International Journal of Surgery 65 (2019) 120–127

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.elsevier.com/locate/ijsu

Original Research

Repair of complex abdominal wall hernias with a cross-linked porcine acellular matrix: cross-sectional results of a Dutch cohort study

Ruth Kaufmann (MD, PhD)[a,*,1], Lucas Timmermans[a,1], Yu T. van Loon[b,c], Joseph P.A.M. Vroemen[d], Johannes Jeekel[e], Johan F. Lange[a]

[a] Department of Surgery, Erasmus University Medical Center, Wytemaweg 80, 3015 CN, Rotterdam, the Netherlands
[b] Department of Surgery, Zuyderland Medical Center, Henri Dunantstraat 5, 6419 PC, Heerlen, the Netherlands
[c] Department of Surgery, Elisabeth TweeSteden Hospital, Dr. Deelenlaan 5, 5042 AD, Tilburg, the Netherlands
[d] Department of Surgery, Amphia Hospital, Molengracht 21, 4818 CK, Breda, the Netherlands
[e] Department of Neuroscience, Erasmus University Medical Center, Wytemaweg 80, 3015 CN, Rotterdam, the Netherlands

ARTICLE INFO

Keywords:
Complex hernia
Contamination
Incisional hernia
Biological mesh
Complication
Quality of life

ABSTRACT

Background: The use of synthetic mesh in potentially contaminated and contaminated incisional hernias may lead to a higher morbidity and mortality. Biological meshes may provide a solution, but since these meshes are rarely used, little is known about long-term results. The aim of this cohort study was to evaluate the long-term clinical efficacy and patient satisfaction following Permacol™ in complex abdominal wall hernia repair (CAWHR) patients in a cross-sectional fashion.

Materials and methods: All patients were operated for CAWHR with Permacol™ in the Netherlands between 2009 and 2012. The design was a multicenter cross-sectional cohort study. The STROCSS statement was followed. Patients were interviewed, underwent abdominal examination, and completed quality-of-life questionnaires. ClinicalTrials.gov Identifier NCT02166112. Research Registry Identifier researchregistry4713.

Results: Seventy-seven patients were seen in the outpatient clinic. Their hernias were classified as potentially contaminated in 25 patients (32.5%) and infected in 52 patients (67.5%). The mean follow-up was 22.2 ± 12.6 months. The most frequent postoperative complication was wound infection (n = 21; 27.3%), meshes had to be removed in five patients (6.5%). By the time of their visit to the outpatient clinic, 22 patients (28.6%) had a recurrence of whom ten (13%) had undergone reoperation. Thirty-nine patients (50.6%) had bulging of the abdominal wall. Quality-of-life questionnaires revealed that patients graded their health status with a mean 6.8 (± 1.8) out of 10 points.

Conclusion: Bulging and recurrence are frequently observed in patients treated with Permacol™ for CAWHR. Considering both recurrence and bulging as undesirable outcomes of treatment, a total of 46 patients (59.7%) had an unfavorable outcome. Infection rates were high, but comparable with similar patient cohorts. Quality-of-life questionnaires revealed that patients were satisfied with their general health, but scored significantly lower on most quality-of-life modalities of the Short Form-36 questionnaire.

1. Introduction

As a rule nowadays incisional hernia is repaired with a mesh-assisted technique [1]. In potentially contaminated and infected incisional hernia the use of conventional synthetic mesh is controversial and may be dangerous: infected meshes are invalidating to the patient and may eventually be life-threatening.

Contamination can be caused by the presence of stoma, enterocutaneous fistula, bowel leakage, reanastomosis procedure, and burst abdomen, or may be present after the removal of an infected mesh. The grade of contamination is an important factor in the treatment of incisional hernia. Therefore, the Ventral Hernia Working Group (VHWG) developed a hernia grading system to classify the different grades of contamination and its treatment complexity in abdominal wall hernia repair (grade 1: low risk to grade 4: infected) [2].

The so-called complex abdominal wall hernia repair (CAWHR) is a

* Corresponding author. Erasmus University Medical Center Rotterdam, Room Ee-173, Wytemaweg 80, 3015 CN, Rotterdam, the Netherlands.
E-mail addresses: ruth.kaufmann@gmail.com (R. Kaufmann), l.timmermans@erasmusmc.nl (L. Timmermans), tinavanloon@gmail.com (Y.T. van Loon), josvroemen@gmail.com (J.P.A.M. Vroemen), j.jeekel@erasmusmc.nl (J. Jeekel), j.lange@erasmusmc.nl (J.F. Lange).
[1] Ruth Kaufmann and Lucas Timmermans contributed equally to this article.

https://doi.org/10.1016/j.ijsu.2019.03.023
Received 31 December 2018; Received in revised form 24 February 2019; Accepted 24 March 2019
Available online 01 April 2019
1743-9191/

surgical challenge. Patients often have multiple comorbidities and risk factors increasing the risk for postoperative complications and hernia recurrence. Patients who need CAWHR often undergo strictly planned, staged repair of their hernia defect [3]. At first, the aim is to achieve a reduction of bacterial load in the operation field by surgically debriding the operative area, temporary placing of conventional meshes or use of Vacuum-Assisted Therapy (VAC) or skin grafts to cover any granulating open abdominal defect. These surgical techniques are mostly combined with antibiotic treatment. Thereafter, definitive repair of the remaining hernia is planned. This staged repair is time consuming, uncomfortable for the patient, and is associated with higher healthcare costs and a decrease in quality of life.

