



Mesh-augmented versus direct abdominal closure in patients undergoing open abdomen treatment

M. O. Jakob¹ · C. Schwarz² · T. Haltmeier¹ · J. Zindel¹ · T. Pinworasarn¹ · D. Candinas¹ · P. Starlinger² · G. Beldi¹

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Abstract

Background Open abdomen (OA) may be required in patients with abdominal trauma, sepsis or compartment syndrome. Vacuum-assisted wound closure and mesh-mediated fascial traction (VAWCM) is a widely used approach for temporary abdominal closure to close the abdominal wall. However, this method is associated with a high incidence of re-operations in short term and late sequelae such as incisional hernia. The current study aims to compare the results of surgical strategies of OA with versus without permanent mesh augmentation.

Methods Patients with OA treatment undergoing vacuum-assisted wound closure and an intraperitoneal onlay mesh (VAC-IPOM) implantation were compared to VAWCM with direct fascial closure which represents the current standard of care. Outcomes of patients from two tertiary referral centers that performed the different strategies for abdominal closure after OA treatment were compared in univariate and multivariate regression analysis.

Results A total of 139 patients were included in the study. Of these, 50 (36.0%) patients underwent VAC-IPOM and 89 (64.0%) patients VAWCM. VAC-IPOM was associated with reduced re-operations (adjusted incidence risk ratio 0.48 per 10-person days; CI 95% = 0.39–0.58, $p < 0.001$), reduced duration of stay on intensive care unit (ICU) [adjusted hazard ratio (aHR) 0.53; CI 95% = 0.36–0.79, $p = 0.002$] and reduced hospital stay (aHR 0.61; CI 95% = 0.040–0.94; $p = 0.024$). In-hospital mortality [22.5 vs 18.0%, risk difference –4.5; confidence interval (CI) 95% = –18.2 to 9.3; $p = 0.665$] and the incidence of intestinal fistula (18.0 vs 22.0%, risk difference 4.0; CI 95% = –10.0 to 18.0; $p = 0.656$) did not differ between the two groups. In Kaplan–Meier analysis, hernia-free survival was significantly increased after VAC-IPOM ($p = 0.041$).

Conclusions In patients undergoing OA treatment, intraperitoneal mesh augmentation is associated with a significantly decreased number of re-operations, duration of hospital and ICU stay and incidence of incisional hernias when compared to VAWCM.

Keywords Open abdomen · Vacuum-assisted wound closure and mesh-mediated fascial traction · Mesh augmentation · Non-absorbable mesh

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✉ G. Beldi
guido.beldi@insel.ch

¹ Department of Visceral Surgery and Medicine, University Hospital, Bern, Switzerland

² Department of Surgery, General Hospital, Medical University of Vienna, Vienna, Austria

Introduction

Open abdomen (OA) treatment with temporary abdominal closure using negative-pressure wound therapy has become a standard of care in trauma patients undergoing damage control surgery [1]. OA is also increasingly used in non-trauma patients with abdominal sepsis or abdominal compartment syndrome as a life-saving procedure, especially in the growing older population with increased comorbidities and limited physiologic reserve [2].

Temporary abdominal closure needs to ensure the integrity of the abdominal wall and to compartmentalize abdominal contents to avoid treatment-related complications (e.g., intestinal fistula, inability to close the abdominal wall).

Several methods for temporary abdominal closure have been described of which vacuum-assisted wound closure and mesh-mediated fascial traction (VAWCM) has been reported to be associated with the lowest fistula rate with high rates of fascial closure [3]. However, using the VAWCM technique, multiple surgical revisions are often required for definitive abdominal closure, which may lead to a prolonged ICU and total hospital duration of stay [4]. In addition, these patients exhibit a high rate of incisional hernias of up to 66% during long-term follow-up potentially because of local fascial traction [5].

