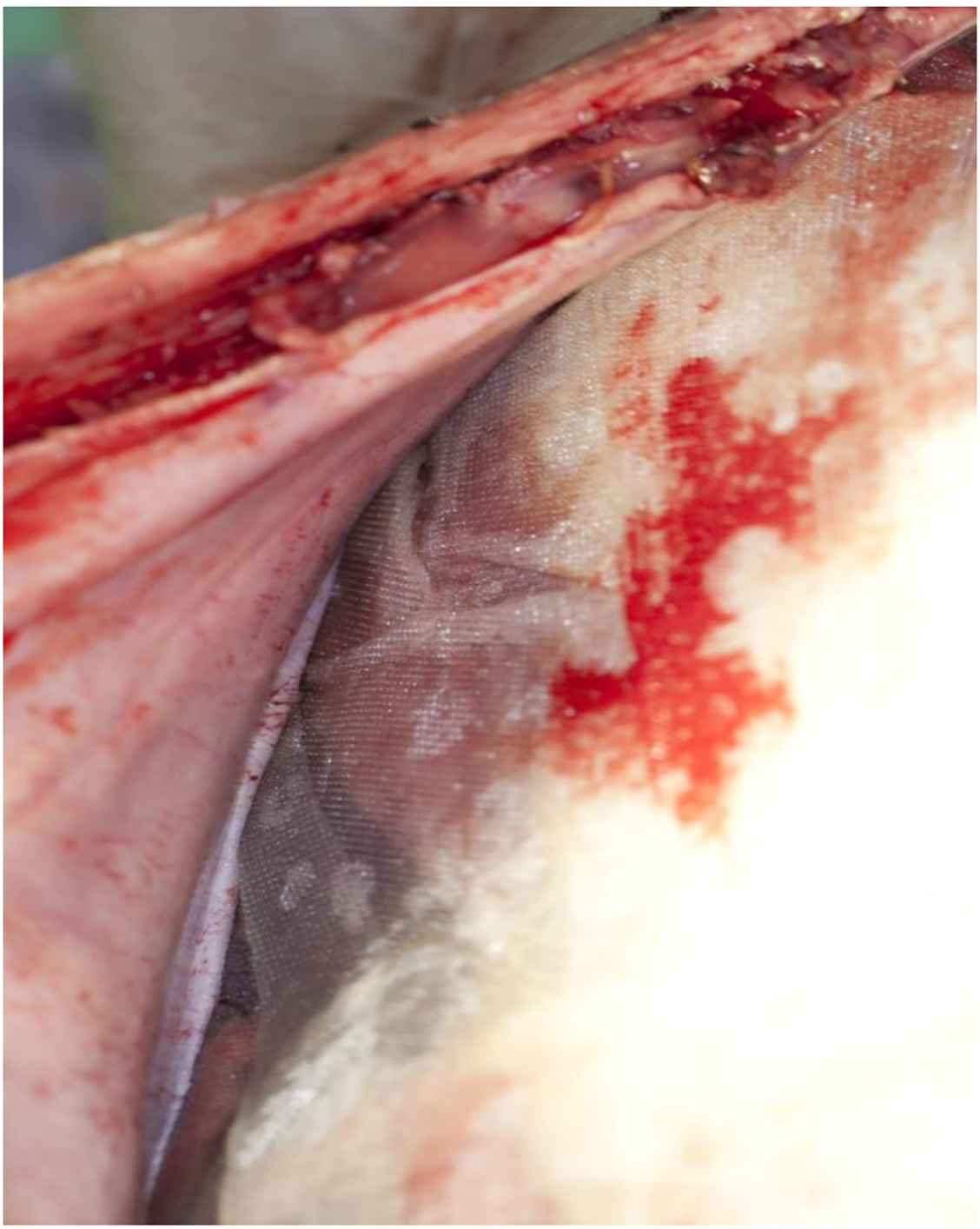

FIGURE 3 | The Suprasorb-CNP film easily detached from the abdominal wall.

done. These four sites were then covered each with a suction pad. These pads were handcrafted (**Figure 2**), and a Jackson drain^{R} in the center was wrapped with Kerlix^{R} gauze and covered with the Suprasorb CNP^{R} film, closed around with a running suture. After suture fixation of the intestine pads and positioning of the liver and pancreas pad, the whole intestine convolute was covered with the foil. Each Jackson drain^{R} was led separately out of the abdomen, connected with the suction unit. A continuous NP was applied for 8 h, four experiments with −60 mmHg, three with −80 mmHg. This NP, well below the values of other systems, was chosen on the assumption that the full amount of NP will affect the intestine surface. After 8 h of suction, the abdomen was reopened, the surface areas were inspected, and the treated organ parts were removed for histological investigation. The histological specimens were examined both on the foil-bearing sections and on the adjacent foil-free sections. These were seen as a control group without foil therapy, with NP application only.

Primary Endpoint

Damage to the intestine: histological findings, microcirculatory impairments, necrosis signs, damage of liver and pancreas tissue, triggering of pancreatitis. Histological findings for foil-bearing and foil-free sections.

Secondary Endpoints

Degree of attachment of the foil, macroscopic findings: traces at all the surfaces, fistula formation of the areas of anastomosis, foil-covered and free areas, bowel surface, gall fistula formation. Suction delivery rates.

RESULTS

All test animals could be kept in a stable circulatory state during the entire anesthesia period; hyperthermia episodes were not observed. After 8 h of treatment and reopening of the abdominal cavity, the covering film was removed.

Secondary Endpoints (Macroscopic Appearance)

The film was easy to remove without any visible impairment on all animals whether treated on −80 or −60 mmHg (**Figure 3**). There was no fluid accumulation found in any animal, no visible

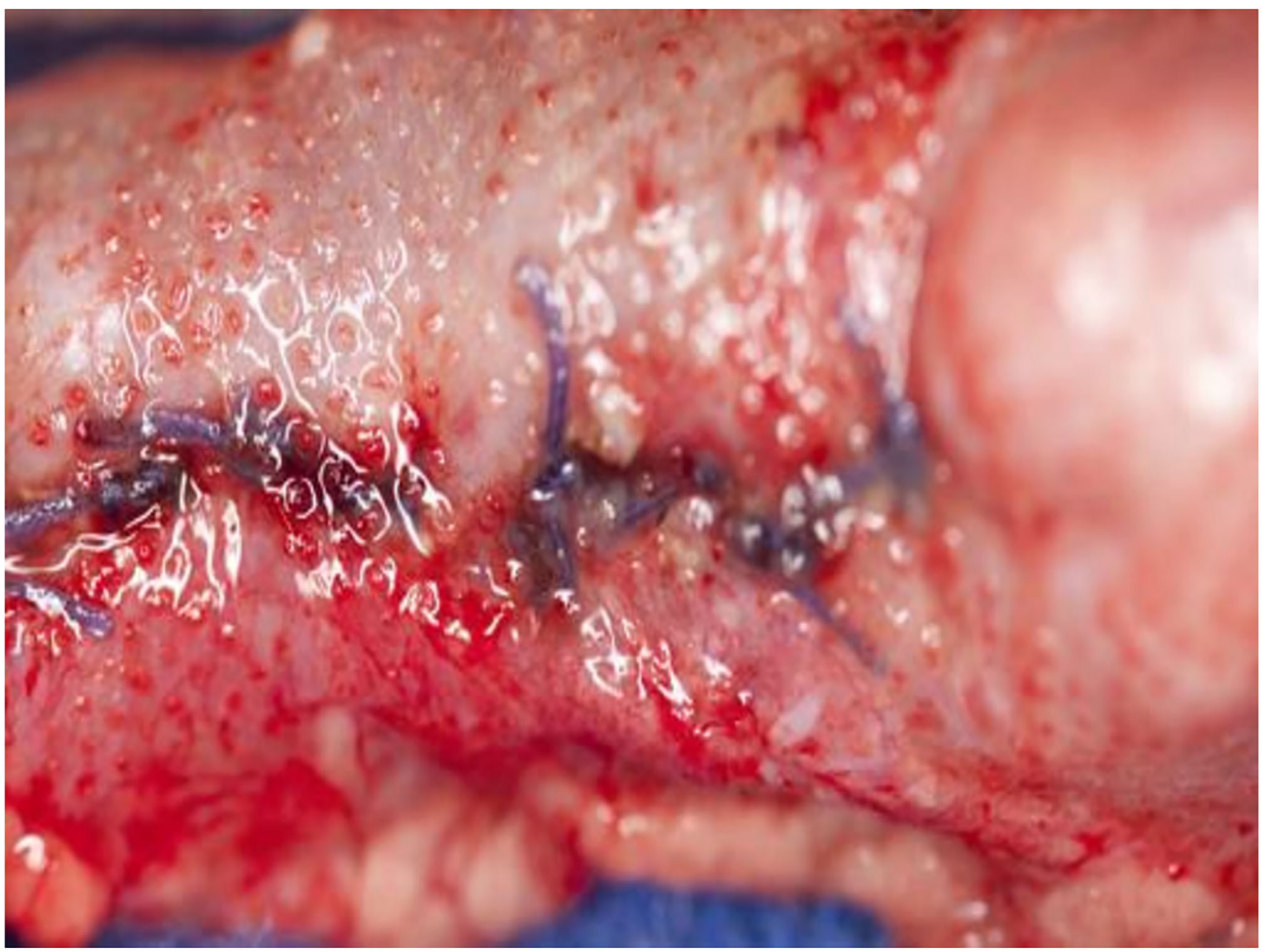

FIGURE 4 | Colon defect closed with single sutures after 8 hours of NP application.

TABLE 1 | Histological findings for small bowel, colon, liver, and pancreas of animals 1–7, indicating corresponding negative pressure.

Animal number	Negative pressure	Small bowel	Colon	Liver	Pancreas
1	−80 mmHg	Extension of: serosa, subserosa, Lamina muscularis propria	Extension of: Serosa, subserosa	Extension of: Serosa, Granulocytic infiltration	Extension of: Serosa
2	−80 mmHg	Extension of: Serosa, subserosa Partially: Lam.muscul.propr. Sparse lymphocutic infiltr	Extension of: Serosa, Subserosa, Lam. muscul. propria	Gallbladder bed: necrosis, Subcapsulary edema	Extension of: Serosa
3	−80 mmHg	Extension of: Serosa, Subserosa, Lam.muscularis propria Blood vessels (no structural damage)	Extension of: Serosa, subserosa, Lam. muscul. propria	Gallbladder bed: necrosis, Granulocytic infiltration	Extension of: Serosa
4	−60 mmHg	Extension of: Serosa Partially subserosa Sparse superficial parts of the Lam.muscularis propria	Extension of: Serosa	Sparse granulocytic infiltration	Sparse granulocytic infiltration
5	−60 mmHg	Extension of: Serosa, subserosa Very sparse parts of the Lam.muscularis propria	Extension of: Serosa, subserosa	Sparse granulocytic infiltration	Sparse granulocytic infiltration
6	−60 mmHg	Extension of: Serosa, subserosa Partially Lam.muscularis propria	Extension of: Serosa, subserosa Partially Lam.muscularis propria	Subcapsulary edema of the gallbladder bed	Serosa extensions
7	−60 mmHg	Extension of: Serosa, subserosa Minimal parts of Lam.muscularis propria	Extension of: Serosa, subserosa Isolated superficial parts of Lam.muscularis propria	Gallbladder bed: Subcapsulary edema	Serosa extensions

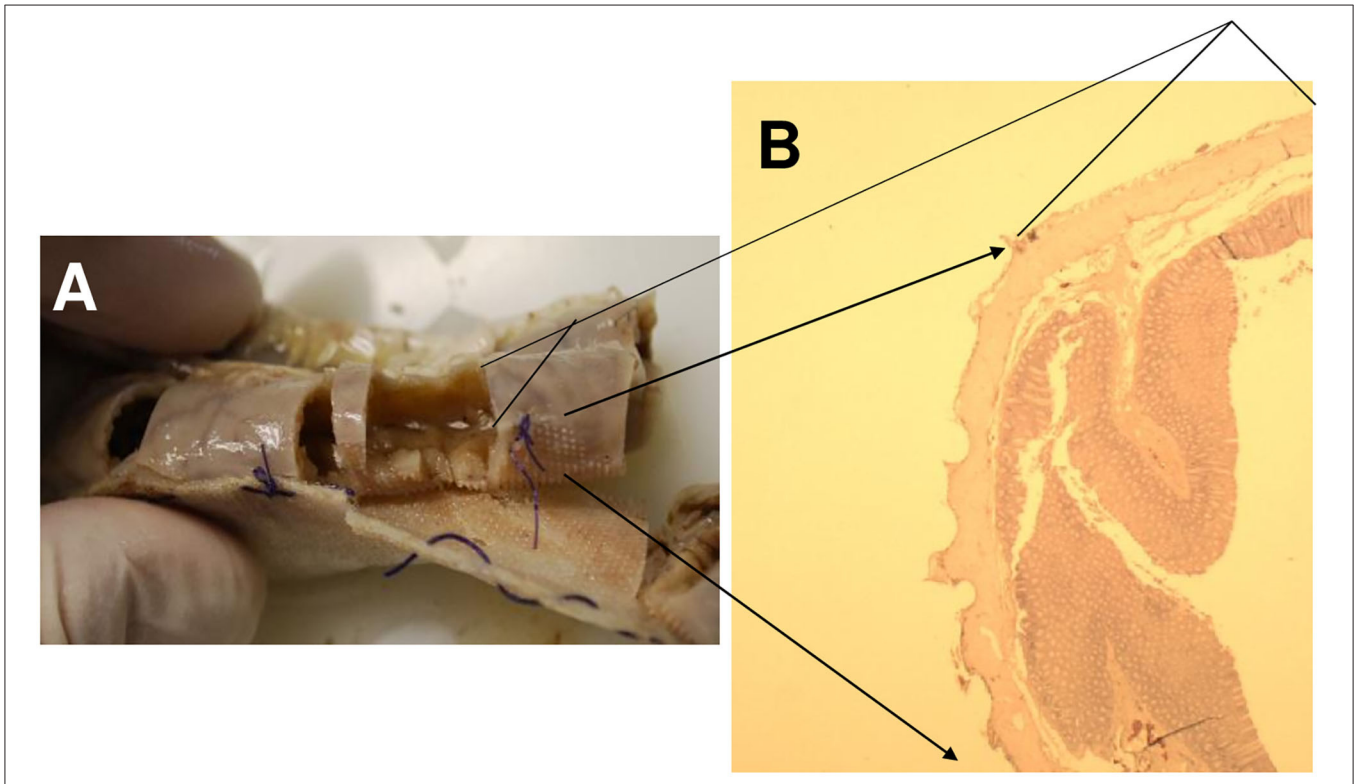

FIGURE 5 | Animal 1, −80 mmHg. **(A)** Small intestine resection. Section after removal of the patch with a paving stone-shaped pattern (delimited by arrows). Non-patch area with smooth surface marked by bars. **(B)** Small intestine wall from the "patch" section near the anastomosis. Superficially with extensions (arrow) consisting of serosa, subserosa, and L. muscularis propria. This is with a paving stone-shaped surface (arrow). Underlying layers without pathological changes. Section marked with a bar from the non-patch area with a smooth surface (bar, corresponding to the bar in the macro illustration opposite).

