Biologic mesh implantation is associated with serious abdominal wall complications in patients undergoing emergency abdominal surgery: A randomized-controlled clinical trial

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BACKGROUND: Open, emergency abdominal surgery is associated with a high incidence of fascial dehiscence and incisional hernia. Implantation of biologic meshes potentially reinforces the abdominal wall and therefore decreases such complications. The aim of this prospective randomized study was to compare the outcome after prophylactic intraperitoneal implantation of a biologic Strattice mesh (Allergan, Dublin, Ireland) with standard abdominal closure in patients undergoing emergency abdominal surgery.

METHODS: A two-arm randomized clinical trial was performed in patients undergoing emergency abdominal surgery at Bern University Hospital, University of Bern, Switzerland, from April 2016 to March 2019. Patients were randomly assigned to prophylactic implantation of a biological intraperitoneal mesh using Strattice, Allergan (mesh group), or standard abdominal closure using a single, continuous running suture (no-mesh group). Because of safety concerns, patient enrollment was closed prematurely.

RESULTS: Eligibility for inclusion was assessed in 61 patients. A total of 48 patients were randomized (21 in the mesh group, 28 in the no-mesh group). No differences in baseline characteristics were found. Abdominal wall complications requiring reoperations were more frequent in the mesh group compared to the no-mesh group (5 [83.3%] of 13 vs. 1 [14.3%] of 13 patients, $p = 0.026$). Mesh-associated abdominal wall complications included nonintegration of the mesh into the abdominal wall, dissolution of the mesh, and mesh-related infections.

CONCLUSION: In patients undergoing emergency abdominal surgery, intraperitoneal biologic Strattice mesh implantation is associated with significantly more frequent abdominal wall complications requiring reoperation. Therefore, the use of such meshes cannot be recommended in the contaminated environment of emergency abdominal surgery. (*J Trauma Acute Care Surg.* 2020;89: 1149–1155.

LEVEL OF EVIDENCE: Therapeutic, level I.
KEY WORDS: Biologic mesh; emergency surgery; abdominal wall complications; hernia prophylaxis.

Incisional hernia is a common complication after abdominal surgery with a reported rate of 13% to 23% in the general surgical population.[1,2] In patients undergoing emergency abdominal surgery, impaired wound healing in response to the systemic inflammatory environment and the high incidence of surgical site infection (SSI) render the abdominal wall even more susceptible to an incisional hernia with rates up to 54%.[3–5] Incisional hernias are associated with a high morbidity rate, including intestinal incarceration, chronic discomfort, and pain, and often require revisional surgery and implantation of a synthetic mesh.[6,7] Fascial dehiscence as a result of suture failure can occur in up to 24% of at risk patients with an associated mortality rate of up to 44%.[8]

The running slowly absorbable suture is the standard abdominal wall closure in elective and emergency abdominal surgery.[9] Prophylactic, synthetic mesh implantation reduced the incidence of incisional hernia in the elective situation.[10,11] In the emergency setting and in the presence of intra-abdominal contamination, synthetic mesh implantation reduced re-operation and the length of hospital stay in the short-term and hernia formation in the long-term without increasing the risk for intestinal fistula formation.[12,13] However, recent studies report increased incidences of chronic SSI or seromas with the use of such meshes.[12–14] Thus, alternatives to synthetic meshes need to be sought to combine advantages of mesh implantation and overcome disadvantages, especially chronic SSI. The Strattice Reconstructive Matrix Tissue (Allergan, Dublin, Ireland) showed a high resistance against infections in animal models and usage of biologic meshes reduced the occurrence of SSI in patients[15,16] and was therefore tested in this study.

The hypothesis of the current study was that prophylactic implantation of biologic Strattice meshes in patients undergoing emergency abdominal surgery reduces the rate of incisional hernias and is not associated with mesh-associated complications. Therefore, we prospectively compared outcomes after abdominal wall closure using a single running suture versus prophylactic intraperitoneal biologic Strattice mesh implantation in patients undergoing emergency laparotomy. The primary outcome of this study was the incidence of incisional hernia 18 months postoperatively. Secondary outcomes included chronic mesh infection and intestinal fistula.