Therefore, novel strategies to support the abdominal wall in these patients are required. Synthetic mesh implantation has been shown to effectively support the abdominal wall [6]. However, the use of such meshes in OA may have been limited due to the lack of robust data and due to reports of mesh related complications [7]. We have previously shown that the use of synthetic meshes in patients with peritonitis or fascial dehiscence is an effective approach [8, 9]. Thus, a therapeutic algorithm that includes mesh-augmented definitive abdominal closure (VAC-IPOM) in this severely ill patient population has been developed and introduced at the Bern University Hospital in 2005. The aim of this large two-centre study was to compare this VAC-IPOM technique with the current standard of care (VAWCM) in patients undergoing OA treatment.

Materials and methods

Study design

All consecutive patients treated for OA between January 2005 and December 2015 from two centers were analyzed. The participating centers were the Department for Visceral Surgery and Medicine, Bern University Hospital, Switzerland (patients with VAC-IPOM) and the Department for Surgery, Medical University of Vienna, General Hospital Vienna, Austria (patients with VAWCM). Patients not using the VAC-IPOM technique at the University Hospital of Bern ($n = 22$) were excluded from the study. Cantonal ethics committee of Bern, Switzerland and the institutional review board of the Medical University of Vienna, Austria have approved this study.

Outcome parameters

The primary outcome parameter was hernia-free survival. Secondary outcome parameters comprised of general complications such as re-operations, duration of hospital stay, duration of stay on intensive care unit (ICU), mortality and mesh-associated complications such as intestinal fistula and surgical site infection (SSI). SSI infection was defined

according to CDC criteria [10]. Intestinal fistula was defined as the persistent leakage of bowel contents within 100 days of the initial OA.

Surgical strategy

VAWCM group

OA was covered with abdominal dressings and dynamic tension on fascia was applied to avoid fascial retraction. Dynamic tension on fascia was applied either via vessel loops or temporary inlay meshes as previously described [11, 12]. The vessel loops were sutured to the anterior sheet of the rectus muscle and constant tension was applied to approximate the fascial edges. In addition, 18 (22.2%) patients received a temporary large-pore polypropylene inlay mesh. The mesh was sutured to the fascial edges with non-absorbable sutures and was removed at definitive abdominal closure. The fasciae were closed with absorbable loops.

VAC-IPOM group

The technique has been previously published [13]. Briefly, patients with OA were treated for one or two cycles with abdominal dressings to stabilize the patients' conditions. After this initial period, intraperitoneal onlay mesh implantation was performed using dual-layered-, large pore, synthetic meshes. Meshes were placed with an overlap of at least 5 cm on all sides. The meshes were fixed in all corners with a non-absorbable polypropylene suture (Prolene[®], Ethicon) and the edges were attached to the peritoneum with the same suture. The fascia was partially or completely closed with a PDS running suture (PDS[®], Ethicon). A vacuum dressing (V.A.C.[®], KCI) was then placed on the mesh and continuous suction was applied (25–75 mmHg suction). Wound treatment included: (1) vacuum dressings until an adequate formation of granulation tissue was achieved and (2) skin re-adaptation with non-resorbable sutures (Dermalon[®], Covidien).

Statistical analysis

Data were reported as median and interquartile ranges (IQR), or numbers and percentages, as appropriate. Patients' groups were compared using Fisher's exact test and Mann–Whitney *U* test for categorical and continuous variables, respectively. Time-to-event outcomes were analysed using the log-rank test. Effects are reported as risk differences or c-statistics with 95% confidence intervals (CI). The primary endpoint hernia-free survival, was analyzed with Kaplan–Meier curves and a log-rank test for statistical comparison. The effect of mesh treatment on hernia-free survival and secondary outcomes was adjusted in multivariable regression

analyses. Clinically important and potential confounder variables (age, gender, BMI, emergency primary operation, malignancy, ASA score, immunosuppressive drugs) were tested in univariable models and included in the multivariable model if the *p* value was below 0.2. Logistic, Cox or Poisson regression were fitted for binary, time-to-event or count outcomes, respectively. Results were reported as odds

ratio (OR), hazard ratio (HR) or incidence risk ratio (IRR) with 95% CI and *p* values. A two-sided *p* value of <0.05 was considered statistically significant. All statistical tests were performed using SPSS Statistics (Version 17.0.0, SPSS Inc., Chicago, IL).