sign of damage or traces of discolored fluids, and no signs of fistula formation on the whole bowel surfaces. The mean amount of fluids collected was 507 ml (500–800), and all fluids were clear. The pads were cut out with the attached parts of the intestine. The anastomotic area of the small intestine and the colon showed no sign of damage or leakage, and no fistula formation. The

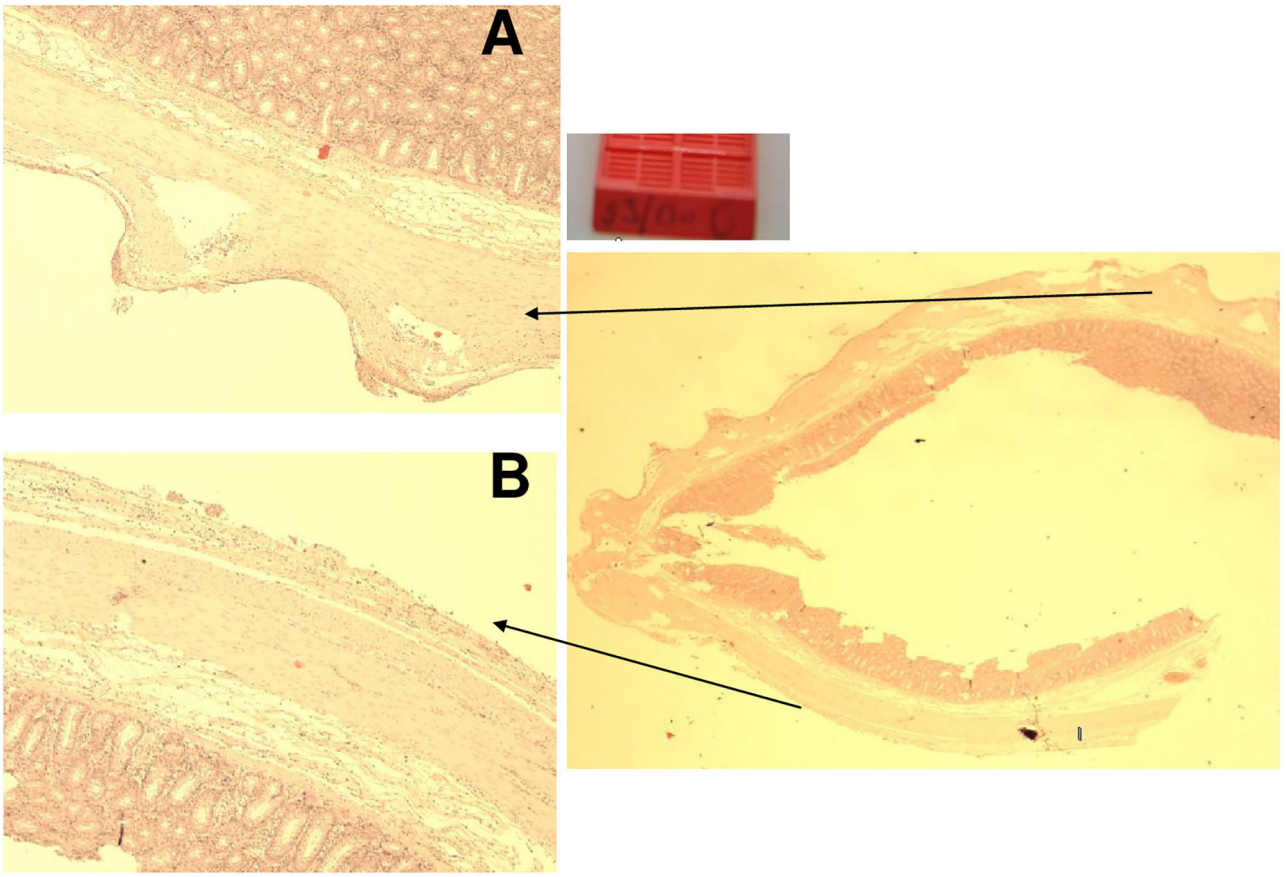

FIGURE 6 | Animal 3, −80 mmHg. **(A)** Histology small intestine from the patch area. Extensions with serosa, subserosa, and lamina muscularis propria. Extended vessels in the lamina muscularis propria with intact structure (no rupture). **(B)** Histology from the non-patch area. Smooth surface.

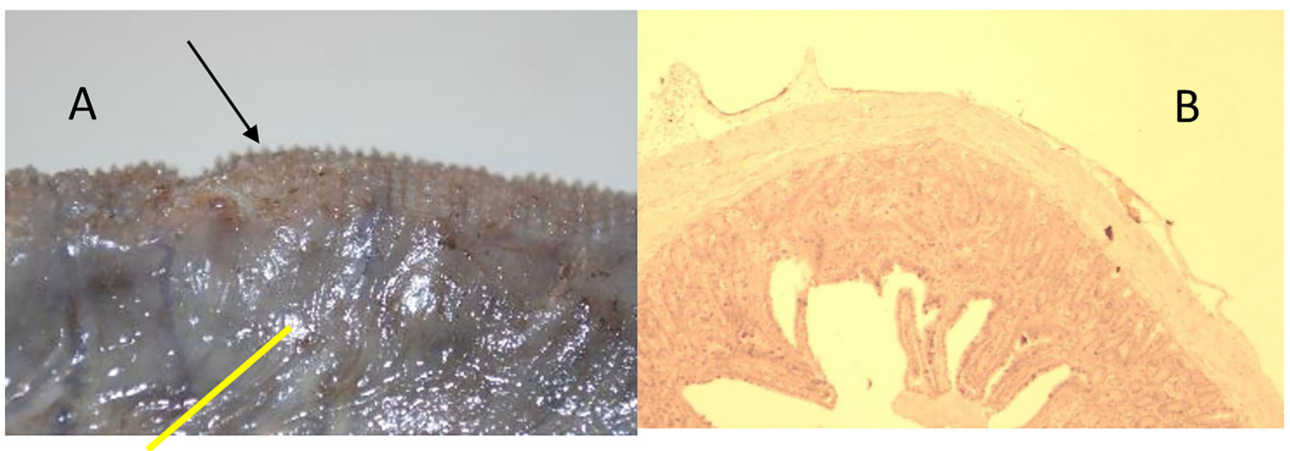

FIGURE 7 | Animal 1, −80 mmHg. **(A)** Colon resection. Section after removing the patch with a paving stone-shaped pattern (arrows). Non-patch area with a smooth surface (yellow bar). **(B)** Colon wall from the "Patch" section. Superficially with extension consisting of serosa and subserosa. Underlying wall layers without pathological changes.

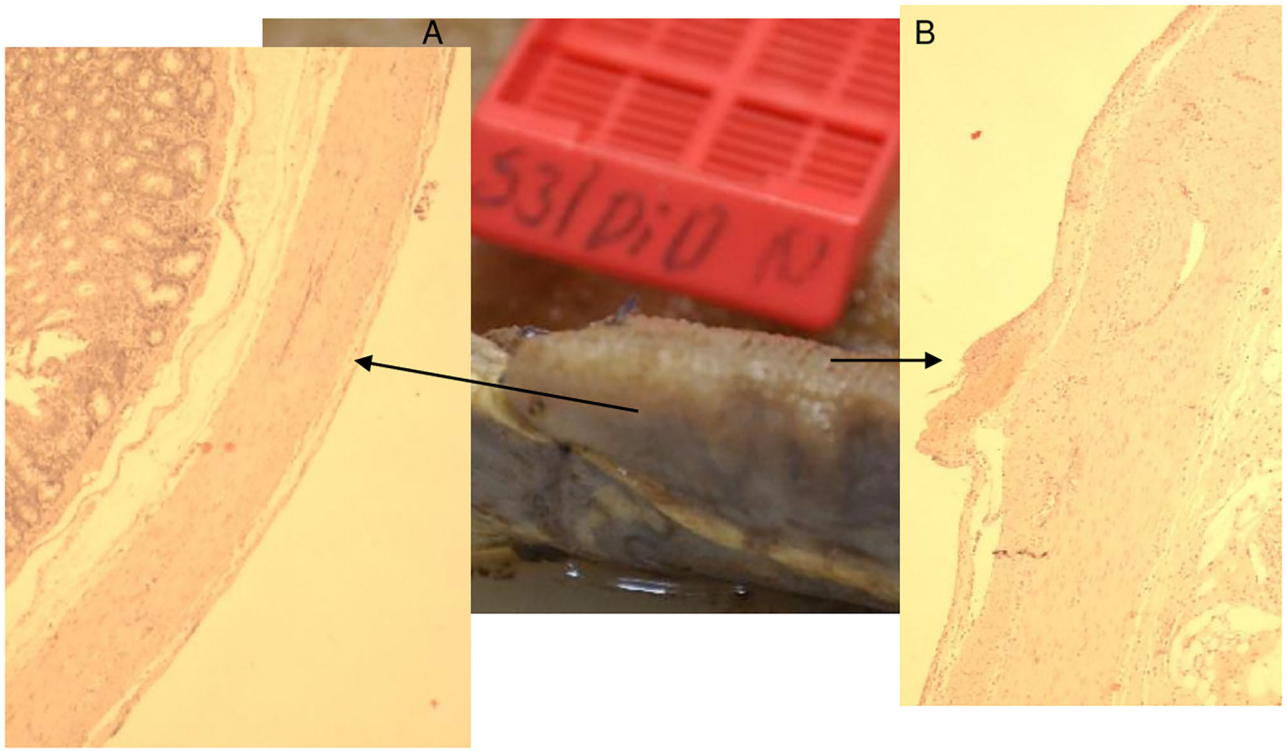

FIGURE 8 | Animal 3, −80 mmHg Colon histology. **(A)** Without patch, smooth surface. **(B)** Spikes with serosa, subserosa, and hardly any lamina muscularis propria.

surface of the translucent serosa layer with the negative imprints of the film was seen with the aspect of a healing wound with macroscopic well-perfused tissue (**Figure 4**). In the same way, the bed of the gallbladder and untreated parts of the liver around were cut out, and the contact parts and free parts around of the pancreas were excised. All liver and pancreas surface areas showed no sign of pathology, the bed of the removed gallbladder was inconspicuous, and especially no sign of gall fistula formation was seen. All surfaces on which the film was applied showed the same pattern of protrusion as the pores of the film. These were typically missing in places that were not in contact with the film.

Primary Endpoints (Histology)

The macroscopic described protrusion as found in all areas covered by the porous film was found in the same way in the histological cross sections and was made exclusively by serosa. Sparse granulocytic infiltration was seen in some areas. No signs of bleeding, no signs of thrombosis, or no other pathology was found in these areas. As a control, the uncovered surfaces showed no extensions and no other pathological changes.

The histological findings of the intestine, liver, and pancreas are described in **Table 1**. The investigated areas of anastomosis with pad and parts of them on the untreated surface did not give a different histological appearance (**Figure 5**). The difference between −80 and −60 mmHg was found on the examined small and large intestine wall. Whereas, extensions of the serosa and subserosa was found on all areas in contact with the film, extensions of the lamina muscularis propria was seen in nearly all histological specimens of intestine on animals treated with −80 mmHg. Especially on animal 3, extensions of blood vessels were also seen in the lamina muscularis propria plane of small intestine but were not accompanied by pathology such as thrombosis and rupture (**Figure 6**). In particular, the large intestine had less effect on the lamina muscularis propria than the small intestine with the −80-mmHg treatment, and no effect on the deeper wall layer similarly with small intestine with the −60-mm treatment (**Figures 7–9**). On animals 4–7, treated with −60 mmHg, the extensions of the lamina muscularis propria were found as spares, superficial, minimal, or none, on the histological sections of the intestine (**Table 1**, **Figure 10**). On all figures, parts without extensions represent areas without foil covering and are seen as a control. These areas showed an intact serosa form and no histological changes to the wall layers of the small intestine and large intestine. Histological findings on liver sections were typical for findings after removal of the gallbladder: edema, necrosis, and granulocytic infiltration (**Figure 11**). Around the resection bed and on the surface in contact with suction pads, the findings were such as sparse lymphocytic infiltration and extension of the serosa capsule, but unchanged liver tissue (**Figure 12**). The portions of the liver without a film covering showed no pathological changes whatsoever on the liver surface or on the underlying parenchyma. Similar findings were found on the pancreas surface: extensions of the serosa capsule on the film contact side and unchanged pancreas tissue on all

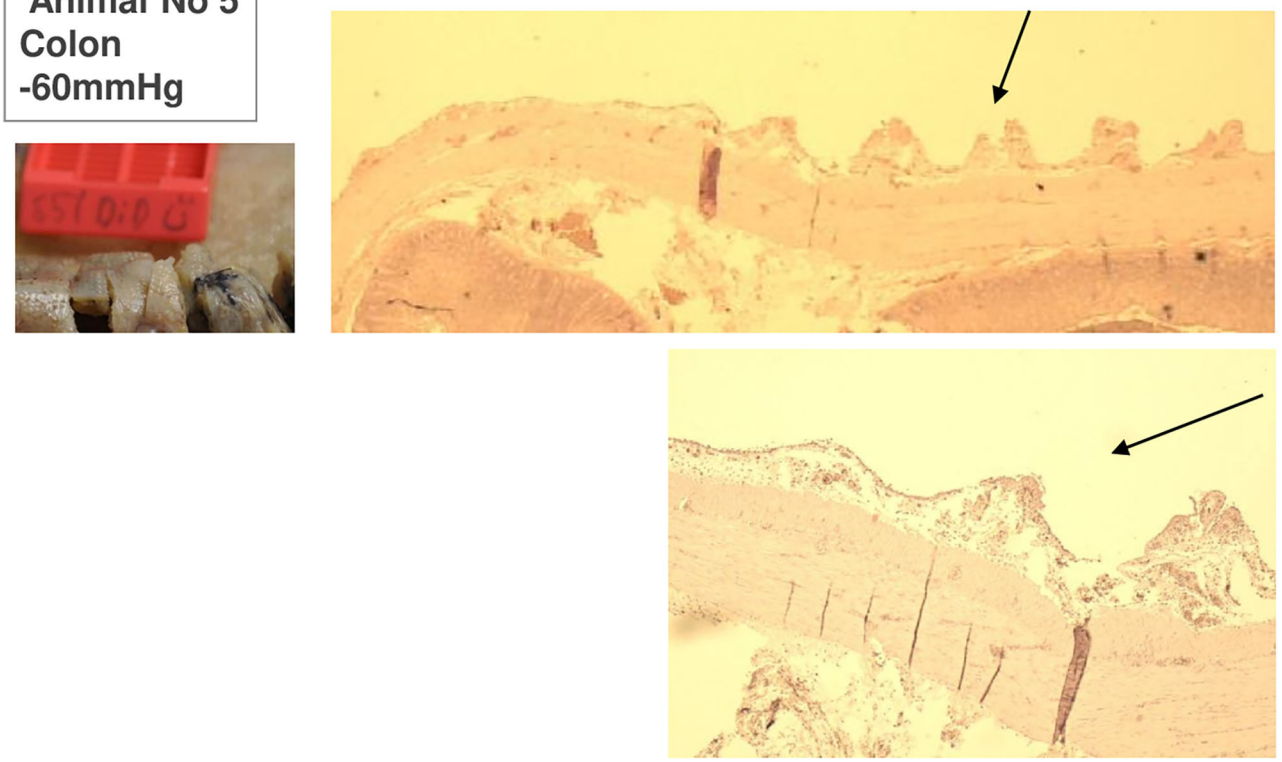

FIGURE 9 | Animal 5, −60 mmHg. Colon histology. Transition patch and non-patch area. In the patch area (arrows) extensions of the serosa and subserosa. Lamina muscularis propria would not be pulled along.

sections (**Figure 13**). In particular, no sign of the onset of pancreatitis was found. The parts not covered with the film showed no capsular expansion and no pathological changes in the pancreatic parenchyma.