PATIENTS AND METHODS

Trial Design

This study was designed as a randomized-controlled clinical trial including patients that underwent midline laparotomy or laparoscopy with expected conversion to midline laparotomy for abdominal emergencies. Exclusion criteria were moribund patients indicated as an American Society of Anesthesiologists physical status classification system score of 5, patients with septic shock requiring vasoactive medication, pregnancy, prior mesh implantation, and known sensitivity against porcine material or polysorbate 20. Patients were included from April 2017 until March 2019. Participants were enrolled and assigned to interventions by surgeons who received appropriate training. Patients fit to decide were asked to participate in the study and had to sign the corresponding consent form. For patients who were not conscious, their legal representatives received oral and written information, evaluated the putative will of the patient and signed the form. The study was registered at ClinicalTrials.gov (HPACS-trial; NCT01110798). The study was approved by the Ethical Committee of the Swiss Canton of Bern (KEK-BE, 2016-02212). The trial protocol can be found in Supplemental

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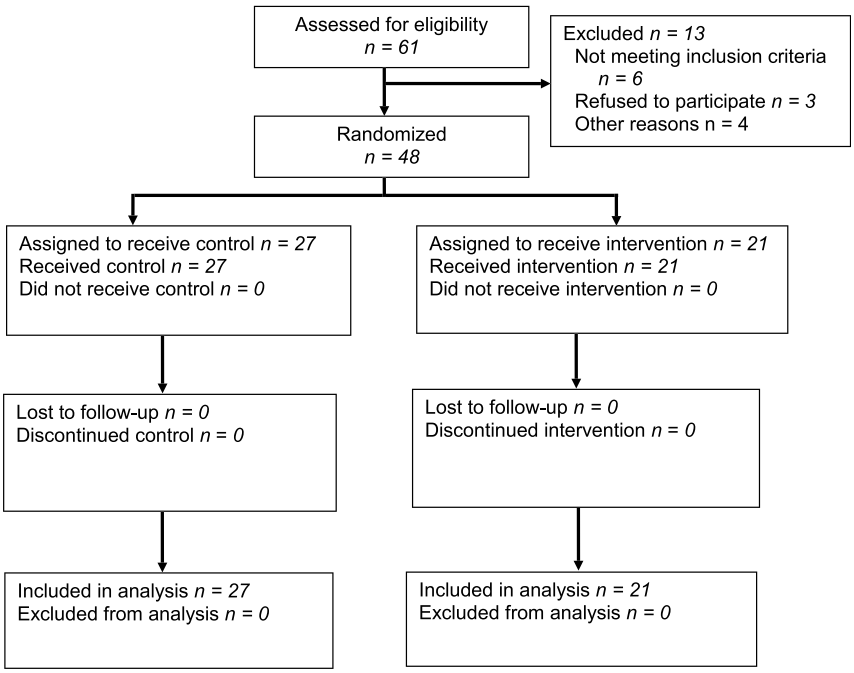

Figure 1. Consolidated Standards of Reporting Trials flow diagram.

Digital Content 1 (Supplementary Fig. 1, http://links.lww.com/TA/B764). This study was financially supported by Strattice, Allergan.

Randomization

The randomization was performed in 1:1 ratio between the investigational and the control group. Randomization was performed by computer-generated random number tables in permutated blocks of 10 patients while considering patients above and below a body mass index of 28 kg/m^2 to balance these strata in both groups. Random allocation sequence was generated using the online software randomization.com (http://www.randomization.com). Allocation was implemented directly in the electronic case report form (REDCap; Vanderbilt University, Nashville, TN). Only system administrators had access to the list to ensure concealment of allocation.

Procedures

Experimental Intervention

Emergency abdominal surgery was performed according to the standard of care at the Bern University Hospital, University of Bern, Switzerland. At the end of the operation, an acellular porcine dermal mesh (Strattice Reconstructive Tissue Matrix; Allergan) was implanted. The mesh had a width of at least 15 cm with an overlap of the incision of at least 5 cm in all quadrants. The mesh was placed intra-abdominally and fixed with single stitches using Prolene 2/0 in all four corners visualized by exposing the inner abdominal wall. After the initial fixation of the mesh in all quadrants, the boarders of the mesh were fixed using polydioxanon 2/0 running sutures while visually controlling for potential herniation of intestinal contents between the mesh and the abdominal wall. Afterwards, the abdominal wall was closed as described in the control group. Skin closure was performed using single stitches with gaps between stitches of at least 2 cm. Dry dressings were applied on the incision site. Alternatively, the skin was left open and treated with subcutaneous vacuum-assisted closure dressing.