Table 1 Patients' characteristics

	VAWCM (n=89)	VAC-IPOM (n=50)	<i>p</i>
Age, median in years (IQR)	55 (48–67)	61 (55–72)	0.046
Male patients (%)	52 (58.4%)	30 (60.0%)	1.000
Body mass index in kg/m ² (IQR)	24.8 (21.0–29.2)	27.3 (23.1–35.0)	0.172
Known malignancy (%)	36 (41.8%)	27 (54.0%)	0.212
Type 2 diabetes (%)	15 (17.0%)	6 (12.0%)	0.471
Cardiac disease (%)	47 (52.8%)	23 (46.0%)	0.483
Pulmonary disease (%)	16 (18.0%)	20 (40.0%)	0.008
Liver disease (%)	18 (20.2%)	14 (28.0%)	0.303
Kidney disease (%)	20 (22.5%)	9 (18.0%)	0.665
Anticoagulation preoperative (%)			
Phenprocoumon	1 (1.2%)	5 (10.4%)	0.024
Platelet aggregation inhibitors	5 (6.0%)	4 (8.3%)	0.723
Dual anticoagulation	11 (13.1%)	2 (4.2%)	0.132
Immunosuppressors (%)			
Immunosuppressive drugs	1 (1.2%)	4 (8.2%)	0.090
Cortisone	5 (6.2%)	2 (4.1%)	
Both	4 (4.9%)	–	
ASA score (%)			
2	35 (41.7%)	8 (16.3%)	<0.001
3	43 (51.2%)	18 (36.7%)	
4	3 (3.6%)	22 (44.9%)	
5	3 (3.6%)	2 (4.1%)	
Type of primary surgery (%)			
Hepatobiliary surgery	4 (4.5%)	1 (2.0%)	0.011
Pancreatic surgery	6 (6.7%)	–	
Upper GI surgery	14 (15.7%)	6 (12.0%)	
Resection of intestine with preserved continuity	23 (25.8%)	9 (18.0%)	
Resection of intestine without preserved continuity	19 (21.3%)	10 (20.0%)	
Pancreatic necrosectomy	3 (3.4%)	–	
Multivisceral resections	4 (4.5%)	10 (20.0%)	
Vascular surgery	2 (2.2%)	4 (8.0%)	
Other	14 (15.7%)	10 (20.0%)	
Emergency primary procedure (%)	41 (46.1%)	26 (52.0%)	0.596
Prior laparotomies, no. (IQR)	3 (1–4)	2 (1–3)	0.030
Duration of primary operation in minutes (IQR)	195 (135–318)	240 (163–300)	0.416
Incision at primary procedure (%)			
Median laparotomy	64 (75.3%)	49 (98.0%)	0.007
Transverse Laparotomy	11 (12.9%)	1 (2.0%)	
Combined	9 (10.6%)	–	
Laparoscopy	1 (1.2%)	–	

ASA American Society of Anaesthesiology, IQR interquartile range

Results

Meshes used in the VAC-IPOM group include polypropylene-based mesh in 39 (78%) patients, (Parietene composite[®], Medtronic, in 34 (87.2%) patients; Dynamesh[®], FEG Textiltechnik mbH, in 4 (10.3%) patients; Vipro[®], Ethicon, in 1 (2.5%) patient) and polyester-based meshes (Parietex composite[®], Medtronic) in 11 (22%) patients. Patients' characteristics are shown in Table 1.