DISCUSSION

For this experiment, a compromise had to be found between ethical feasibility, costs, and meaningfulness. It is believed that this was found in a full day's experiment with small domestic pigs under general anesthesia over the entire term. Open-abdomen NP therapy has a minimal duration of 24–48 h, and treatments can last up to several weeks. The results of this 8-h study must be seen as approximations of a much more sensitive but very comparable system (11) in relation to human tissue. The small intestine, for example, has an empty diameter of ∼1 cm and the wall diameter half of a human small intestine (12). In addition, the direct pad-to-intestine contact was reinforced by the direct cable routing to the suction pump, in contrast to the distribution effect when the film was placed on the intestine over a large area. Thus, in our opinion, the application of −60 and −80 mmHg also has a much stronger impact after a shorter period of time and allows conclusions to be drawn about the expected effects of longer applications on human tissue. Studying the development of a fistula formation of the intestine, first signs as microcirculatory disturbance and signs of necrosis are to be expected (8). As a discreet sign of an incipient microcirculation disorder, we already assessed the pulling out of a vessel with the lamina propria, only seen in test animal 3, but also the clear pulling out of only the lamina propria muscularis, even if this remained without any sign of a functional disorder such as thrombosis or necrobiosis. As these significant changes only occur at −80 mmHg, this was set as the maximum end point for the strength of the suction for further therapeutic use in humans. At −60 mmHg, the described effects were limited mainly on the serosa and subserosa in the form of extracts in the pore pattern of the film, so this was set as the standard pressure for the therapeutic use of the film. We see these results in certain contradiction to the observations of the Lindstedt group: significant reduction in microcirculation of the small bowel loops and omentum with application of NP from −50 to −170 mmHg. A reduction of this effect could be achieved by placing a protection plate. A dependency of the interference effect on the microcirculation was found depending on the distance of the pressure buildup system (8, 13). We also see a discrepancy

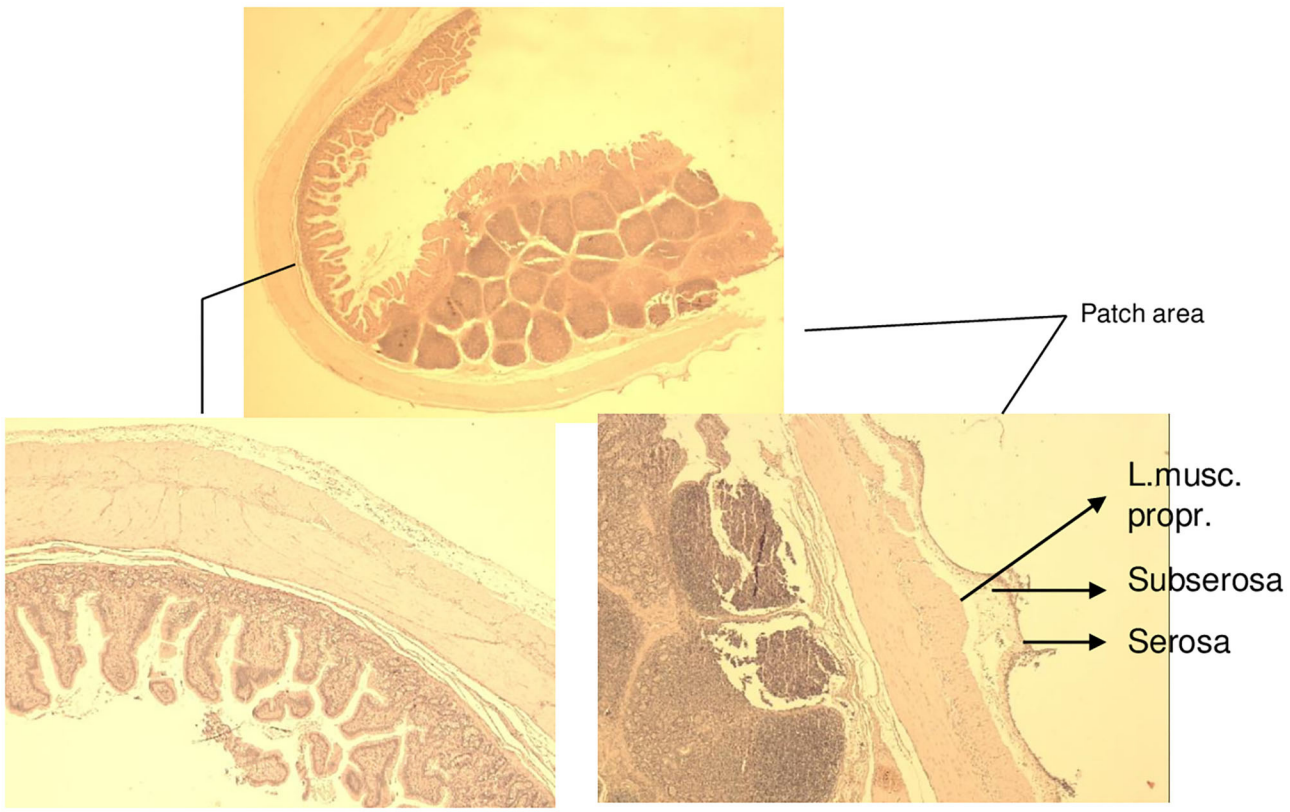

FIGURE 10 | Animal 7, −60 mmHg. Histology small intestine. Patch to non-patch transition area. In the patch area, lobe-shaped extensions are mainly the serosa and subserosa affect. The lamina muscularis propria is only minimally involved. Smooth non-patch area surface.

of these microcirculatory findings with the results of Bjarnason et al. (9); only minimal residual NP was observed below the AB-Thera^R system of applied NP from −50 to −150 mmHg. The main differences to our experiment were the film used (Suprasorb CNP^R vs. AB-Thera/V.A.C^R) and the observation window (histology vs. blood flow determination vs. pressure measurement). The authors of the study (8), Hlebowicz et al., estimated the occasional association of the observed decrease of blood flow with ischemia, promoting the development of intestinal fistulae. Two models are considered as hypotheses: the effect of NP *per se*, which decreases with the distance of the tissue from the application and is more pronounced in soft tissue than in the firm one. On the other hand, based on the effects of the NP application in proximity to the heart muscle, a model of herniation in the direction of the NP application is considered. In our model, the suction application was applied directly to the intestinal loop, and the suction pump was also connected to a direct line. This means on the one hand a very intensive contact directly with the intestinal surface, on the other hand a relatively stable system that hardly leaves any freedom of movement, even if the highest suction power was less than half that of the experiment by Hlebowicz et al. (8). From this point of view, we would tend to the herniation model and assume that the measured perfusion reductions were caused by an incarceration effect or by kinking of vessels. Because, if a perfusion disorder were caused by contact alone, damage would have to be visible histologically in our model after 8 h and also with −60 mmHg. The effect of a protective disc presented in the publication by Lindstedt et al. (14) could confirm this assumption, since it may act as a support for the bowel loop. In any case, it would be interesting to examine our two models together.

The application of the suction pads to the gallbladder bed of the liver after cholecystectomy had no effects on the liver tissue apart from the known serosa extractions, i.e., it showed no differences under the two selected suction settings in comparison to the free liver surface. The same result was also seen in the pancreatic tissue. To our astonishment, this tissue, which is otherwise sensitive to manipulation, showed no effects on the parenchyma itself, with the exception of the serosa extensions mentioned several times. These observations in comparison with the abovementioned perfusion model would in turn underline the hernia model, since both organs and especially the pancreatic tissue would have to show effects of direct negative pressure on the perfusion in the histomorphology. The truth could be in between. With our model, we come to a significant reduction in

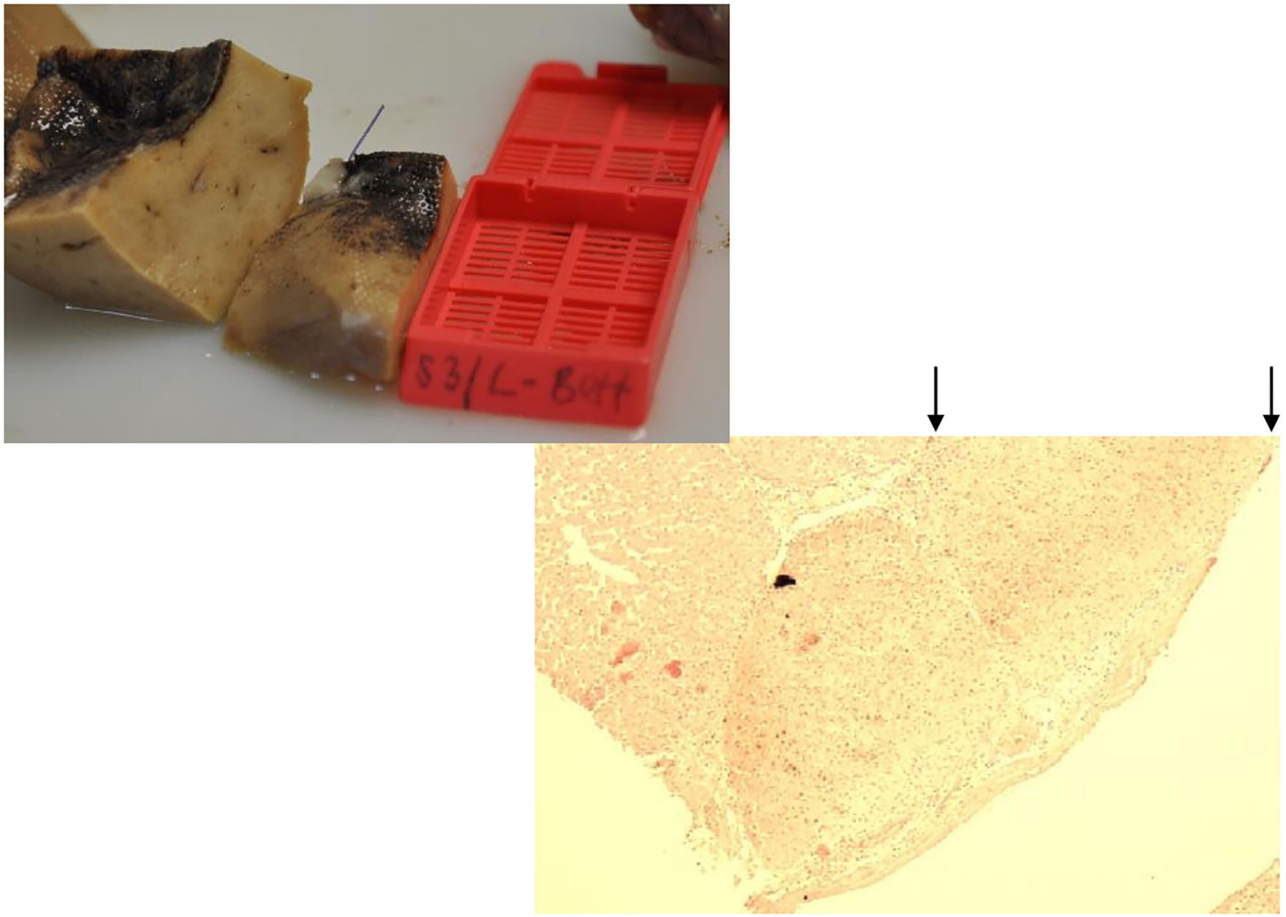

FIGURE 11 | Animal 3, −80 mmHg. Histology from the liver bed: capsular and subcapsular inflammatory infiltrate with necrosis (marked by arrows). Intact liver parenchyma (bars).

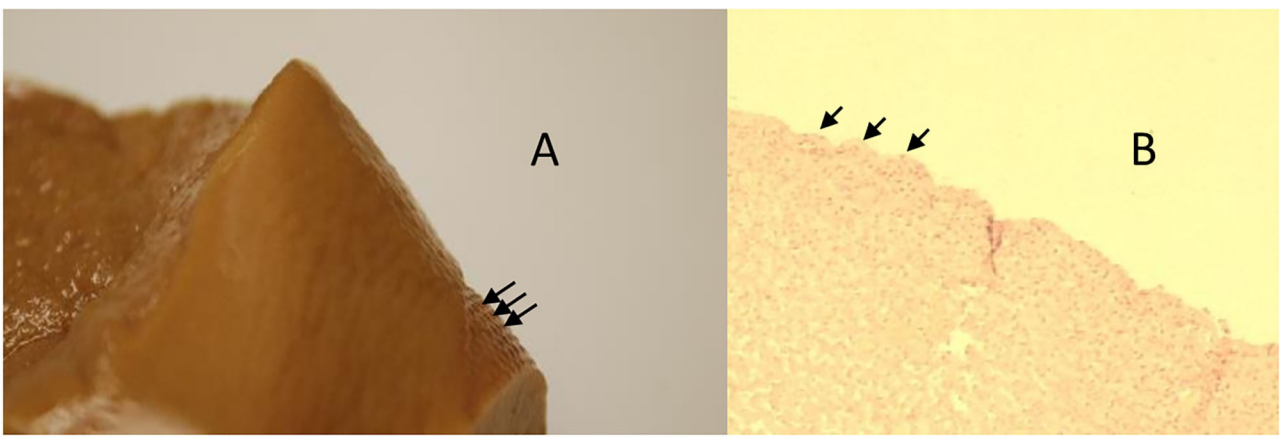

FIGURE 12 | Animal 1, −80 mmHg. **(A)** Partial liver resection. Arrows mark areas with a paving stone surface, corresponding to the patched area. **(B)** Liver cut from the "patch" section. Superficially with a lobular shape (arrow) consisting of capsule and underlying, not pathologically altered liver cells.

the suggested suction strength of −60 mmHg to the widespread use of −120 mmHg, but with a completely different structure of the film used. Possibly a direct influence on perfusion, especially in the intestinal wall, begins even with stronger suction values of −80 mmHg and more. Lindstedt et al. (14) describe only a slight protective effect of the protective disc at −120 mmHg compared

FIGURE 13 | Animal 1, −80 mmHg. **(A)** Partial pancreatic resection. Arrows rewrite the section after patch removal with paving stone pattern. Non-patch area marked by bars and with a smooth surface. **(B)** Pancreas from "Patch" section. Superficial tip-shaped extension of the serosa coating (arrow). All underlying wall layers are regular without pathological changes. No inflammatory infiltrates.

to a clear effect at −50 mmHg: large protective effect through the stabilization of the disc with little pressure, little effect against the strong NP *per se*.

As conclusions from our results, the application of −60 mmHg is given a guide value for the use of the Suprasorb-CNP system in the abdomen. In any case, the value of −80 mmHg should never be exceeded, if intestinal tissue comes into contact with the foil tested in this study.