Control Intervention

After abdominal surgery, the abdominal wall was closed with a running suture using polydioxanon 1 loops in a 4:1 ratio. The distance of the sutures to the fascial border was 1 cm, and the distance between two stitches was not more than 1 cm. The total length of the suture was at least four times the total length of the abdominal incision. Skin closure was performed using single stitches with gaps between stitches of at least 2 cm. Alternatively, the skin was left open and treated with subcutaneous vacuum-assisted closure dressing.

Outcomes

The current study was designed to study hernia-free survival following mesh implantation versus closure of the abdominal wall with a continuous, single running suture. Secondary outcomes comprised in particular potential disadvantages of prophylactic mesh implantation such as SSI, abdominal wall-related complications, and intestinal fistula.

Power Analysis

Sample size calculation was based on the primary outcome of the trial, that is, hernia-free survival. The incidence of incisional hernia in patients undergoing emergency surgery varies between 33% and 54% after a mean follow-up of 16.7 months and a median follow-up of 74 months, respectively.[5,17] Recent data show that mortality rates after emergency general surgery range between 3.7% to 6.8% for a 30-day follow-up.[18,19] For the purpose of this sample size calculation, the following incidences of hernia in the group without

TABLE 1. Baseline and Surgical Characteristics

	All Patients (n = 48)	Mesh Group (n = 21)	No-Mesh Group (n = 27)	p*
Baseline characteristics				
Male sex	28 (58.3)	13 (61.9)	15 (55.6)	0.771
Age, y**	71.0 (12.0)	69.0 (11.0)	71.0 (15.0)	0.546†
BMI, kg/m^2**	25.5 (6.1)	25.5 (4.2)	25.4 (8.0)	0.634†
ASA score				
2	12 (25.0)	6 (28.6)	6 (22.2)	0.271
3	15 (31.3)	9 (42.9)	6 (22.2)	
4	18 (37.5)	5 (23.8)	13 (48.1)	
5	3 (6.3)	1 (4.8)	2 (7.4)	
Heart disease	13 (27.1)	7 (33.3)	6 (22.2)	0.516
Pneumopathy and nicotine abuse	11 (22.9)	2 (9.5)	9 (33.3)	0.083
Liver disease	2 (4.2)	0 (0.0)	2 (7.4)	0.497
Renal insufficiency	18 (37.5)	8 (38.1)	10 (37.0)	1.000
Diabetes mellitus	7 (14.6)	1 (4.8)	6 (22.2)	0.118
Malignant disease	21 (43.8)	10 (47.6)	11 (40.7)	0.771
Anticoagulants and antiaggregants	13 (27.1)	7 (33.3)	6 (22.2)	0.516
Immunosuppressive drugs	5 (10.4)	2 (9.5)	3 (11.1)	1.000
Previous abdominal surgery	31 (64.6)	12 (57.1)	19 (70.4)	0.377
Surgical characteristics				
Indication for surgery				
Small bowel obstruction	14 (29.2)	6 (28.6)	8 (29.6)	1.000
GIT perforation and anastomotic leak	12 (25.0)	4 (19.0)	8 (29.6)	0.510
Trauma	8 (16.7)	4 (19.0)	4 (14.8)	0.715
Large bowel obstruction	5 (10.4)	2 (9.5)	3 (11.1)	1.000
Nontraumatic bleeding	4 (8.3)	1 (4.8)	3 (11.1)	0.621
Mesenteric ischemia	2 (4.2)	2 (9.5)	0 (0.0)	0.186
Other	3 (6.3)	2 (9.5)	1 (3.7)	0.574
Duration of operation, min**	120.0 (90.0)	134.0 (108.0)	96.0 (61.0)	0.015†
Surgeon				
Attending	7 (14.6)	4 (19.0)	3 (11.1)	0.865
Fellow	38 (79.2)	16 (76.2)	22 (81.5)	
Resident	3 (6.3)	1 (4.8)	2 (7.4)	
Bowel resection	24 (50.0)	9 (42.9)	15 (55.6)	0.561
Stoma formation	14 (29.2)	5 (23.8)	9 (33.3)	0.536
Intraoperative PRBC transfusion	5 (10.4)	1 (4.8)	4 (14.8)	0.369
Abdominal fluid at time of operation				
Clear	28 (58.3)	13 (61.9)	15 (55.6)	0.248
Serosanguinous	1 (2.1)	1 (4.8)	0 (0.0)	
Bloody	1 (2.1)	1 (4.8)	0 (0.0)	
Purulent	12 (25.0)	5 (23.8)	7 (25.9)	
Fecal	6 (21.4)	1 (4.8)	5 (18.5)	
Mannheim peritonitis index	14 (11)	13.5 (10.5)	14 (12)	0.730
Vacuum-assisted wound therapy	4 (8.3)	2 (9.5)	2 (7.4)	1.000