Therefore a single-stage hernia repair would be a better alternative. In single-stage hernia repair the surgeon has to cope with the presence of contamination. In this situation biological meshes may provide a solution. These meshes, made of collagen of either human or animal origin, are associated with a lower infection risk and might increase the strength of primary repair [4]. However, little known is about long-term results, since these meshes are expensive and rarely used [5].

Permacol™ is a mesh prosthesis consisting of type I collagen, derived from porcine dermis. The mesh is produced by Sofradim, Trévoux, France; part of Covidien–Medtronic, New Haven, Connecticut, USA. The porcine dermis is processed to remove hair, cells, cell components, as well as other antigens present in the tissue [6]. After decellularization and degradation of the porcine dermal tissue, a 3D structure of collagen remains. Thereafter, the collagen fibers are chemically cross-linked with hexamethylene diisocyanate to increase the strength of the mesh and to slow-down the degradation of the mesh [3,6]. During degradation, ingrowth of host fibroblasts and collagen replacement can take place. This so-called xenograft remodeling begins directly after implantation and takes several months to years. In this article Permacol™ is referred to as cross-linked porcine acellular dermal matrix (X-PADM).

The aim of this study was to evaluate the indication for the use of cross-linked porcine acellular matrix and to assess the results of CAWHR in potentially contaminated and infected abdominal wall hernia (VHWG classification grade 3 and 4 [2]). We also assessed patient satisfaction following Permacol™ (X-PADM) repair.

2. Materials and methods

2.1. Patients

Patients were eligible for inclusion in this multi-center cohort study if they had been operated in the Netherlands between 2009 and 2012, with X-PADM mesh for the indication CAWHR. CAWHR was defined as a repair for a potentially contaminated to infected hernia, which is grade 3 to grade 4 according to the system developed by the VHWG [2]. Data of patients who had passed away within a year after X-PADM implantation were also analyzed.

2.2. Study design

A list with anonymized operation dates was disclosed to the research group by the company (Covidien–Medtronic, New Haven, Connecticut, USA). This list comprehended a registry of all X-PADM prostheses that were sold to hospitals in the Netherlands within the time-span of 2009–2012. This list contained only patients with grade 3 and grade 4 hernia according to the VHWG [2]. Additional information to match the operation dates with patient records was gathered from all hospitals, that had used X-PADM in the past to treat complicated abdominal wall defects. These hospital were both academic hospitals and community hospitals. Patients records were identified via contact with the operating surgeons. They identified their own patients from the list of anonymized operation dates.

All living patients received written information on the study and an invitation to participate. If informed consent was received, we invited patients to the outpatient clinic. During this visit, patients were interviewed to collect baseline parameters and their medical and abdominal operations history. Patient files were also retrospectively assessed to complete baseline parameters. Baseline parameters were defined as age, gender, BMI, length of follow-up, smoking history, and occupational heavy lifting. Medical history was focused on medical conditions like COPD/chronic coughing, steroid use, malignancy, diabetes, general abdominal operations and specific abdominal wall operations.

All patient underwent physical examination. Quality-of-life parameters were assessed with the following three questionnaires: EuroQol (EQ-5D-5L), Short Form-36 (SF-36) and Body Image Questionnaires (BIQ). The operating surgeons were interviewed on the indication for the use of X-PADM. The STROCSS statement was followed [7].

2.3. Outcomes

The primary endpoints were recurrence of abdominal wall hernia and bulging of the abdominal wall after X-PADM implantation. Both incisional hernia and recurrence were defined as any abdominal wall gap with or without bulge in the area of a postoperative scar perceptible or palpable by clinical examination or imaging [8]. Bulging was defined as a substantial increase in abdominal circumference, not explicable by weight gain, in the absence of a palpable or objectifiable fascia defect, and observed by either the patient or the doctor [9–11]. All patients were diagnosed by clinical examination.

Secondary outcomes included postoperative complications i.e. occurrence of wound infection, mesh infection, intra-abdominal abscess, skin abscess, seroma, hematoma, necrotic abdominal wall, fistulas, and burst abdomen. Also mesh explantations, additional abdominal operations, visits to the outpatient clinic, and quality-of-life parameters were recorded. The results of SF-36 were compared with the results of an incisional hernia population [12] together with the general Dutch population [13]. Patient files of deceased patients were also analyzed.