The following clinical studies will have to show whether this system can represent an extension of the spectrum of NP therapy. Many areas of septic abdomen treatment, deep abscess treatment in the abdomen, necrotizing pancreatitis, anastomotic treatment in infectious environment, and also fistula treatment leave a lot to be desired. We hope to be able to provide an impetus through this study.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The animal study was reviewed and approved by Austrian Ministry, according to animal testing law (BGBI.Nr.501/1988 i.d.g.F.).

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

REFERENCES

1. Amin AI, Shaikh IA. Topical negative pressure in managing severe peritonitis: a positive contribution? *World J Gastroenterol.* (2009) 15:3394–7. doi: 10.3748/wjg.15.3394
2. DeFranzo AJ, Argenta L. Vacuum assisted closure for the treatment of abdominal wounds. *Clin Plast Surg.* (2006) 33:213–24. doi: 10.1016/j.cps.2005.12.007
3. Cheatham ML, Malbrain ML, Kirkpatrick A. Results from the conference of experts on intra-abdominal hypertension and abdominal compartment syndrome. II. Recommendations. *Intens Care Med.* (2007) 33:951–62. doi: 10.1007/s00134-007-0592-4
4. Acosta S, Bjarnason T, Petersson U, Palsson B, Wanhainen A, Svensson M, et al. Multicenter prospective study of fascial closure rate after open abdomen with vacuum and mesh mediated fascial traction. *Br J Surg.* (2011) 98:735–43. doi: 10.1002/bjs.7383
5. 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. doi: 10.1111/j.1463-1318.2006.01154.x
6. Stevens P. Vacuum assisted closure of laparostomy wounds: a critical review of the literature. *Int Wound J.* (2009) 6:259–66. doi: 10.1111/j.1742-481X.2009.00614.x
7. Becker HP, Wilms A, Schwab R. Small bowel fistulas and the open abdomen. *Scand J Surg.* (2007) 96:263–71. doi: 10.1177/145749690709600402
8. Hlebowicz J, Hansson J, Lindstedt S. Microvascular blood flow response in the intestinal wall and the omentum during negative wound pressure therapy of the open abdomen. *Int J Colorectal Dis.* (2011) 27:397–403. doi: 10.1007/s00384-011-1317-2
9. Bjarnason T, Montgomery A, Hlebowicz J, Lindstedt S, Peterson 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. doi: 10.1007/s00268-010-0937-y
10. Csiszko A, Balog K, Godo ZA, Juhasz G, Peto K, Deak A, et al. Pressure distribution during negative pressure wound therapy of experimental abdominal compartment syndrome in a porcine model. *Sensors.* (2018) 18:897–908. doi: 10.3390/s18030897
11. Gonzalez LM, Moeser AJ, Blikslager AT. Porcine models of digestive disease: the future of large animal translational research. *Transl Res.* (2015) 166:12–27. doi: 10.1016/j.trsl.2015.01.004
12. Kararli T. Comparison of the gastrointestinal anatomy, physiology, and biochemistry of humans and commonly used laboratory animals. *Biopharm Drug Disposition.* (1995) 16:351–80. doi: 10.1002/bdd.2510160502

13. Lindstedt S, Malmsjö M, Hlebowicz J, Ingemansson R. Comparative study of the microvascular blood flow in the intestinal wall, wound contraction and fluid evacuation during negative pressure wound therapy in laparostomy using the V.A.C. abdominal dressing and the ABThera abdomen negative pressure therapy system. *Int Wound J.* (2015) 12:83–8. doi: 10.1111/iwj.12056
14. Lindestedt S, Malmsjö M, Hansson J, Hlebowicz J, Ingemansson R. Pressure transduction and fluid evacuation during conventional negative pressure wound therapy of the open abdomen and NPWT using a protective disc over the intestines in laparostomy. *Ann Surg.* (2012) 255:171–5. doi: 10.1186/1471-2482-12-4

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

frontiers in Surgery

ORIGINAL RESEARCH
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Long Term Outcome After Open Abdomen Treatment: Function and Quality of Life

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Background: Open abdomen treatment (OAT) is widely accepted to manage severe abdominal conditions such as peritonitis and abdominal compartment syndrome but can be associated with high morbidity and mortality. The main risks in OAT are (1) entero-atmospheric fistula (EAF), (2) failure of primary fascial closure, and (3) incisional hernias. In this study, we assessed the long-term functional outcome after OAT to understand which factors impacted most on quality of life (QoL)/daily living activities and the natural course after OAT.

Materials and Methods: After a retrospective analysis of 165 consecutive OAT patients over a period of 10 years (2002–2012) with over 65 clinical parameters that had been performed at our center (1), we initiated a prospective structured follow-up approach. All survivors were invited for a clinical follow-up. Forty complete datasets including clinical and social follow-up with SF-36 scores were available for full analysis.

Results: The patients were dominantly male (75%) with a median age of 52 years. Primary fascial closure (PC) was achieved in 9/40 (23%), while in 77% a planned ventral hernia (PVH) approach was followed. A total of 3/4 of the PVH patients underwent a secondary-stage abdominal wall reconstruction (SSR), but 2/3 of these reconstructed patients developed recurrent hernias. Fifty-five percent of the patients with PC developed an incisional hernia, while 20% of all patients developed significant scarring (Vancouver Scar Score >8). Scar pain was described by 15% of the patients as "moderate" [Visual Analog Scale (VAS) 4–6] and by 10% as "severe" (VAS > 7). While hernia presence, PC or PVH, and scarring showed no impact on QoL, male sex and especially EAF formation significantly reduced QoL.

Discussion: Despite many advantages, OAT was associated with relevant mortality and morbidity, especially in the early era before the implementation of a structured concept at our center. Follow-up revealed that hernia incidence after OAT and secondary reconstruction were high and that 25% of patients qualifying for a secondary

reconstruction either did not want surgery or were unfit. Sex and EAF formation impacted significantly on QoL, which was lower than in the general population. With regard to hernia incidence, new strategies such as prophylactic mesh implantation upon fascial closure should be discussed analogous to other major abdominal procedures.

Keywords: open abdomen treatment, abdominal compartment syndrome, long term outcome, planned ventral hernia, peritonitis, SCAR, enteroatmospheric fistula

INTRODUCTION

In the recent years, open abdomen treatment (OAT) has become a widely accepted treatment strategy for severe abdominal conditions such as peritonitis and abdominal compartment syndrome (1). However, OAT can be associated with inherent high morbidity and mortality (2). Atema et al. reported in a recent review of OAT in non-trauma patients an overall mortality rate of 30% (3). The main procedure-inherent risks in patients undergoing OAT are (1) the development of an entero-atmospheric fistula (EAF), (2) failure of primary fascial closure (PC) resulting in a planned ventral hernia (PVH), and (3) high rates of incisional hernias after PC. Recent studies have demonstrated that a structured approach including (a) the use of a visceral protection layer, (b) mesh-mediated fascial traction, and (c) negative pressure wound treatment reduces the above-mentioned complications significantly (4).

The rate of incisional hernia development after primary fascial closure in OAT may be higher than in usual laparotomy which has an incidence of 5–20% in the general patient population (5). In OAT, incisional hernia incidence after PC was reported to be as high as 35–65% (6). Incisional hernia rates of this proportion are also known for other high-risk situations such as abdominal aortic aneurysm repair or obese patients (7). While in the early era of OAT a planned ventral hernia was often accepted as unavoidable, recent evidence shows that achieving PC as soon as possible is associated with reduced complications (2). For example, The World Society of Emergency Surgery suggests early fascial closure as the key strategy for the management of open abdomen with a grade 1B recommendation (8). The recent literature also suggests that early closure should be achieved within 10 days (4, 9). Thus, while hospital discharge with PVH after OAT becomes less frequent, the incidence of an incisional hernia after open abdomen treatment is high (6). The presence of an incisional hernia is associated with a higher rate of readmissions and subsequent operations (10). Furthermore, patients with incisional hernias experience a lower health-related quality of life (QoL) on physical components and a worse body image (11). It is unclear what can be done to prevent incisional hernias after OAT, and this aspect will receive more attention as high rates of delayed primary closure in OAT become more and more feasible.

As mentioned above, the second major problem after OAT is presented by the formation of entero-atmospheric fistulas (incidence of 7 to 19%), which is associated with high morbidity and mortality (2, 12). A prospective analysis of the International Register of Open Abdomen from Coccolini et al. has shown that EAF formation is—among other factors—potentially influenced by the duration of OAT, the patients' characteristics (such as malignancy or inflammatory bowel disease), and the timing of restarting enteral nutrition. Despite the caution regarding an untoward effect of negative pressure on hollow viscera, Coccolini et al. showed no existing link between negative pressure treatment and EAF development (12). A study by our working group showed that the combined use of a visceral protection layer and negative pressure wound treatment effectively reduced the formation of EAF formation in OAT patients with peritonitis (4).

Historically, the traditional method to close the OAT-induced fascial defect was to neglect midline closure, let a ventral hernia develop, and then repair this hernia in a secondary-stage abdominal wall reconstruction 6 to 12 months later (PVH approach). This technique was often combined with a temporary abdominal closure using an absorbable or non-absorbable mesh and negative pressure wound therapy. Hereby the laparotomy is allowed to granulate, followed in some cases by split-thickness skin grafting (13, 14). Logically, this results in excessive scarring. Multiple studies in burn damage survivors have shown that abnormal scarring can be associated with reduced QoL (15). For OAT, however, compiled data on esthetic and functional outcomes including scarring by using an objective score (Vancouver Scar Scale, VSS) were not available.

In this study, we assessed the long term clinical, functional and QoL outcome in OAT patients of the early era at our institution to understand which factors (PVH *vs*. PC, EAF formation, scarring, recurrent incisional hernia) impacted most on QoL and the natural course after OAT.

METHODS

The primary study was conceived in 2012, after consultation with the local ethics committee. As a first step, data were systematically gathered from all medical records of 174 patients that underwent OAT in our hospital (University Hospital of Bonn) over a period of 10 years (2002–2012) for different indications (**Supplementary Figure 1**). After quality control, 165 patient records were available for full analysis, and more than 65 clinical variables were extracted from the records. The overall results of the retrospective analysis are published elsewhere (16). Over time, the patients had been treated with different approaches for OAT according to era. The earliest cohort of the patients was often treated using a PVH approach

Abbreviations: OAT, open abdomen treatment; QoL, quality of life; EAF, entero-atmospheric fistula; PC, primary fascial closure; PVH, planned ventral hernia; VSS, Vancouver Scar Score.

using an absorbable polyglactin (Vicryl) mesh as a temporary abdominal closure, with a planned secondary-stage abdominal wall reconstruction at the earliest after 6 months. The most recent cohort of patients was treated using a standardized algorithm ("Koblenz algorithm") that uses a combination of mesh-mediated fascial traction, visceral protection, and vacuum-assisted wound closure (17). To address long-term outcome, we initiated a structured follow-up approach with telephone and written contact and invited all 95 survivors of the historic cohort for a clinical follow-up. The patients who were willing to participate after informed consent received the German 36-Item Short Form Health Survey (SF-36) questionnaire to assess QoL. The widely accepted SF-36 relies on patient self-reporting and consists of eight scaled scores, which are the weighted sums of the questions in their section. Each scale is directly transformed into a 0–100 scale on the assumption that each question carries an equal weight: the lower the score the more disability and, *vice versa*, the higher the score the less disability is displayed.

A total of 53 patients were not available or did not respond to our contact attempts. We performed a clinical follow-up examination in 42 patients of that cohort but had to exclude two patients due to incomplete SF-36 data. Thus, 40 complete datasets including clinical follow-up were available for analysis (**Supplementary Figure 1**). The median follow-up time of these 40 patients in this follow-up was 4.4 years after the index operation and OAT. In our clinical follow-up examination, QoL was assessed by SF-36 as mentioned, the presence of a clinically relevant incisional hernia was recorded, and an objective scar assessment using the VSS was performed. The modified Vancouver Scar Scale provides a standardized assessment of scarring. It scores the scar on four parameters: pigmentation, vascularity, pliability, and height (18). In addition, we used a verbal numerical rating scale as an assessment method of scar-related pain and itching in those patients.

In this study, we thus report the outcome of 40 long-term survivors of OAT concerning functional, esthetic, and QoL outcome, including data on primary fascial closure and method, presence of EAF, hernia presence, scar condition, and QoL as assessed with the SF-36 questionnaire.

STATISTICS

Descriptive and inferential statistics were used in data analysis using SPSS Statistics Version 24 (IBM, Armonk, New York, USA). Intergroup differences were calculated for the SF-36 score using Students' *t*-test followed by Bonferroni correction. Clinical parameters were analyzed for possible correlations using Pearson's correlation coefficient. *P*-values were two-sided, and statistical significance was set at 0.05.

RESULTS

Epidemiology

The epidemiologic and clinical data of the 40 patients participating in the follow-up study are presented in **Table 1**. Median patient age was 52 years, and sex was predominantly male.

TABLE 1 | Epidemiologic data, comorbidities and potential influencing factors of postoperative outcome.

***N* total = 40**	***n*, (%)**
Sex: m	30 (75)
f	10 (25)
Malignancy at time of index procedure	5
ASA (19) at time of index procedure: I	0 (0)
II	7 (18)
III	23 (58)
IV	9 (23)
V	1 (1)
Index Procedure: Colorectal	11 (28)
Pancreas	12 (30)
Small bowel	3 (7)
HPB	6 (15)
Other	8 (20)
Indication for OAT: Peritonitis/anastomotic leakage	22 (55)
Hemorrhage	3 (7)
Pancreatitis	7 (18)
Abdominal compartment syndrome	3 (7)
Other	5 (13)
Obesity (BMI >30 kg/m²)	10 (25)
Cardiovascular disease	14 (35)
Immunosuppression	3 (7)
Renal failure	5 (13)
Prior malignancy	9 (23)
Lung disease	2 (5)
Diabetes mellitus	7 (18)
Prior abdominal surgery	16 (40)

Peritonitis was the most common indication for open abdomen treatment.

Clinical Course

The median hospital stay was 71 days, and the median duration of OAT (from index operation until the closure of the abdominal wall) was 13 days, and this was achieved with a median of 6.5 procedures (scheduled reoperations). The survival rate of the entire historic patient cohort was 57%. Seven (18%) of the patients developed an entero-atmospheric fistula at some point along the duration of OAT. A vacuum-assisted wound closure method was used in 25 cases (63%).