Values are numbers (percentages) unless indicated otherwise.
*Fisher's exact test unless indicated otherwise.
**Values are medians (IQRs).
†Mann-Whitney *U* test.
BMI, body mass index; ASA, American Society of Anesthesiologists Physical Status Classification System; GIT, gastrointestinal tract; PRBC, packed red blood cell.

prophylactic mesh were used: 18% at 12 months and 35% at 18 months. We estimated that 10% of patients will have died at 12 months and 15% at 18 months. According to our own findings and other published reports, we expected an incidence of incisional hernia with prophylactic mesh repair of 6% after a mean follow-up of 16.7 months.[5,20] We assumed that the effect of mesh repair would mainly be on hernias and only have a minimal effect on mortality. Consequently, we used a hazard ratio of 0.4 for the sample size calculation. We considered a cumulative loss to follow-up of 15% at 18 months.

For the sample size calculation, we defined the level of significance at a two-sided 5% and power of 80%. Using an unweighted log-rank test with local alternatives, this resulted in a required sample size of 118 patients overall and 59 per group, respectively. Sample size calculation was done in Stata (Stata Statistical Software, StataCorp 2017; StataCorp LLC, College Station, TX) using the artsurv command.

Interim Analysis

Because of serious safety concerns of the studied medical device, an initially unplanned interim analysis was performed 25 months after the inclusion of the first patient. Based on the results of the interim analysis, the study was prematurely terminated.

Statistics

Normality of distribution of continuous variables was assessed using histograms, skewness, and the Shapiro-Wilk test. Data were reported as median and interquartile ranges (IQRs), or numbers and percentages, as appropriate. The intervention and control group were compared using Fisher's exact test and Mann-Whitney *U* test for categorical and continuous variables, respectively. A two-sided *p*-value of <0.05 was considered statistically significant. Statistical tests were performed by using SPSS Statistics (version 25; SPSS Inc., Chicago, IL).

RESULTS

Demographics

Eligibility for inclusion was assessed in 61 patients. Of these, 48 patients were included in the study. A total of 21 patients (43.8%) were randomized into the mesh group and 27 patients (56.2%) into the no-mesh group. Figure 1 shows the Consolidated Standards of Reporting Trials flow diagram.

Intraoperative Characteristics and Postoperative Outcome

The duration of the operation was significantly longer if a mesh was implanted (134.0 minutes [IQR, 108.0 minutes] vs. 96.0 minutes [IQR, 61.0 minutes] without mesh implantation, $p = 0.015$). Other surgical characteristics were not significantly different when comparing the mesh group versus the no-mesh group (Table 1). The grade of intra-abdominal contamination was not significantly different between groups, reflected by the intraoperative aspect of the abdominal fluid ($p = 0.248$) and the Mannheim peritonitis index ($p = 0.730$). Implantation of an intra-abdominal mesh was not associated with postoperative ileus or hematoma formation ($p = 0.246$ and 1.000, respectively)