Short-term outcome

Detailed operative characteristics and postoperative results are shown in Table 2. There was no difference of the intestinal fistula rate and in-hospital mortality between VAWCM and VAC-IPOM. The median number of re-operations after initiation of OA was 5 (IQR 2–13) for VAWCM and 3 (IQR 2–5) for VAC-IPOM (Fig. 1). The incidence of re-operations during hospitalisation per 10-person days after

initiation of OA was 1.28 for VAWCM and 0.62 for VAC-IPOM. Therefore, the adjusted incidence risk ratio for re-operation was 0.48 for VAC-IPOM [95% confidence interval (CI), 0.39–0.58, $p < 0.001$] (Table 3). Duration of ICU stay was significantly longer for VAWCM compared to VAC-IPOM [adjusted hazard ratio 0.53 (CI 95%, 0.36–0.79), $p = 0.002$] (Fig. 2a). Complete fascial closure was achieved in 66 (74.2%) patients for VAWCM versus 13 (26.0%) patients for VAC-IPOM [risk difference –48.2 (CI 95%, –63.3 to –33.0), $p < 0.001$]. Duration of hospital stay was significantly longer for VAWCM compared to VAC-IPOM [adjusted hazard ratio 0.61 (CI 95%, 0.40–0.94), $p = 0.024$] (Fig. 2b).

Long-term outcome

Median follow-up was 681 days (311–1091) for VAWCM and 426 (178–1058) for VAC-IPOM ($p = 0.201$). SSI at last follow-up was found in 3 patients for VAWCM [after a

Table 2 Operative and postoperative results

	VAWCM (n=89)	VAC-IPOM (n=50)	Effect measure (95% CI)	p
Occurrence of OA after primary surgery in days (IQR)	11 (4–16)	11 (7–17)	0.53 (0.43 to 0.63)	0.605
Leakage of gastric anastomosis (%)	5 (5.6%)	1 (2.0%)	–3.6 (–9.8 to 2.5)	0.419
Leakage of small intestinal anastomosis (%)	12 (13.5%)	9 (18.0%)	4.5 (–8.3 to 17.3)	0.471
Leakage of colonic anastomosis (%)	3 (3.4%)	5 (10.0%)	6.6 (–2.5 to 15.7)	0.136
Leakage of pancreatic anastomosis (%)	1 (1.1%)	1 (2.0%)	0.9 (–3.6 to 5.3)	1.000
Leakage of small intestine and colon (%)	–	1 (2.0%)	2.0 (–1.9 to 5.9)	0.360
VAC therapy (%)	87 (97.8%)	45 (90.0%)	–7.8 (–16.6 to 1.1)	0.098
Duration of redo-surgery in minutes (IQR)	70 (43–110)	111 (80–181)	0.72 (0.61 to 0.80)	<0.001
Incidence of intestinal fistula until 100 days after OA (%)	16 (18.0%)	11 (22.0%)	4.0 (–10.0 to 18.0)	0.656
Occurrence of intestinal fistula before OA (%)	7 (7.9%)	4 (8.0%)	0.1 (–9.2 to 9.5)	1.000
Intestinal fistula during OA treatment (%)	9 (10.1%)	7 (14.0%)	3.9 (–7.6 to 15.4)	0.582
Type of intestinal fistula (%)				
Small intestine	13 (14.6%)	9 (18.0%)	3.4 (–9.5 to 16.3)	0.633
Enterotomospheric	3 (3.4%)	2 (4.0%)	0.6 (–6.0 to 7.2)	1.000
In-hospital mortality (%)	20 (22.5%)	9 (18.0%)	–4.5 (–18.2 to 9.3)	0.665
Reason for mortality (%)				
Cardiopulmonary insufficiency	2 (2.2%)	–	–2.2 (–5.3 to 0.8)	1.000
Sepsis/multi-organ failure	12 (13.5%)	6 (12.0%)	–1.5 (–13.0 to 10.0)	1.000
Underlying disease	3 (3.4%)	2 (4.0%)	0.6 (–6.0 to 7.2)	0.633
Other ^A	3 ^a (3.4%)	1 ^b (2.0%)	–1.4 (–6.7 to 4.0)	1.000
Patients requiring intensive care (%)	85 (95.5%)	47 (94.0%)	–1.5 (–9.4 to 6.4)	0.702
Days at intensive care unit (IQR)	20 (6–36)	11 (6–16)	0.37 (0.27 to 0.46)	0.002
Termination of OA treatment after initiation in days (IQR)	28 (9–63)	3 (0–7)	0.13 (0.06 to 0.19)	<0.001
Fascia closed (%)	66 (74.2%)	13 (26.0%)	–48.2 (–63.3 to –33.0)	<0.001
SSI at discharge (%)	16 (18.0%)	27 (54.0%)	36.0 (20.1 to 52.0)	<0.001
Duration of hospital stay in days (IQR)	66 (33–109)	49 (34–72)	0.40 (0.3 to 0.49)	0.007