Fascial Closure and Hernia Development

Primary closure was achieved in nine cases (22%), and a planned ventral hernia approach had to be employed in 31 patients (**Figure 1**). Twenty-three of the 31 PVH patients (74%) underwent a secondary-stage abdominal wall reconstruction procedure to achieve a definitive abdominal wall closure. In 16 cases, a mesh enhanced procedure was used. In nine cases, the fascial edges could not be approximated, and a mesh was used as an abdominal wall substitute in inlay position. In seven cases,

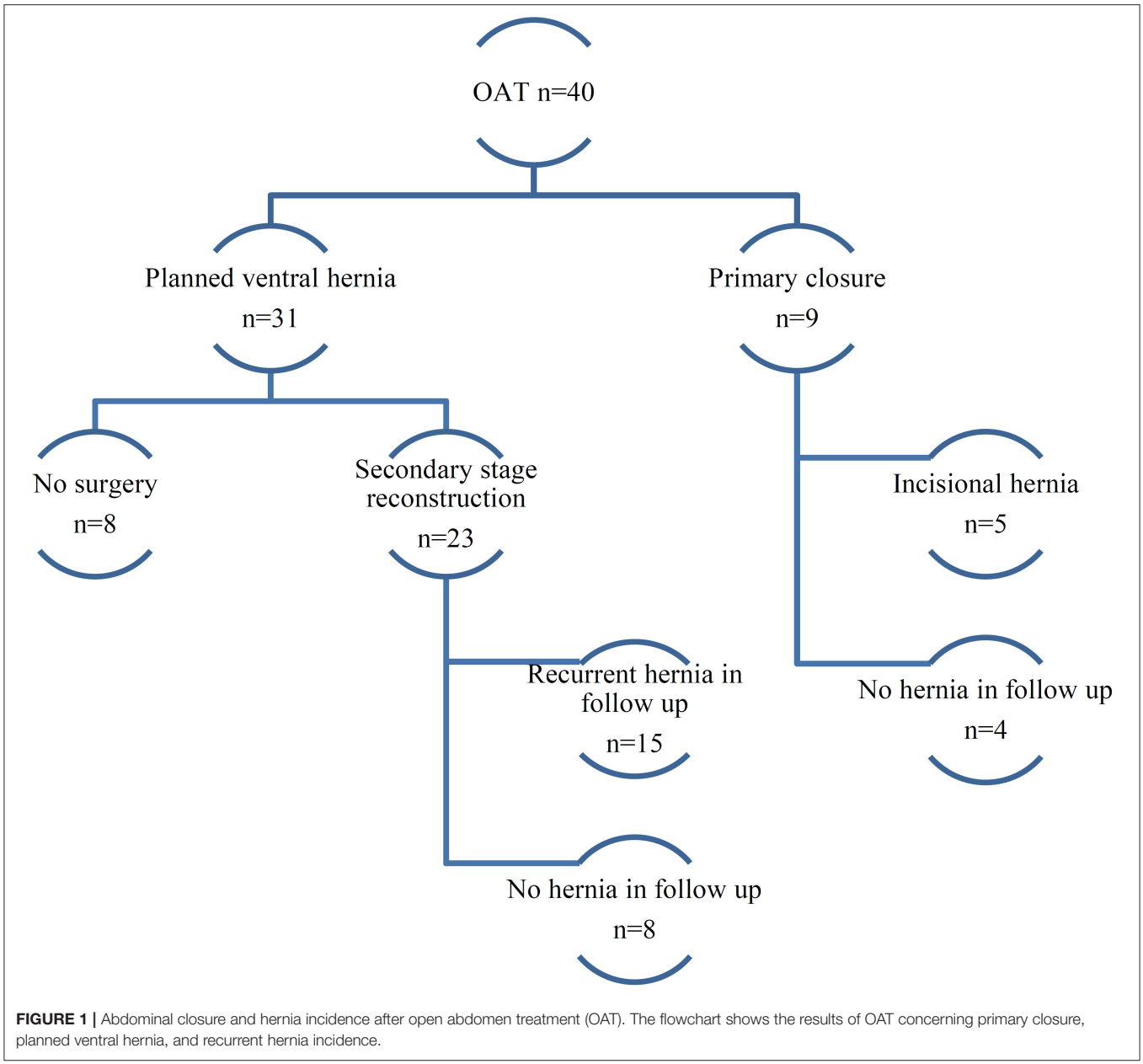


FIGURE 1 | Abdominal closure and hernia incidence after open abdomen treatment (OAT). The flowchart shows the results of OAT concerning primary closure, planned ventral hernia, and recurrent hernia incidence.

an anterior component separation as described by Ramirez et al. (20) was necessary to close the fascial defect. One patient required an upper thigh myocutaneous flap to reconstruct the abdominal wall (**Figure 2**).

One-fourth of the patients with a planned ventral hernia did not undergo secondary reconstruction for several reasons: the majority of them deemed the perioperative risk too high to attempt a procedure or the surgeon refrained from it for the same reason. Of the nine patients where a primary fascial closure was achieved, five (55%) developed a subsequent incisional hernia. Two of them underwent more than two attempts at abdominal wall reconstruction. Of the 23 patients in whom a secondary-stage reconstruction was performed, 15 (65%) eventually developed a recurrent incisional hernia. As expected, all of the patients without primary fascial closure and who did not receive a reconstruction developed a (planned ventral) hernia. In our clinical follow-up, a total of 28 (70%) patients presented with a clinically relevant abdominal hernia.

Scarring

In our cohort, 10 patients developed mild scars, with VSS < 4. Twenty-two (55%) of the patients presented with a score between 4 and 8, while eight of them had a VSS score >8 that represents significant scarring (**Figure 3**).

Itching was not a problem for 33 (83%) of the patients, and seven patients complained about only mild itching, none of severe itching. The majority of the patients did not report

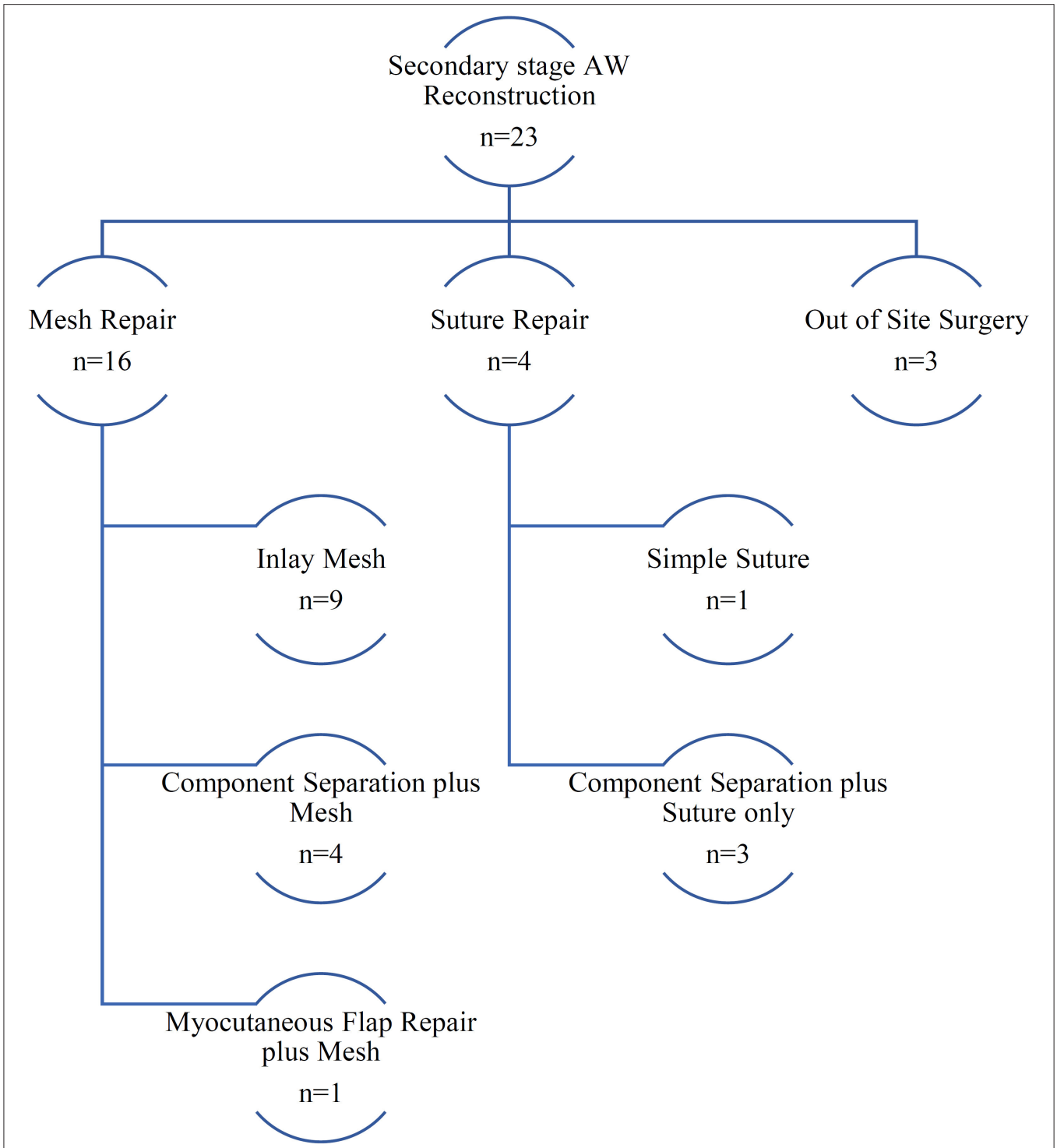
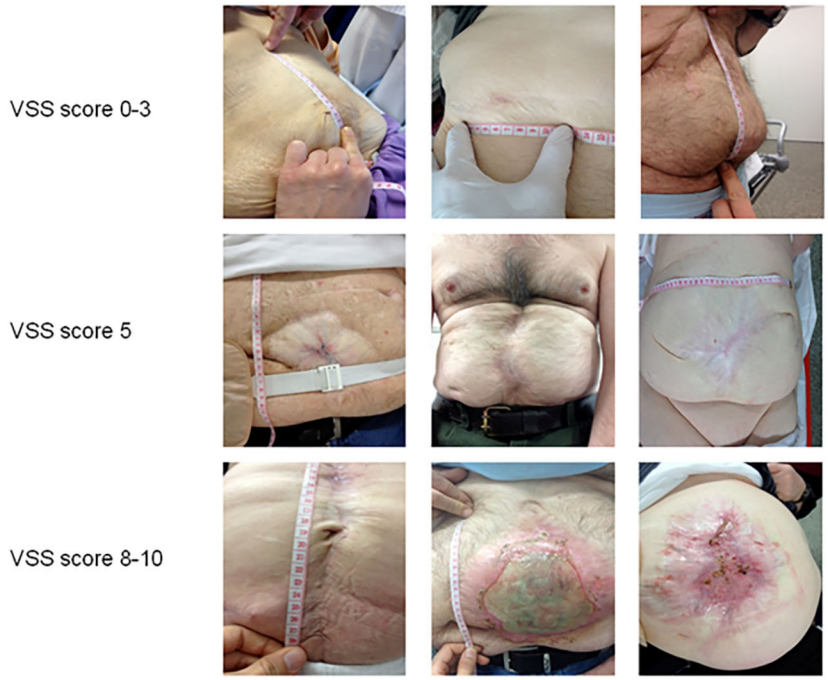


FIGURE 2 | Secondary-stage abdominal wall reconstruction techniques. The flowchart shows a synopsis of techniques used for secondary-stage abdominal wall reconstruction at our center.

significant scar pain, with four patients reporting only mild pain (two and three on the VAS Pain Scale). Six patients complained about moderate pain (4–6 in the VAS Pain Scale), while four patients experienced severe pain with VAS > 7. Eight (20%) patients developed ulcers on the scar tissue, some of which were microbially contaminated (**Figure 3**,



VSS	n	%
<3	10	25
4 to 8	22	55
>8	8	20

SI		
No Itching	33	83
Mild Itching	7	17
Severe Itching	0	0

Scar Pain		
No Pain (1)	26	65
Mild Pain (2-3)	4	10
Moderate Pain (4-6)	6	15
Severe Pain (7-10)	4	10

FIGURE 3 | Vancouver Scar Scale (VSS) assessment combined with scar itching and pain scores. Shown are the VSS assessment scale and scar itching and scar pain results with clinical examples from our cohort.

bottom picture; refer to **Supplementary Material** for data on bacterial contamination).

Quality of Life

Quality of life as assessed by SF-36 showed impaired physical role functioning in men as well as in women when compared to the normal population (21). The SF-36 scores are known to be sex dependent; therefore, they are given to men and women separately (**Figure 4**).

It was also analyzed which clinical findings after OAT impacted on QoL as measured by the SF-36 questionnaire. The presence of a clinically evident hernia or EAF and also the factors sex, primary fascial closure, and scarring (VSS score low *vs.* high) were compared. While hernia presence, primary closure *vs.* planned ventral hernia, and scarring showed no statistically significant differences, the factors sex and especially EAF formation impacted significantly on QoL (**Table 2**).

DISCUSSION

OAT is a specialized treatment that can prove to be life-saving for critical situations of abdominal sepsis but is inherently associated with high morbidity. Survivors of OAT face various factors that potentially limit their quality of life.

In this long-term follow-up with over 4 years after the index procedure of a single-center patient cohort after OAT, we show that several aspects of OAT must be addressed to achieve a satisfactory outcome. Overall survival was decent at best with 95/165 patients (58%). Due to the evolution of OAT at our institution which reflects the advances in OAT strategies in general, survival has improved to over 64% in the current era. The primary fascial closure rates which are the focus of surgical management (as only fascial closure as a "surgical factor" significantly reduces mortality and morbidity) were also relatively low in this historic cohort (only 9/40 patients, 23%). Recent algorithms such as the utilization of a consequent three-column approach (fascial traction, visceral protection, negative pressure wound treatment) have significantly improved primary closure rates over time not only at our institution (22). In the historic cohort reported here, a primary closure was not achieved in the majority of cases, which would not be acceptable compared to contemporary standards. Interestingly, primary fascial closure *vs.* planned ventral hernia was not a factor that impacted on quality of life. This could, in part, explain why only 75% of PVH patients were scheduled for secondary reconstruction, the reasons being mainly 2-fold: either the surgeon deemed the patient unfit for surgery or the patient refused secondary reconstruction due to lack of hernia-related complaints and/or fear of complications. More than half of the patients after successful PC and 65% of patients after a secondary reconstruction for PVH eventually developed a recurrent ventral hernia. Comparably, in the recent literature, the incidence of an incisional hernia after OAT is high, reaching up to 65% (6). This is comparable to other high-risk situations as abdominal aortic aneurysm operation (7), transplantation (23), or obesity and considerably higher than hernia incidence after elective laparotomy (5). In some of the above-mentioned instances, the use of prophylactic mesh implantation may reduce incisional

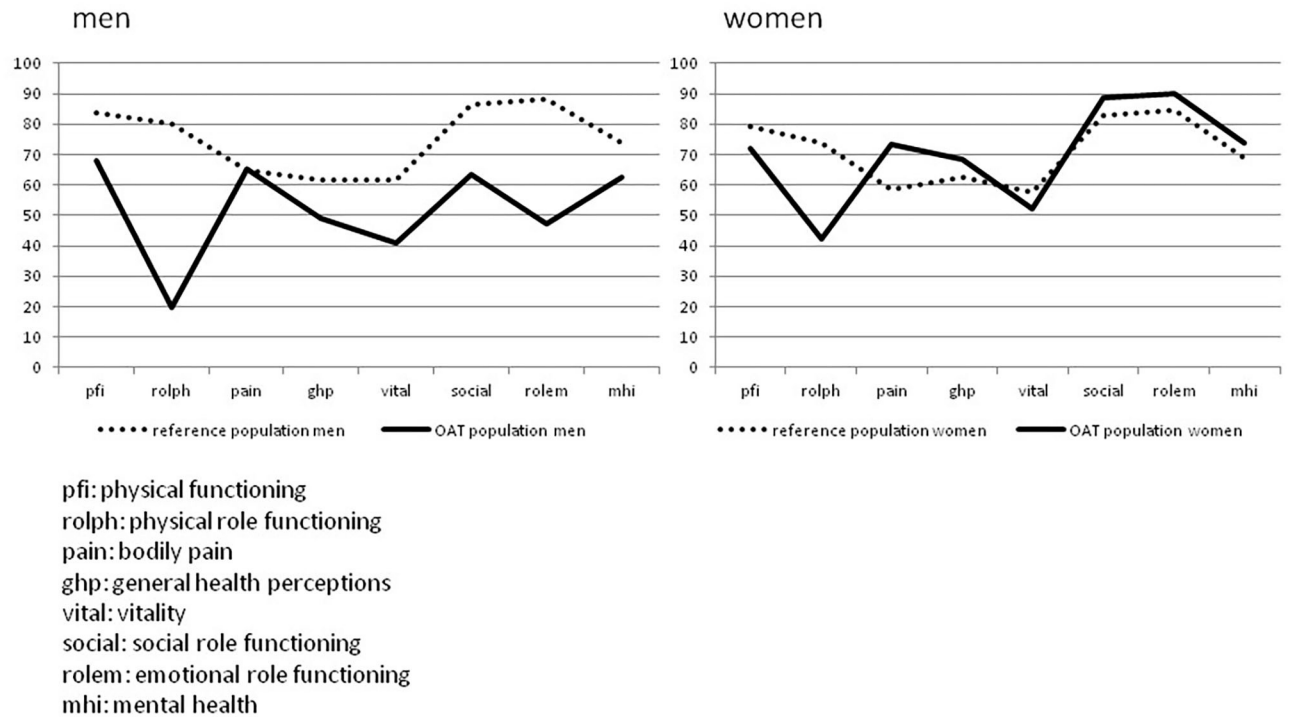


FIGURE 4 | SF-36 results of open abdomen treatment (OAT) cohort ($n = 40$), visual comparison to general population. Shown are the SF-36 QoL results of men ($n = 30$) and women ($n = 10$) after OAT compared to the general population (21).