TABLE 2. Postoperative Outcome

	All Patients (n = 48)	Mesh Group (n = 21)	No-Mesh Group (n = 27)	*p Value**
Postoperative ileus	3 (6.3)	0 (0.0)	3 (11.1)	0.246
Postoperative hematoma	2 (4.2)	1 (4.8)	1 (3.7)	1.000
Postoperative fascial dehiscence	4 (8.3)	3 (16.7)	1 (4.0)	0.292
Postoperative seroma	0 (0.0)	0 (0.0)	0 (0.0)	n/a
Abdominal wall complication				
Overall	13 (27.1)	6 (28.6)	7 (25.9)	1.000
Uncomplicated SSI**	7 (53.8)	1 (16.6)	6 (85.7)	
Serious complications requiring redosurgery (Dindo ≥3)**	6 (46.2)	5 (83.3)	1 (14.3)	0.026
Postoperative length of stay†	7.0 (7.0)	7.0 (7.0)	7.0 (8.0)	0.639‡
In-hospital mortality	3 (6.3)	2 (9.5)	1 (3.7)	0.574
Mortality at 30 d	4 (8.3)	3 (14.3)	1 (3.7)	0.306

Values are numbers (percentages) unless indicated otherwise.
*Fisher's exact test unless indicated otherwise.
**Subgroup of patients with abdominal wall complications (n = 13).
†Values are medians (IQRs).
‡Mann-Whitney *U* test.

(Table 2). Mesh implantation was not associated with a lower rate of postoperative fascial dehiscence (3 [16.7%] of 21 patients with mesh vs. 1 [4.0%] of 27 patients without mesh implantation, $p = 0.292$).

Abdominal Wall Complications

Overall, 13 patients (27.1%) developed abdominal wall complications. The incidence of abdominal wall complications was not different between groups ($p = 1.000$) (Table 2). However, the incidence of abdominal wall complications that required surgical reoperation (Clavien-Dindo grade, ≥3) was significantly more frequent in the mesh group (5 [38.5%] of 13 patients with mesh and 1 [7.7%] of 13 patients without mesh implantation, $p = 0.026$). We observed three distinct types of complication after mesh implantation (Supplemental Digital Content 2, Supplementary Table 1, http://links.lww.com/TA/B765). First, the mesh did not integrate in the abdominal wall (Fig. 2, n = 1) and led to fascial dehiscence requiring mesh explantation including a complex reconstruction of the abdominal wall. Second, the mesh nearly completely dissolved leading to fascial dehiscence (Fig. 3, n = 1). Third, in presence of infection, mesh implantation led to more severe abdominal wall complications (n = 3) including necrosis of the abdominal wall, severe peritonitis with a hematoma within the abdominal wall, and late onset mesh infection. The latter case was diagnosed during colostomy reversal 112 days after mesh implantation where the patient had no obvious signs of infection (Fig. 4).

DISCUSSION

In this prematurely terminated, prospective, randomized controlled study, implantation of a biologic Strattice mesh was associated with significantly more abdominal wall complications requiring revisional surgery in comparison with standard abdominal wall closure. Based on these results, such meshes cannot be recommended in patients undergoing emergency abdominal surgery.

In patients undergoing emergency abdominal surgery, impaired primary fascial closure and fascial dehiscence are common complications. Synthetic meshes are a good option to reenforce the abdominal wall and reduce reoperations and incisional hernia.[12,13] However, the concept of prophylactic, synthetic mesh placement in patients with abdominal emergencies can be complicated by chronic infection requiring partial mesh explantation in up to 14.3% of patients.[13] Thus, development and testing of novel mesh types based on alternative materials with the same stability