IQR interquartile range, OA open abdomen, SSI surgical site infection

^AOther included: ^a death due to brain oedema ($n = 1$), pulmonary embolism ($n = 1$), perforation of aorta ($n = 1$) and ^bdeath due to liver failure ($n = 1$)

median of 648 days (151–1207)] and 12 patients for VAC-IPOM [after a median of 269 days (55–454), $p=0.001$]. Hernia-free survival showed a significant curve separation when comparing VAC-IPOM with VAWCM ($p=0.041$) (Fig. 3).

Mesh-related complications

SSI at last follow-up did not differ when comparing polypropylene-based meshes with polyester-based meshes [$n=9$ (28.1%) vs $n=3$ (33.3%), $p=1.000$]. A higher but not significant incidence of SSI was found when fascial closure was not achieved [$n=11$ (34.4%)] compared to fascial closure [$n=1$ (12.5%), $p=0.240$]. Partial mesh explantation due to persistent SSI was necessary in 4 (9.8%) patients. There was no difference in partial mesh explantation when comparing polypropylene-based meshes with polyester-based meshes ($n=3$ polypropylene versus $n=1$ polyester mesh, $p=1.000$). We did not find a difference in incidence of intestinal fistula until 100 days after OA ($n=10$ polypropylene versus $n=1$ polyester mesh, $p=0.416$).

Discussion

The current study shows that VAC-IPOM in patients with OA treatment decrease re-operations, duration of hospital and ICU stay, and the incidence of incisional hernia, when

compared with VAWCM, which represents the current standard of care.

OA treatment with temporary abdominal closure should address three main clinical problems: (1) survival of the patient; (2) prevention of short-term complications of the abdominal wall; (3) reduction of long-term complications.

To improve survival and to prevent multi-organ injury in OA, the initial management of abdominal sepsis includes removal of inflammatory ascites [14, 15]. This is mainly achieved by vacuum therapy, which is offered by both, VAC-IPOM and VAWCM and thereby potentially explains the comparable in-hospital mortality.

To reduce short-term complications, the integrity of the abdominal wall should be restored as soon as hemodynamic stabilization and removal of septic foci have been achieved. Repetitive abdominal dressings in this setting as required by VAWCM are potentially unnecessary or even harmful leading to a marked increase in duration of stay on ICU.

The fascial closure rate of the current series with VAWCM was similar to a previously published meta-analysis, i.e., 73.1% [3]. However, the fasciae of 25.8% of patients using the VAWCM technique were not closed and a planned ventral hernia was the consequence, which could be prevented by the VAC-IPOM technique. In the VAC-IPOM group, fascial closure was not required in the majority of patients because this technique was sufficient to stabilize the abdominal wall and prevented excessive fascial traction. Therefore, high tension to achieve fascial closure can be avoided.

Intestinal fistula is a putative complication in patients with OA and might potentially further complicate the clinical course [16]. The current series supports a growing body of literature showing that the incidence of enterocutaneous fistula in the contaminated abdomen is not different when compared to a cohort without synthetic, intraperitoneal mesh implantation [8, 9, 17–19]. Visceral protection with dual-layered meshes seems to be a key element in prevention of mesh-related intestinal fistula in these patients [20]. Because of this additional barrier function, the VAC-IPOM technique also allows bedside subcutaneous VAC treatment, avoiding unnecessary re-operations.