TABLE 2 | Analysis of clinical findings impacting on SF-36.

Sectors SF-36	Sex	Hernia	PC	EAF	VSS
	Male vs. Female	**Yes vs. No**	**Yes vs. No**	**Yes vs. No**	**VSS Low < 3 vs. High > 8**
Vitality	ns	ns	ns	ns	ns
Physical functioning	ns	ns	ns	ns	ns
Bodily pain	ns	ns	ns	ns	ns
General health perceptions	female*	ns	ns	no EAF*	ns
Physical role functioning	ns	ns	ns	ns	ns
Emotional role functioning	female*	ns	ns	no EAF*	ns
Social role functioning	female*	ns	ns	no EAF**	ns
Mental health	ns	ns	ns	no EAF**	ns
Overall physical	ns	ns	ns	ns	ns
Overall mental	female*	ns	ns	no EAF*	ns

*Table shows the comparison of mean SF-36 sector results and the following factors were compared: male vs. female sex, presence or absence of a clinically evident hernia, primary fascial closure, development of an entero-atmospheric fistula, and a low VSS score (<3) vs. a high one (>8). Non-statistically significant differences are stated as "ns." Where a statistically significant difference was detected, it is marked accordingly, i.e., EAF formation impacts significally on the SF-36 sector "general health perceptions" [two-sided t-test, *$p < 0.05$ and **$p < 0.01$, the original mean value data is given in Supplements (**Supplementary Table 2**)].*

hernia incidence (24). Furthermore, recent studies showed a significant reduction in incisional hernia incidence after "onlay" mesh reinforcement compared with suture only and superior to "sublay" mesh (5). As such, onlay mesh reinforcement may have the potential to improve the standard treatment for high-risk patients including OAT.

OAT may result in excessive scar tissue which may affect QoL in the long term. This is especially true for patients after OAT where PC of the fascia (and/or skin) cannot be achieved and who may be discharged with a granulating laparostomy. Excessive scarring after burn injuries is known be associated with reduced QoL and is related to disruption of daily activities, altered sleep patterns, anxiety, depression, and issues of social acceptance (15). Furthermore, hypertrophic scars might be itchy and painful and cause serious functional and cosmetic disability (25). We assessed scar formation in our follow-up cohort for the first time after

OAT in a standardized manner by utilizing the Vancouver Scar Scale. Even though we found a high percentage of VSS > 3 scar formation (in 30 patients, 75%), we did not find a correlation of the VSS score (low VSS *vs.* high VSS) with QoL. This could be related to the fact that no patient experienced severe scar itching and only 10% experienced severe scar pain, which are factors known to impair QoL after burn injuries and have since been added to the VSS score (26). Although previous studies did show a correlation between VSS and pain as well as itching, we could not detect such correlation. However, pain and itching correlated significantly among themselves, with Pearson's $P = 0.533$. While the subject of scar tissue development after OAT is much less well-understood as scarring after burn damage, further research in this area may provide ways of minimizing scar-related problems, ensuring better aesthetic results as well as less scar tissue complications in these patients. One finding that the authors noticed was a colonization of multi-resistant bacterial strains in unstable scars of some patients (especially after granulating laparostomy; see **Figure 1**, bottom picture, and **Supplementary Figure 3**), which have to be addressed before secondary reconstruction is attempted. Concerning quality of life, we found that the sector "physical role functioning" was most impaired after OAT—especially in men—compared to the general population. This is not a surprising finding in our cohort because men, in particular, may find persisting disabilities after OAT a hindrance to former job-related physical labor or activities in daily life. The inherent sex difference in QoL, when assessed with SF-36, was also seen in our data with better QoL reported by 10 females of the cohort. The biggest negative impact on QoL was seen in patients with EAF formation; here the sectors "general health perception," "emotional and social role functioning," and "mental health" as well as the overall mental status score were negatively affected. We conclude that the avoidance of EAF formation, best achieved by the consequent use of visceral protection and early midline closure, is paramount not only for survival and morbidity but also to preserve QoL in OAT patients. Naturally, our study has several limitations: the small sample size and single-center setup limit generalizability in some aspects. It could be argued that a selection bias may have distorted the clinical follow-up because some patients were reached but did not want to participate in the clinical follow-up study. According to the patients' statements, several reasons were mentioned: some patients avoided hospitalization due to the previous traumatic experience, some argued that the distance to our center was too far, and several patients did not want a follow-up due to lack of complaints. It is therefore conceivable that especially the last group manages well with a stable abdomen and that the rate of patients with planned ventral hernia may be distortedly high in our follow-up cohort. The small sample size may have impacted on the SF-36 analysis especially in the subgroups and hindered the detection of all potential factors that logically would influence QoL (such as PC of the fascia). For the same reason, multivariate analysis was not feasible in this cohort, which would be interesting in a larger, multicentric database[1].

To summarize, we show that an early-era approach to OAT before the implementation of a structured concept such as the "Koblenz algorithm" with (a) fascial traction, (b) visceral protection, and (c) negative pressure therapy resulted in relevant mortality and morbidity. Our follow-up strategy identified a significant proportion of patients that would qualify for a secondary reconstructive procedure, but only about 2/3 of patients discharged with a planned ventral hernia wanted reconstructive surgery and were deemed fit. Of all clinical factors tested, only sex and EAF formation impacted on quality of life, which was generally lower in OAT patients compared to the general population concerning bodily role functioning. Hernia rates after PC were still high with over 50%, and prophylactic measures such as a prophylactic mesh implantation upon fascial closure should be discussed in the future analogous to other major and emergency abdominal procedures.

DATA AVAILABILITY STATEMENT

The original contributions generated for this study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethikkomitee der Medizinischen Fakultät Bonn. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

MW and SM contributed to the conception and design of the study. AT and AJ performed most of the data collection. MW and AT drafted the manuscript. All the authors contributed to data collection and manuscript revision and approved the manuscript.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fsurg.2021.590245/full#supplementary-material

[1] Available online at: https://www.eurahs.eu/.

REFERENCES

1. Miller PR, Meredith JW, Johnson JC, Chang MC. Prospective evaluation of vacuum-assisted fascial closure after open abdomen: planned ventral hernia rate is substantially reduced. *Ann Surg.* (2004) 239:608–14. doi: 10.1097/01.sla.0000124291.09032.bf
2. Sugrue M. Abdominal compartment syndrome and the open abdomen: any unresolved issues? *Curr Opin Crit Care.* (2017) 23:73–8. doi: 10.1097/MCC.0000000000000371

3. Atema JJ, Gans SL, Boermeester MA. Systematic review and meta-analysis of the open abdomen and temporary abdominal closure techniques in non-trauma patients. *World J Surg*. (2015) 39:912–25. doi: 10.1007/s00268-014-2883-6
4. Willms AG, Schaaf S, Zimmermann N, Schwab R, Güsgen C, Vilz TO, et al. The significance of visceral protection in preventing enteroatmospheric fistulae during open abdomen treatment in patients with secondary peritonitis: a propensity score-matched case-control analysis [published online ahead of print, 2019 Jul 15]. *Ann Surg*. (2019). doi: 10.1097/SLA.0000000000003440. [Epub ahead of print].
5. Jairam AP, Timmermans L, Eker HH, Pierik REGJM, van Klaveren D, Steyerberg EW, et al. Prevention of incisional hernia with prophylactic onlay and sublay mesh reinforcement versus primary suture only in midline laparotomies (PRIMA): 2-year follow-up of a multicentre, double-blind, randomised controlled trial. *Lancet*. (2017) 390:567–76. doi: 10.1016/S0140-6736(17)31332-6
6. Berrevoet F. Prevention of incisional hernias after open abdomen treatment. *Front Surg*. (2018) 5:11. doi: 10.3389/fsurg.2018.00011
7. Antoniou GA, Georgiadis GS, Antoniou SA, Granderath FA, Giannoukas AD, Lazarides MK. Abdominal aortic aneurysm and abdominal wall hernia as manifestations of a connective tissue disorder. *J Vasc Surg*. (2011) 54:1175–81. doi: 10.1016/j.jvs.2011.02.065
8. Coccolini F, Roberts D, Ansaloni L, Ivatury R, Gamberini E, Kluger Y, et al. The open abdomen in trauma and non-trauma patients: WSES guidelines. *World J Emerg Surg*. (2018) 13:7. doi: 10.1186/s13017-018-0167-4
9. Regner JL, Kobayashi L, Coimbra R. Surgical strategies for management of the open abdomen. *World J Surg*. (2012) 36:497–510. doi: 10.1007/s00268-011-1203-7
10. Rios-Diaz AJ, Cunning JR, Broach RB, Metcalfe D, Elfanagely O, Serletti JM, et al. One-year health care utilization and recurrence after incisional hernia repair in the United States: a population-based study using the nationwide readmission database. *J Surg Res*. (2020) 255:267–76. doi: 10.1016/j.jss.2020.03.070
11. van Ramshorst GH, Eker HH, Hop WCJ, Jeekel J, Lange JF. Impact of incisional hernia on health-related quality of life and body image: a prospective cohort study. *Am J Surg*. (2012) 204:144–50. doi: 10.1016/j.amjsurg.2012.01.012
12. Coccolini F, Ceresoli M, Kluger Y, Kirkpatrick A, Montori G, Salvetti F, et al. Open abdomen and entero-atmospheric fistulae: an interim analysis from the International Register of Open Abdomen (IROA). *Injury*. (2019) 50:160–6. doi: 10.1016/j.injury.2018.09.040
13. Doble JA, Pauli EM. Management of open abdomen. In: Docimo S, Pauli EM, editors. *Clinical Algorithms in General Surgery*. Cham: Springer International Publishing (2019). p. 809–11. doi: 10.1007/978-3-319-98497-1_195
14. Huang Q, Li J, Lau W. Techniques for abdominal wall closure after damage control laparotomy: from temporary abdominal closure to early/delayed fascial closure—a review. *Gastroenterol Res Pract*. (2016) 2016:1–15. doi: 10.1155/2016/2073260
15. Finlay V, Burrows S, Kendell R, Berghuber A, Chong V, Tan J, et al. Modified Vancouver Scar Scale score is linked with quality of life after burn. *Burns*. (2017) 43:741–6. doi: 10.1016/j.burns.2016.11.007
16. von Websky M, Jedig A, Willms A, Jafari A, Matthaei H, Kalff J, et al. Prognosefaktoren der offenen Abdominalbehandlung in der Viszeralchirurgie. *Zentralblatt Für Chir - Z Für Allg Visz Thorax-Gefäßchirurgie*. (2017) 142:259–66. doi: 10.1055/s-0042-119303
17. Willms A, Gusgen C, Schaaf S, Bieler D, von WM, Schwab R. Management of the open abdomen using vacuum-assisted wound closure and mesh-mediated fascial traction. *Langenbecks ArchSurg*. (2015) 400:91–9. doi: 10.1007/s00423-014-1240-4
18. Baryza MJ, Baryza GA. The Vancouver scar scale: an administration tool and its interrater reliability. *J Burn Care Rehabil*. (1995) 16:535–8. doi: 10.1097/00004630-199509000-00013
19. Doyle DJ, Goyal A, Bansal P, Garmon EH. American Society of Anesthesiologists Classification (ASA Class) [Updated 2020 Apr 7]. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing (2020). Available online at: https://www.ncbi.nlm.nih.gov/books/NBK441940/ (accessed March 09, 2021).
20. 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. doi: 10.1097/00006534-199009000-00023
21. Ellert U, Bellach BM. Der SF-36 im Bundes-Gesundheitssurvy-Beschreibung einer aktuellen Normstichprobe. *Gesundheitswesen*. (1999) 61:184–90.
22. Willms A, Muysoms F, Güsgen C, Schwab R, Lock J, Schaaf S, et al. The open abdomen route by EuraHS: introduction of the data set and initial results of procedures and procedure-related complications. *Hernia*. (2017) 21:279–89. doi: 10.1007/s10029-017-1572-4
23. Ayvazoglu Soy EH, Kirnap M, Yildirim S, Moray G, Haberal M. Incisional hernia after liver transplant. *Exp Clin Transplant*. (2017) 15:185–9. doi: 10.6002/ect.mesot2016.P65
24. Muysoms FE, Detry O, Vierendeels T, Huyghe M, Miserez M, Ruppert M, et al. Prevention of incisional hernias by prophylactic mesh-augmented reinforcement of midline laparotomies for abdominal aortic aneurysm treatment: a randomized controlled trial. *Ann Surg*. (2016) 263:638–45. doi: 10.1097/SLA.0000000000001369
25. Mauck MC, Shupp JW, Williams F, Villard MA, Jones SW, Hwang J, et al. Hypertrophic scar severity at autograft sites is associated with increased pain and itch after major thermal burn injury. *J Burn Care Res*. (2018) 39:536–44. doi: 10.1093/jbcr/irx012
26. Choi Y-H, Kim K-M, Kim H-O, Jang Y-C, Kwak I-S. Clinical and histological correlation in post-burn hypertrophic scar for pain and itching sensation. *Ann Dermatol*. (2013) 25:428. doi: 10.5021/ad.2013.25.4.428

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Lessons Learned in 11 Years of Experience With Open Abdomen Treatment With Negative-Pressure Therapy for Various Abdominal Emergencies

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Introduction: Open abdomen (OA) treatment with negative-pressure therapy (NPT) was initiated for perforated diverticulitis and subsequently extended to other abdominal emergencies. The aim of this retrospective study was to analyze the indications, procedures, duration of NPT, and the outcomes of all our patients.