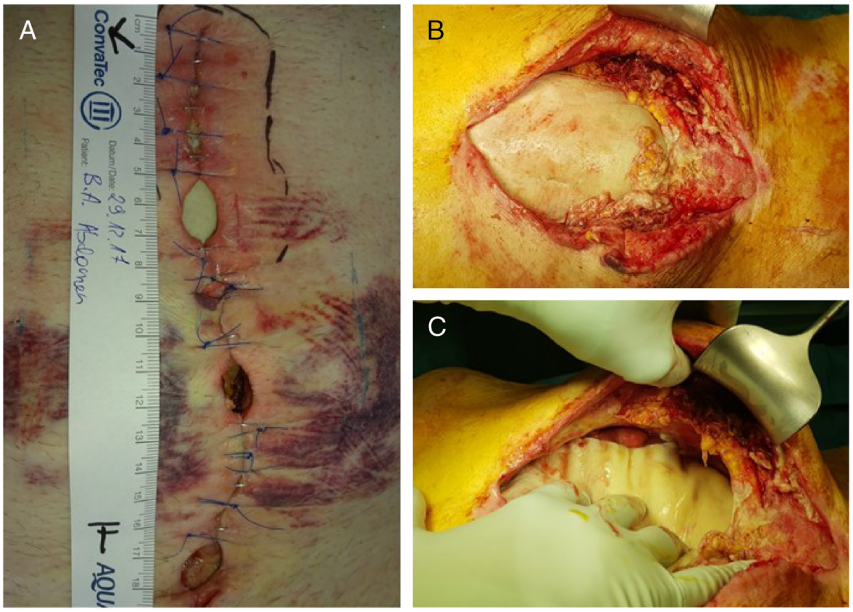

Figure 2. The Strattice mesh failed to integrate in the abdominal wall. Twenty days postoperatively, the abdomen had to be revised because of fascial dehiscence. Intraoperatively, the mesh was not integrated in the abdominal wall. (*A*) Intraoperative situs with the exposed mesh. Clinical apparent fascial dehiscence was only prevented by skin sutures. (*B*) The fascia was retracted. No clear foreign body reaction was found in the abdominal wall in proximity to the mesh. (*C*) The mesh was removed with no effort.

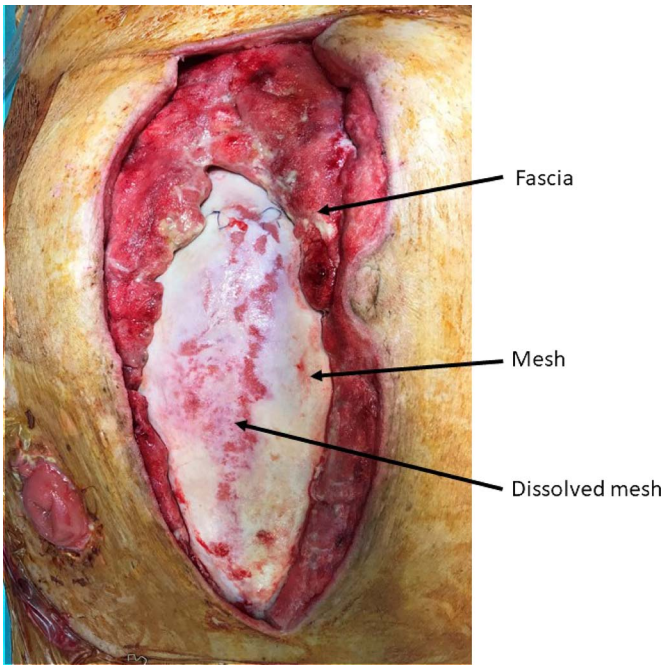

Figure 3. The Strattice mesh was resorbed in presence of intra-abdominal infection. Twenty days postoperative, the abdomen had to be revised because of fascial dehiscence. Intraoperatively, the mesh was partially dissolved, and the abdominal fasciae were retracted. The intra-abdominal contents are visible through the dissolved mesh.

but higher resistance to infection are needed. The Strattice acellular porcine dermal mesh has been chosen for the current study because of its highly reported success and low incidence for hernia recurrence compared with several other biologic meshes.[21,22] However, this prospective randomized controlled clinical trial did not recapitulate these findings in the setting of emergency abdominal surgery. Thus, primary mesh augmentation with polypropylene meshes or early abdominal closure remains the only alternatives in the context of damage-control surgery.[23]

Biologic and biosynthetic meshes have been proposed to potentially overcome SSI in the contaminated abdomen.[16,24] Over the last decade, different mesh materials have been approved by the US Food and Drug Administration[25]; however, some studies did not report a reduction in the incidence of SSI when using biologic meshes.[26] The current study further supports these findings, revealing that the intra-abdominal implantation of a biologic mesh increases the incidence of serious abdominal wall-related complications in the contaminated abdomen. This observation is of particular importance because biologic meshes are expensive, whereas large-pore polypropylene-based meshes may be better suited to reinforce the abdominal wall in the presence of contamination.[27]