The frequency of SSI in this population is high and may be complicated by chronic mesh infection [21]. Even though mesh removal is a putative complication for chronic SSI (especially in patients with peritonitis), mesh explantation is rarely necessary [22].

At long-term follow-up, incisional hernia is the most important complication in patients after OA [23, 24]. Even in a series of patients with a very high fascial closure rate of 88%, the rate of incisional hernias remained high with an incidence of at least 28.6% [25]. These high incidences

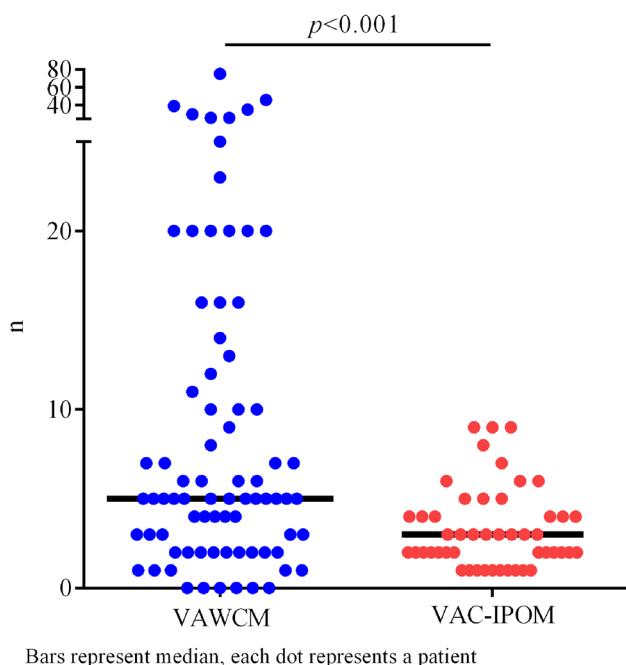


Fig. 1 Re-operations after initiation of open abdomen until discharge

Table 3 Unadjusted and adjusted effect of mesh-augmentation on important outcome variables