Methods: All consecutive patients treated with intra-abdominal NPT from January 1, 2008 to December 31, 2018 were retrospectively analyzed.

Results: A total of 438 patients (44% females) with a median (range) age of 66 (12–94) years, BMI of 25 (14–48) kg/m^2, and ASA class I, II, III, and IV scores of 36 (13%), 239 (55%), 95 (22%), and 3(1%), respectively, were treated with NPT. The indication for surgery was primary bowel perforation in 163 (37%), mesenteric ischemia in 53 (12%), anastomotic leakage in 53 (12%), ileus in 53 (12%), postoperative bowel perforation/leakage in 32 (7%), abdominal compartment in 15 (3%), pancreatic fistula in 13 (3%), gastric perforation in 13 (3%), secondary peritonitis in 11 (3%), burst abdomen in nine (2%), biliary leakage in eight (2%), and other in 15 (3%) patients. A damage control operation without reconstruction in the initial procedure was performed in 164 (37%) patients. The duration of hospital and intensive care stay were, median (range), 28 (0–278) and 4 (0–214) days. The median (range) duration of operation was 109 (22–433) min and of NPT was 3(0–33) days. A trend to shorter duration of NPT was observed over time and in the colonic perforation group. The mean operating time was shorter when only blind ends were left *in situ*, namely 110 *vs*. 133 min ($p = 0.006$). The mortality rates were 14% at 30 days, 21% at 90 days, and 31% at 1 year. An entero-atmospheric fistula was observed in five (1%) cases, most recently in 2014. Direct fascia closure was possible in 417 (95%) patients at the end of NPT, but least often (67%, $p = 0.00$) in patients with burst abdomen. During follow-up, hernia repair was observed in 52 (24%) of the surviving patients.

Conclusion: Open abdomen treatment with NPT is a promising concept for various abdominal emergencies, especially when treated outside normal working hours. A low

rate of entero-atmospheric fistula formation and a high rate of direct fascia closure were achieved with dynamic approximation of the fascia edges. The authors recommend an early-in and early-out strategy as the prolongation of NPT by more than 1 week ends up in a frozen abdomen and does not improve abdominal sepsis.

Keywords: negative-pressure therapy, open abdomen, damage control surgery, abdominal sepsis, second look exploration

INTRODUCTION

Open abdomen (OA) treatment seems to be effective in treating critically ill patients with abdominal sepsis. However, the indication remains controversial as it is a resource-consuming and a non-anatomic situation with the potential of severe adverse effects (1–3). Temporary abdominal closure (TAC) with negative-pressure therapy (NPT) allows not only the patient to be resuscitated at the intensive care unit (ICU) but also the decision on the definitive surgical procedure to be postponed to a second look in an elective situation with an experienced colorectal surgeon and the aim of avoiding creation of a temporary stoma (4–6).

We initially adopted damage control surgery (DCS) for the clinical situation of perforated diverticulitis with generalized peritonitis, where we were able to report a high rate of restoration of bowel continuity in prospective studies and ultimately in a small randomized controlled trial (7–9). With the aid of dynamic sutures, we demonstrated a high rate of direct fascia closure and a low rate of hernia development (10). Simultaneously, we extended the indication for DCS with NPT to other abdominal emergencies, such as mesenteric ischemia, to allow the decision on the extent of bowel resection to be postponed to a second-look operation or to avoid stoma creation in patients with obstructed colon. After open decompression and regeneration of the overstretched colon, safe reconstruction is facilitated in a second-look operation. Moreover, in all situations outside normal working hours, and especially when working hours are subject to restrictions, the surgeon on duty can postpone the decision of performing an anastomosis DCS whenever he has doubts.

The aim of this retrospective analysis was to analyze the indications, procedures, and the outcomes of all consecutive patients treated with OA and NPT at our university hospital in the last 11 years.

PATIENTS AND METHODS

Clinical data from 438 consecutive patients treated with open abdomen at our department from January 1, 2008 to December 31, 2018 were documented in an Excel database, where data from already published prospective studies were integrated. OA treatment was indicated by the performing surgeon on duty in cases outside study protocols. Negative pressure was applied with VAC^{R} or ABThera^{TM} therapy (KCI, San Antonio, TX). To avoid fascia retraction and enhance direct fascia closure, dynamic sutures with vessel loops or approximation of the fascia edges by negative pressure was applied as published. To prevent entero-atmospheric fistula formation, direct contact between the intra-abdominal sheet of the NPT system and the intestinal sutures was avoided by covering the sides with omental fat, whenever possible. The technique to be administered for closure of the abdominal wall at the end of the OA treatment was determined by the surgeon in charge and recorded as continuous or interrupted using absorbable or non-absorbable suture material.

Statistical analysis of the data was conducted with SPSS 26.0 (Chicago, IL). Analysis was performed with the chi-square test for categorical variables or Fisher's exact test for nominal variables. Overall survival rate was calculated with a Kaplan–Meier estimate.

RESULTS

From January 1, 2008 to December 31, 2018, 438 patients (194 females) with a median (range) age of 66 (12–94) years, a body mass index (BMI) of 25 (14–48) kg/m^2, and American Society of Anesthesiologists (ASA) class I–IV scores of 36 (13%), 239 (55%), 95(22%), and 3 (1%), respectively, were treated with NPT at our department.

The indication for emergency surgery is shown in detail in **Table 1**. Besides the main indication, primary bowel perforation with 163 (37%) and anastomotic leakage, intestinal ischemia, and ileus with 53 (12%) were the most frequent indications for the DCS procedure. Eighty-three (19%) patients suffered from a malignant disease and 21 (5%) patients were immunocompromised for solid organ transplantation. Besides, the mean ± SD operating time was 120 ± 66 min. Definitive surgery was performed in 272 (62%) and a damage control operation without reconstruction in 164 (37%) patients. In the group of patients with colonic perforation ($n = 199$), the surgical time was shorter in the damage control group, with a median (mean) time of 110 (118) min *vs.* 133 (145) min in the group where reconstruction or stoma creation was performed during the emergency surgery ($p = 0.006$). No significant difference was observed in the median (mean) durations of NPT between these two groups, namely 2 (4.3) *vs.* 3 (4.9) days.

Outcome parameters are depicted in **Table 2**. The median (range) hospital stay was 28 (0–278) days, and the median (range) duration of NPT was 3 (0–27) days (see **Figure 1**). Admission to the ICU was not necessary in 184 patients, and the median

Abbreviations: DCS, damage control surgery; OA, open abdomen; TAC, temporary abdominal closure; NPT, negative-pressure therapy; HP, Hartmann's procedure; ICU, intensive care unit; n, number; PA, primary anastomosis without ileostomy.

TABLE 1 | Clinical Data.

Indication for surgery	*n*	%	Female n (%)	Age Median(range)	ASA Score Mean	BMI Median(range)
Primary bowel perforation	163	37%	71 (44%)	67 (12–92)	3.0	25 (14–40)
Anastomotic leakage	53	12%	20 (38%)	64 (36–82)	3.0	24 (14–43)
Intestinal ischemia	53	12%	21 (40%)	74 (25–95)	3.3	25 (15–37)
ILEUS	53	12%	28 (53%)	67 (21–90)	2.9	25 (14–48)
Postoperative bowel perforation	32	7%	15 (47)%	66 (26–83)	3.2	24 (15–45)
Abdominal compartment	15	3%	7 (47%)	76 (37–88)	3.4	23 (17–33)
Gastric perforation	13	3%	7 (54%)	55 (33–87)	3.3	27 (18–38)
Pancreatic fistula	13	3%	4 (31%)	60 (44–78)	3.4	26 (15–29)
Secondary peritonitis	11	3%	6 (55%9)	58 (38–77)	3.2	26 (20–33)
Burst abdomen	9	2%	7 (78%)	73 (64–80)	3.1	33 (25–40)
Biliary leakage	8	2%	2 (25%)	56 (20–84)	3.3	25 (18–44)
Other	15	3%	6 (40%)	62 (42–90)	3.3	27 (22–33)
Total	438	100%	194 (44%)	66 (12–95)	3%	25 (14–48)

BMI, body mass index.

TABLE 2 | Outcome.

	Mortality rate (%)		Survival rate (%)		Hospital stay	ICU stay	NPT	Rate (%)	
Indication for surgery	**30-day**	**90-day**	**1 year**	**5 year**	**Median(range) days** $n = 254$			**Fascia closure**	**DCS**
Primary bowel perforation	11%	17%	76%	66%	24 (1–257)	3 (1–61)	3 (1–28)	98%	64%
Anastomotic leakage	17%	25%	69%	60%	34.5 (3–98)	9 (1–35)	4 (1–33)	91%	28%
Intestinal ischemia	19%	26%	58%	52%	20.5 (2–128)	4 (1–51)	2 (1–21)	100%	47%
ILEUS	15%	19%	64%	54%	22 (0–176)	2.5 (1–144)	3 (2–21)	98%	21%
Postoperative bowel perforation	9%	22%	67%	56%	43 (4–278)	10 (1–170)	4.5 (1–17)	97%	9%
Abdominal compartment	20%	20%	55%	m	28 (4–56)	19 (6–34)	5 (2–18)	87%	0%
Gastric perforation	0%	15%	80%	80%	37 (13–110)	29 (16–69)	6 (1–33)	92%	8%
Pancreatic fistula	15%	23%	48%	48%	56.5 (34–192)	9 (3–61)	9 (1–21)	92%	0%
Secondary peritonitis	18%	36%	47%	47%	39 (14–112)	5.5 (1–34)	3 (1–20)	100%	0%
Burst abdomen	11%	22%	76%	31%	38 (12–72)	1 (1–214)	7 (2–24)	67%	0%
Biliary leakage	25%	25%	71%	48%	58.5 (12–140)	8 (2–64)	5 (2–27)	75%	0%
Other	13%	20%	79%	65%	23 (15–73)	5 (1–12)	2 (1–9)	93%	27%
Total	14%	21%	69%	59%	28 (0–278)	4 (1–214)	3 (1–33)	95%	38%

ICU, intensive care unit; NPT, negative pressure therapy; DCS, Damage control surgery; m, missing.

(range) duration of ICU stay for patients admitted to the ICU ($n = 254$) was 4 (1–214) days. The mean duration of NPT was lowest in the group with intestinal ischemia, namely 3.1 days, and highest in the group with pancreatic fistula, namely 10.1 days, followed by burst abdomen (9.8 days) and biliary leakage (9.6 days, $p = 0.027$). No significant difference in ICU or hospital stay was observed between these groups.

The mortality rates were 14% at 30 days, 21% at 90 days, 31% at 1 year, 37% at 3 years, and 41% at 5 years. The 90-day mortality rate was highest in the group with secondary peritonitis (36%), followed by intestinal ischemia (26%), and lowest in the group with gastric perforation (15%) and primary bowel perforation (17%, n.s.) (see **Figures 2**, **3**).

Complete closure of the fascia at the end of NPT was possible in 417 (95%) patients, nine (2%) patients died before removal of NPT, in four (1%) patients a Permacol©, in two (0.5%) patients a Vicryl© mesh was used to close the abdominal wall, and in four (1%) patients complete closure of the abdominal wall was not achieved. The lowest rate of direct fascia closure was observed in the group with burst abdomen (67%), followed by patients with biliary leaks (75%, $p = 0.00$). The mean (confidence interval, CI) of BMI was lowest in the patients who died before the end of NPT, with 21.9 (21.0–24.9) *vs.* 25.2 (25.0–25.5) in the group of complete fascia closure and 31.6 (29.1–34.1, $p = 0.00$) in the group of partial or mesh-mediated fascia closure.

Entero-atmospheric fistula formation as a complication of NPT was observed in five (1%) patients. Ventral hernia repair was performed in 85 patients (19% of all and 24% of all surviving patients). Body mass index was significantly higher in patients with a ventral hernia, namely a mean (95% CI) of 28.1 (27.2–28.9) *vs.* 25.0 (24.7–25.3 kg/m^2, $p = 0.00$).

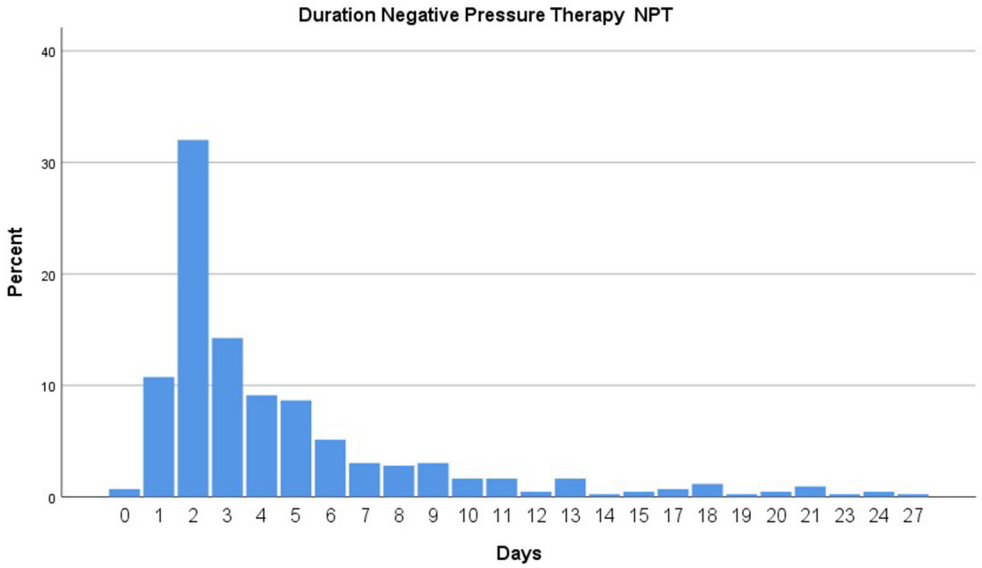

FIGURE 1 | Duration of negative pressure system in place.