The type of mesh-related complication in our study cohort may be attributed to specific mesh properties. The acellular porcine matrix has the theoretical advantage of being biodegradable combined with a low foreign body reaction and should therefore decrease long-lasting mesh infections and overwhelming scarring.[15,28] Such data have been found only in animal models but, as shown by the current study, is not translatable into clinical practice.[15] For instance, the biodegradable properties did result in a near complete loss of the mesh in the presence of SSI in one patient in our cohort. On the other hand, the low foreign body reaction potentially led to failed mesh integration into the abdominal wall and resulted in fascial dehiscence. This observation is in line with experimental data showing that biologic meshes are highly unstable.[29,30]

The limitation of this study is the fact that only one type of biologic mesh was studied, and therefore, the current results may not entirely be translatable to other biologic meshes. However, no study has revealed relevant differences in the resistance to SSI between various types of biologic meshes.[31] No long-term results are available from the current study because (1) the study

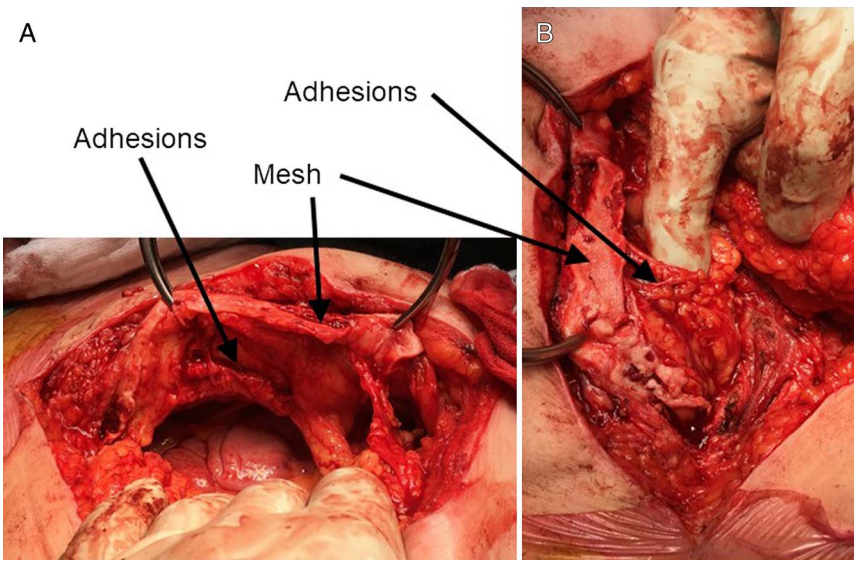

Figure 4. Adhesions and mesh infection in the presence of an intra-abdominal Strattice mesh. (*A, B*) One hundred twelve days after discontinuity resection because of perforated diverticulitis and implantation of a biologic mesh, colostomy reversal was performed. Intraoperatively, serious adhesion formation from the abdominal bowel/omentum to the mesh and mesh infection were observed. The mesh had to be partially removed.

had to be terminated early and (2) mortality was high because a high-risk population was analyzed. Furthermore, surgical revisions for abdominal wall complications were not foreseen as a secondary outcome parameter of the current study and not systematically assessed during the follow-up. However, all electronic patient records were meticulously screened for revisional surgical procedures. It is of importance to note that the current study included patients undergoing open surgery only. Open intraperitoneal mesh implantation has been linked to an increased risk of postoperative complication compared with laparoscopy.[32]

CONCLUSIONS

In the current randomized controlled trial, intraperitoneal biologic Strattice mesh implantation was associated with significantly more frequent high-grade abdominal wall complications in patients undergoing emergency abdominal surgery. Based on these results, the use of such meshes cannot be recommended in the contaminated environment of emergency abdominal surgery.

AUTHORSHIP

M.O.J. contributed in the study design, data acquisition, data analysis, and drafting article. T.H. contributed in the data acquisition, data analysis, and drafting article. D.C. contributed in the study design, data analysis, and revision of article. G.B. contributed in the study design, data analysis, drafting article, and revision of article.

DISCLOSURE

For all authors, no conflicts are declared. This study has been financially supported by Strattice, Allergan.
Trial registration: ClinicalTrials.gov Identifier: NCT 01110798.
Compliance with ethical requirements: Informed consent was obtained from all individual participants included in the study. This study has been approved by the ethics committee of the canton of Bern, Switzerland.

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