	Unadjusted Odds ratio (95% CI)	<i>p</i>	Adjusted Odds ratio (95% CI)	<i>p</i>
In-hospital mortality				
VAC-IPOM	0.76 (0.32–1.82)	0.534	0.45 (0.13–1.61)	0.221
ASA score > 3	2.56 (1.02–6.42)	0.045	3.92 (1.08–14.23)	0.038
Emergency primary procedure	2.04 (0.88–4.71)	0.097	3.60 (1.13–11.44)	0.030
Immunosuppressive drugs	4.72 (1.54–14.46)	0.006	5.14 (1.43–18.44)	0.012
	Unadjusted Odds ratio (95% CI)	<i>p</i>	Adjusted Odds ratio (95% CI)	<i>p</i>
Intestinal fistula at 100 days				
VAC-IPOM	1.29 (0.54–3.04)	0.566	2.06 (0.78–5.42)	0.143
ASA score > 3	0.26 (0.05–1.02)	0.052	0.19 (0.04–0.97)	0.045
Emergency primary procedure	0.38 (0.15–0.94)	0.035	0.47 (0.18–1.20)	0.114
	Unadjusted Hazard ratio (95% CI)	<i>p</i>	Adjusted Hazard ratio (95% CI)	<i>p</i>
Hernia-free survival				
VAC-IPOM	0.30 (0.09–1.02)	0.055	0.36 (0.10–1.27)	0.114
Immunosuppressive drugs	3.02 (0.87–10.5)	0.083	2.74 (0.78–9.64)	0.116
Age	0.97 (0.94–1.00)	0.078	0.97 (0.94–1.01)	0.126
	Unadjusted Hazard ratio (95% CI)	<i>p</i>	Adjusted Hazard ratio (95% CI)	<i>p</i>
Duration of stay on Intensive care unit				
VAC-IPOM	0.52 (0.36–0.77)	< 0.001	0.53 (0.36–0.79)	0.002
Emergency primary procedure	1.26 (0.89–1.78)	0.193	1.29 (0.88–1.89)	0.198
Immunosuppressive drugs	1.67 (0.97–2.90)	0.066	1.38 (0.79–2.43)	0.257
Age	1.01 (1.00–1.03)	0.034	1.01 (1.00–1.03)	0.109
Malignancy	0.67 (0.47–0.95)	0.026	0.77 (0.53–1.13)	0.189
	Unadjusted Hazard ratio (95% CI)	<i>p</i>	Adjusted Hazard ratio (95% CI)	<i>p</i>
Duration of hospital stay				
VAC-IPOM	0.57 (0.38–0.87)	0.008	0.61 (0.40–0.94)	0.024
Age	1.02 (1.00–1.03)	0.029	1.01 (1.00–1.03)	0.115
Malignancy	0.74 (0.49–1.01)	0.138	0.86 (0.58–1.30)	0.484
	Unadjusted Incidence risk ratio (95% CI)	<i>p</i>	Adjusted Incidence risk ratio (95% CI)	<i>p</i>
Re-operations during OA treatment				
VAC-IPOM	0.49 (0.41–0.58)	< 0.001	0.48 (0.39–0.58)	< 0.001
ASA Score > 3	0.70 (0.57–0.85)	< 0.001	1.04 (0.82–1.32)	0.755
Emergency primary procedure	0.89 (0.78–1.02)	0.090	0.89 (0.76–1.04)	0.134
Age	0.99 (0.99–0.99)	< 0.001	1.00 (0.99–1.00)	0.345
Malignancy	0.69 (0.60–0.79)	< 0.001	0.75 (0.64–0.89)	< 0.001
BMI	1.00 (1.00–1.01)	0.117	1.01 (1.00–1.01)	0.016
Male gender	0.81 (0.71–0.92)	0.001	0.90 (0.78–1.04)	0.151

Odds ratios, hazard ratios and incidence risk ratios are shown VAC-IPOM versus VAWCM. Variables with a *p* value below 0.2 on univariable analysis are displayed

Bold values are considered significant ($p < 0.05$)