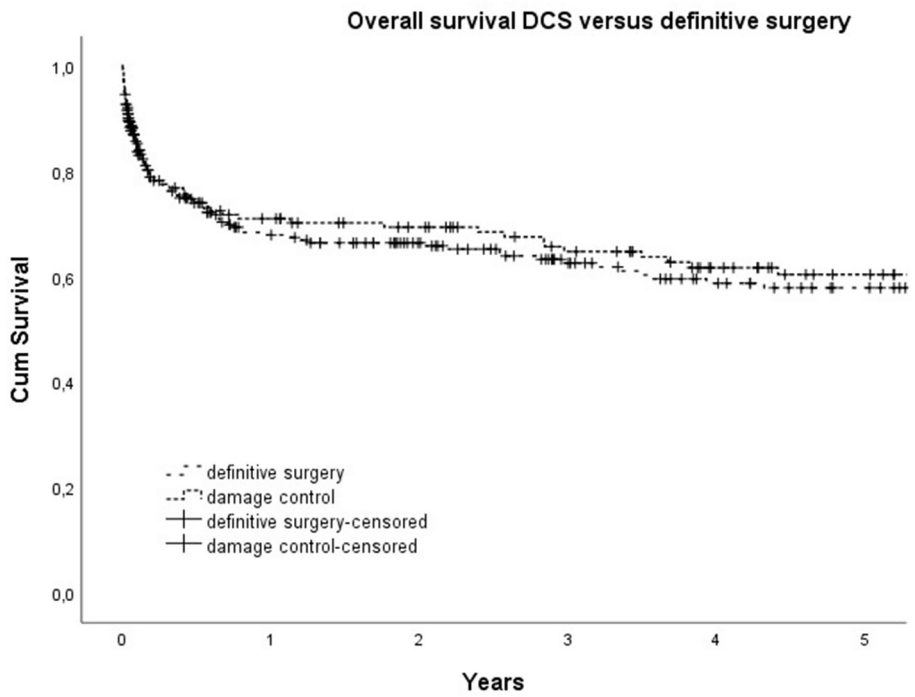

FIGURE 2 | Overall survival for Damage control surgery (DCS) versus definitive surgery.

DISCUSSION

Damage control surgery (DCS), established in the treatment of injured patients by trauma surgeons, has been adopted by general surgeons for various abdominal emergencies (1–4). DCS meets all requirements for an emergency operation: short operating time, immediate clearance of the septic focus, and improving the patient for definitive reconstruction in a second operation at the ICU, if necessary (11). Moreover, this limited procedure can be performed by a general surgeon not specialized in colorectal surgery, a situation that is increasingly encountered especially when working hours are subject to restrictions and

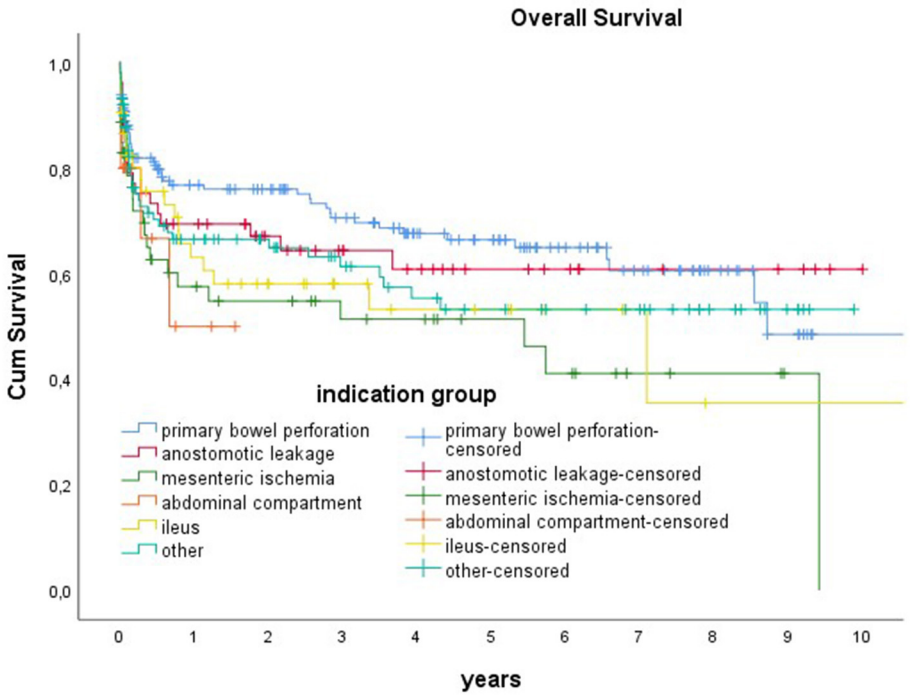

FIGURE 3 | Overall survival for different indications.

there is a reduced availability of specialists. The estimated risk of overtreatment appears to be tolerably low because the use of modern NPT devices means patients can be extubated and treated at the surgical ward until definitive surgery, if the patient improves rapidly after DCS (9, 11, 12).

In the setting of perforated diverticulitis with generalized peritonitis, the concept of DCS is already established (1, 9, 13). We adopted the concept also for patients with anastomotic leakage to allow reanastomosation in the second-look procedure. Of the patients treated with NPT, 53 (12%) had intestinal ischemia, where the aim was to reduce the extent of bowel resection after patient recovery or after recuperation of the intestine following thrombectomy. Another 53 (12%) patients were operated for complicated ileus. After open decompression or reposition of the incarcerated intestine, recovery of the overstretched intestinal wall allowed safe anastomosis in the second-look operation. Moreover, in cases of acute left-sided colonic obstruction due to colon cancer, DCS offers an alternative to diversion or stenting. Under elective conditions and with the aid of a colorectal surgeon, the quality of oncologic resection is enhanced.

Before the introduction of modern NPT devices, a formidable complication, namely the formation of an entero-atmospheric fistula, demanded that a strict indication be observed for OA (2). Recent studies of OA treatment with NPT report rates of entero-atmospheric fistula formation from 5 to 14%, with the risk factors of duration of OA treatment, ischemia, and cancer (14–17). In our cohort of 438 patients, where we strictly avoided direct contact between the plastic sheet and any sewn serosa lesion or an intestinal anastomosis, we demonstrate a low rate of fistula development of 1%. A further problem entailed with OA treatment, namely retraction of the fascia resulting in a ventral hernia, can be resolved with various techniques, as published in cohort studies (10, 17, 18). The technique practiced in our department, dynamic approximation of the fascia edges with vessel loops or approximation of the fascia edges with the aid of negative pressure from the beginning of NPT, resulted in a high 95% rate of direct fascia closure at the end of NPT, comparable to the data of Acosta et al. (18). The lowest rate of fascia closure, namely 67%, was achieved in the patients with burst abdomen due to septic complications or when biliary or pancreatic fistulas were observed. The need for hernia repair in 24% of the surviving patients in our cohort coincides with the published data. BMI could be identified as a risk factor (19–21).

When used as DCS, NPT was terminated in 50% of our patients after 2 days. NPT duration was longest in the group of patients with persistent pancreatic or biliary leakage and in those patients with burst abdomen due to septic complications, where conditioning of the fascia edges was awaited before the abdominal wall was definitively closed. NPT duration in abdominal sepsis is limited by the evolution of a frozen abdomen, limiting the cleansing effect of the negative pressure (22, 23). For this reason, a trend toward an earlier termination of NPT during the observation period was noted. The strategy undertaken at our department is to keep the threshold low for the indication of DCS and NPT, especially outside normal working hours, but

to terminate as early as possible. Decompression laparotomy and NPT in cases of abdominal compartment gave a rare indication in 3% of our patients, while the mean duration was 6 days and fascia closure was achieved in 87% of the patients.

Nine patients died before the end of NPT. At 22, BMI was significantly lower in these patients, indicating that they had malignant or severe chronic disease. A higher BMI was a significant risk factor for complete fascia closure in our cohort of patients. The mortality rates observed in our patients appear to be comparatively low in relation to the literature (24, 25). The effects of OA and NPT on mortality and the risk of overtreatment are still up for discussion, and a prospectively randomized study was announced (12, 26, 27).

In conclusion, OA with NPT is a promising option in various abdominal emergencies, especially when used in a damage control concept and outside normal working hours, where typical and feared complications such as entero-atmospheric fistulas or fascia retraction can be successfully avoided. To demonstrate a supposed positive effect on mortality, a randomized controlled study would be helpful.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

RK-R: design, analysis, and writing. EG: data accuisition, analysis, and writing. DR: data acquisition and analysis. JG: data acquisition. DÖ: design and data validation. AL, PG, and AP: execution and correction. All authors contributed to the article and approved the submitted version.

REFERENCES

1. Cirocchi R, Popivanov G, Konaktchieva M, Chipeva S, Tellan G, Mingoli A, et al. The role of damage control surgery in the treatment of perforated colonic diverticulitis: a systematic review and meta-analysis. *Int J Colorectal Dis.* (2020) 36:867–79. doi: 10.1007/s00384-020-03784-8
2. Regner JL, Kobayashi L, Coimbra R. Surgical strategies for management of the open abdomen. *World J Surg.* (2012) 36:497–510. doi: 10.1007/s00268-011-1203-7
3. 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. doi: 10.1097/00005373-200002000-00001
4. Weber DG, Bendinelli C, Balogh ZJ. Damage control surgery for abdominal emergencies. *Br J Surg.* (2014) 101:e109–18. doi: 10.1002/bjs.9360
5. Perathoner A, Klaus A, Muhlmann G, Oberwalder M, Margreiter R, Kafka-Ritsch R. Damage control with abdominal vacuum therapy (VAC) to manage perforated diverticulitis with advanced generalized peritonitis–a proof of concept. *Int J Colorectal Dis.* (2010) 25:767–74. doi: 10.1007/s00384-010-0887-8
6. Hecker A, Reichert M, Reuß CJ, Schmoch T, Riedel JG, Schneck E, et al. Intra-abdominal sepsis: new definitions and current clinical standards Langenbeck's Archives of Surgery. *Langenbecks Arch Surg.* (2019) 404:257–71. doi: 10.1007/s00423-019-01752-7
7. Kafka-Ritsch R, Birkfellner F, Perathoner A, Raab H, Nehoda H, Pratschke J, et al. Damage control surgery with abdominal vacuum and delayed bowel reconstruction in patients with perforated diverticulitis Hinchey III/IV. *J Gastrointest Surg.* (2012) 16:1915–22. doi: 10.1007/s11605-012-1977-4
8. Gasser E, Alexander P, Reich-Weinberger S, Buchner S, Kogler P, Zitt M, et al. Damage control surgery for perforated diverticulitis: a two center experience with two different abdominal negative pressure therapy devices. *Acta Chir Belg.* (2019) 119:370–5. doi: 10.1080/00015458.2018.1534397
9. Kafka-Ritsch R, Zitt M, Perathoner A, Gasser E, Kaufman C, Czipin S, et al. Prospectively randomized controlled trial on damage control surgery for perforated diverticulitis with generalized peritonitis. *World J Surg.* (2020) 44:4098–105. doi: 10.1007/s00268-020-05762-1
10. Kafka-Ritsch R, Zitt M, Schorn N, Stroemmer S, Schneeberger S, Pratschke J, 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. doi: 10.1007/s00268-012-1586-0
11. Tartaglia D, Costa G, Camillò A, Castriconi M, Andreano M, Lanza M, et al. Damage control surgery for perforated diverticulitis with diffuse peritonitis: saves lives and reduces ostomy. *World J Emerg Surg.* (2019) 14:19. doi: 10.1186/s13017-019-0238-1
12. Zizzo M, Ugoletti L, Lococo F, Pedrazzoli C, Manenti A. Damage control surgery in patients with generalized peritonitis secondary to perforated diverticulitis: the risk of overtreatment. *Tech Coloproctol.* (2018) 22:473–4. doi: 10.1007/s10151-018-1810-5
13. Sohn M, Iesalnieks I, Agha A, Steiner P, Hochrein A, Pratschke J, et al. Perforated diverticulitis with generalized peritonitis: low stoma rate using a "damage control strategy". *World J Surg.* (2018) 42:3189–95. doi: 10.1007/s00268-018-4585-y
14. Atema JJ, Gans SL, Boermeester MA. Systematic review and meta-analysis of the open abdomen and temporary abdominal closure techniques in non-trauma patients. *World J Surg.* (2015) 39:912–25. doi: 10.1007/s00268-014-2883-6
15. Coccolini F, Ceresoli M, Kluger Y, Kirkpatrick A, Montori G, Salvetti F, et al. Open abdomen and entero-atmospheric fistulae: An interim analysis from the International Register of Open Abdomen (IROA). Injury. (2019) 50:160–6. doi: 10.1016/j.injury.2018.09.040
16. Giudicelli G, Rossetti A, Scarpa C, Buchs NC, Hompes R, Guy RJ, et al. Prognostic factors for enteroatmospheric fistula in open abdomen treated with negative pressure wound therapy: a multicentre experience. *J Gastrointest Surg.* (2017) 21:1328–34. doi: 10.1007/s11605-017-3453-7
17. Fortelny RH, Hofmann A, Gruber-Blum S, Petter-Puchner AH, Glaser KS. Delayed closure of open abdomen in septic patients is facilitated by combined negative pressure wound therapy and dynamic fascial suture. *Surg Endosc.* (2014) 28:735–40. doi: 10.1007/s00464-013-3251-6
18. Acosta S, Seternes A, Venermo M, Vikatmaa L, Sörelius K, Wanhainen A, et al. Open abdomen therapy with vacuum and mesh mediated fascial traction after aortic repair: an international multicentre study. *Eur J Vasc Endovasc Surg.* (2017) 54:697–705. doi: 10.1016/j.ejvs.2017.09.002
19. Hofmann AT, Gruber-Blum S, Lechner M, Petter-Puchner A, Glaser K, Fortelny R. Delayed closure of open abdomen in septic patients treated with negative pressure wound therapy and dynamic fascial suture: the long-term follow-up study. *Surg Endosc.* (2017) 31:4717–24. doi: 10.1007/s00464-017-5547-4
20. Petersson P, Petersson U. Dynamic fascial closure with vacuum-assisted wound closure and mesh-mediated fascial traction (VAWCM) treatment of the open abdomen—An updated systematic review. *Front Surg.* (2020) 7:577104. doi: 10.3389/fsurg.2020.577104

21. Berrevoet F. Prevention of incisional hernias after open abdomen treatment. *Front Surg.* (2018) 5:11. doi: 10.3389/fsurg.2018.00011
22. Sugrue M. Abdominal compartment syndrome and the open abdomen: any unresolved issues? *Curr Opin Crit Care.* (2017) 23:73–8. doi: 10.1097/MCC.0000000000000371
23. Leppäniemi A, Kimball EJ, De Laet I, Malbrain ML, Balogh ZJ, De Waele JJ. Management of abdominal sepsis–a paradigm shift? *Anaesthesiol Intensive Ther.* (2015) 47:400–8. doi: 10.5603/AIT.a2015.0026
24. Rausei S, Pappalardo V, Ruspi L, Colella A, Giudici S, Ardita V, et al. Versus delayed source control in open abdomen management for severe intra-abdominal infections: a retrospective analysis on 111 cases. *World J Surg.* (2018) 42:707–12. doi: 10.1007/s00268-017-4233-y
25. Lambertz A, Mihatsch C, Röth A, Kalverkamp S, Eickhoff R, Neumann UP, et al. Fascial closure after open abdomen: initial indication and early revisions are decisive factors–a retrospective cohort study. *Int J Surg.* (2015) 13:12–6. doi: 10.1016/j.ijsu.2014.11.025
26. Rosenzweig M, Berg A, Kuo YH, Onayemi A, Sciarretta J, Davis JM, et al. Are the benefits of rapid source control laparotomy realized after acute colonic perforation? *Surg Infect.* (2020) 21:665–70. doi: 10.1089/sur.2019.272
27. Kirkpatrick AW, Coccolini F, Ansaloni L, Roberts DJ, Tolonen M, McKee JL, et al. Closed or open after source control laparotomy for severe complicated intra-abdominal sepsis (the COOL trial): study protocol for a randomized controlled trial. *World J Emerg Surg.* (2018) 13:26. doi: 10.1186/s13017-018-0183-4

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