95% CI 95% confidence interval; ASA American Society of Anaesthesiology

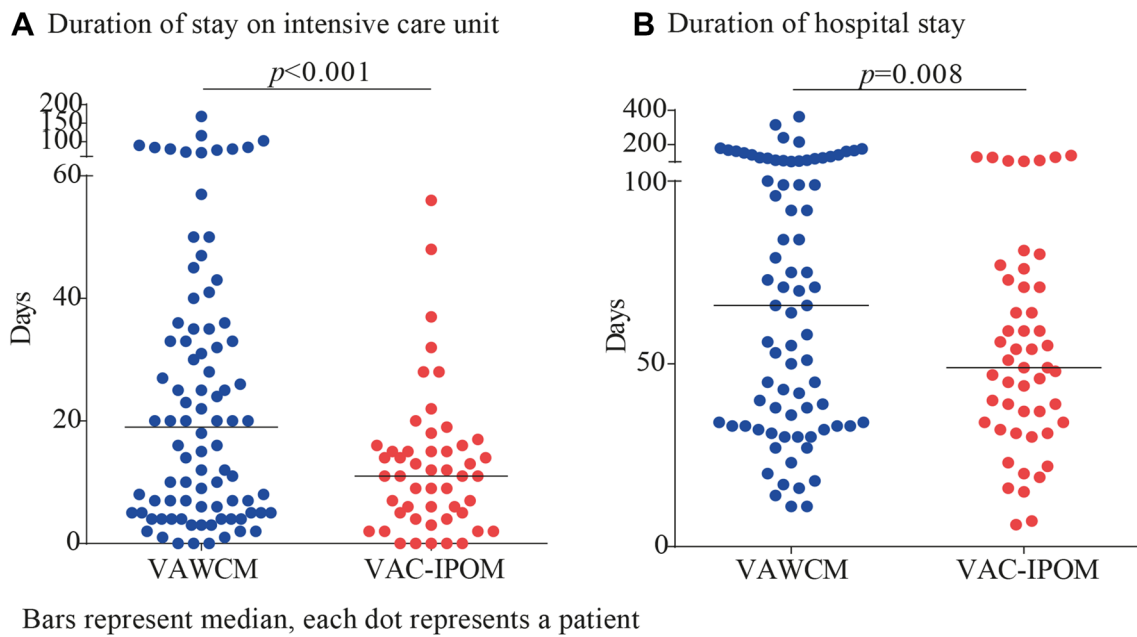


Fig. 2 a Duration of stay on intensive care unit. b Duration of hospital stay

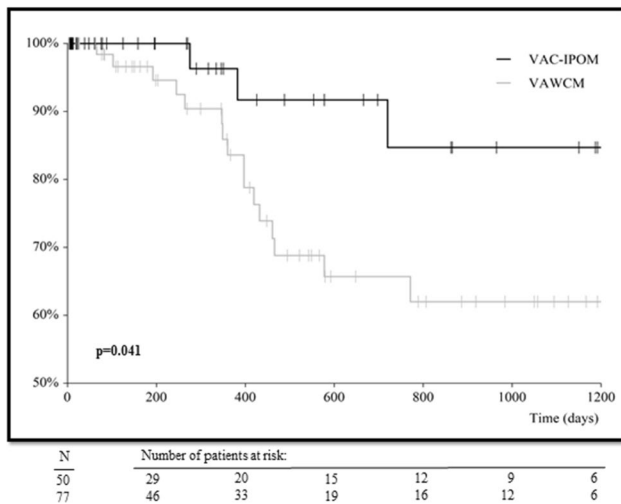


Fig. 3 Hernia-free survival

of incisional hernia and the fact that the collagen structure is comprised in these patients (Fig. SDC 2) indicates the importance of a reinforcement of the abdominal wall. Biologic meshes are an option for the treatment of abdominal wall defects in contaminated fields [26]. However, a recent meta-analysis revealed that biologic meshes were associated with more surgical site complications and hernia recurrence compared to synthetic meshes [27]. Therefore, usage of biologic meshes for such situations should be critically reevaluated [28].

Limitations of this study include its retrospective design and the fact that two different centres were compared with differences in health care. The fact that both hospitals treat a similar number of patients using a comparable surgical spectrum, confounding biases should be reduced. Essentially, prior to data collection, outcome parameters were pre-defined to overcome different definitions. Additionally, the most relevant outcome parameters (Mortality, intestinal fistula, fascial closure, hernia) did not differ compared to other published series [3]. Of note, the current series almost exclusively consists of non-trauma patients.

Conclusion

In the current study, VAC-IPOM in patients with OA decreased re-operations, duration of hospital and ICU stay, and the incidence of incisional hernia compared to VAWCM. Based on these results, abdominal closure using synthetic mesh-augmentation represents a therapeutic option in patients undergoing OA treatment.

Author contributions MOJ: Study design, data analysis, writing. CHS: Data collection, data interpretation. TH: Statistical analysis, writing. JZ: Histology, writing. TP: Data collection, data interpretation. DC: Study design, critical revision of the manuscript. PS: Study design, data analysis, critical revision of the manuscript. GB: Study design, data analysis, critical revision of the manuscript.

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Compliance with ethical standards

Conflict of interest MOJ, CHS, TH, JZ, TP, DC, PS and BG declare no conflict of interest.

Ethical approval Cantonal ethics committee of Bern, Switzerland and the institutional review board of the Medical University of Vienna, Austria have approved this study.

Human and animal rights The study including participant has been performed in accordance with the ethical standard of the Declaration of Helsinki and its later amendments.

Informed consent For this retrospective review, informed consent was not required from both ethical review boards.

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