2.4. Ethical approval

This cohort study was ethically approved by the Ethics Board of the Erasmus University Medical Center in Rotterdam, the Netherlands. After ethical approval in the Erasmus University Medical Center, ethical approval from all ethical comities in all participating hospitals was achieved. The study and its research protocol were also registered at ClinicalTrials.gov with Identifier NCT02166112. The research protocol was not published in a journal. The research protocol was also registered in the Research Registry with Identifier researchregistry4713.

2.5. Statistical analysis

Continuous variables using means and standard deviations (SD) and categorical values with frequencies and percentages were all summarized. Correlations were assessed with Spearman's correlation coefficient and were tested with a two-tailed test of significance. All statistical analyses were performed using SPSS version 21.0.

3. Results

3.1. Patients characteristics

A total of 118 patients met the inclusion criteria, of whom 22 were deceased, 11 did not consent to participate in the study, and eight were lost to follow-up (Fig. 1). Seventy-seven patients (65.3%) were seen at the outpatient clinic (47 male, 30 female, mean age: 60 years). The ventral hernias were classified as potentially contaminated hernia in 25 patients (32.5%; grade 3 VHWG Classification) and infected hernia in 52 patients (67.5%; grade 4 VHWG Classification) [2]. The mean follow-up was 22.2 ± 12.6 months (Table 1).

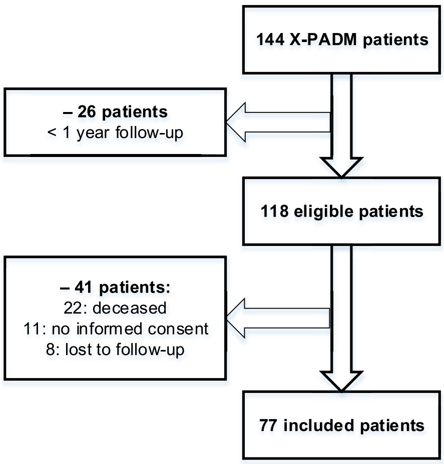

Fig. 1. Flow chart of included patients.

Table 1
Baseline criteria.

Mean follow-up (SD)	22.2 months (± 12.6)
Gender: male vs. female	n = 47 vs. n = 30
Age (SD)	60 year (± 11.4)
Body Mass Index (SD)	28.7 kg/m^2 (± 6.8)
Ventral Hernia Working Group Grade 3	25 (32.5%)
Ventral Hernia Working Group Grade 4	52 (67.5%)
Operations before X-PADM repair	4.8 (range 0–30)
Smoking	40 (57.1%)
Occupational heavy lifting	30 (46.2%)
COPD/chronic coughing	26 (37.7%)
Steroid use	24 (31.2%)
Malignancy	22 (31.4%)
Diabetes	17 (23.9%)

Table 2
Correlations between clinical outcome and risk factors.

	Bulging	Recurrence
Length	0.289	**0.034***
BMI	0.390	0.414
Hernia in history	0.273	**0.007****
History of SSI	0.191	0.082
History of burst abdomen	**0.023***	0.445
History of open abdomen treatment	0.101	**0.031***

*$p < 0.05$.
**$p < 0.01$.

In this cohort the three main risk factors for the development of a complex abdominal wall hernia were smoking (n = 40; 57.1%), occupational heavy lifting (n = 30; 46.2%), and COPD/chronic coughing (n = 26; 37.7%). Other risk factors were steroid use (n = 24; 31.2%), malignancy (n = 22; 31.4%), diabetes (n = 17; 23.9%), and a relatively high BMI (28.7 ± 6.8 kg/m^2). History of burst abdomen was significantly correlated with bulging and both length and hernia in history were significantly correlated with recurrence (Table 2). Other risk factor or patient characteristics were not significantly correlated to either bulging or recurrence.

The main reason for the use of X-PADM was potential contamination in the presence of a stoma (n = 38; 52.1%). Other indications for X-PADM use were enterocutaneous fistulas (n = 25; 34.2%), intra-abdominal abscess (n = 23; 31.9%), wound infection (n = 21; 27.3%), mesh infection (n = 18; 25.0%), open abdomen (n = 17; 23.6%), or anastomotic leakage (n = 10; 13.9%). Some patients had more than one of the previous mentioned indications. Therefore, the total number of indications exceeded the total number of patients.

In most cases the surface area of the actual defect was not defined in the patient's file. Therefore the derived factor “mesh surface” (from the patient's file) was recorded. The most frequently used mesh size was 20 cm by 30 cm (600 cm^2) as used in 22 patients (71.2%). Other sizes were 15 cm by 20 cm (300 cm^2) in 12 patients (22.7%), 20 cm by 40 cm (800 cm^2) in eight patients (12.1%), and 18 cm by 28 cm (504 cm^2) in seven patients (10.6%), respectively.

The meshes were placed in different anatomical planes: sublay in 31 patients (40.3%), intraperitoneal onlay mesh (IPOM) in 20 patients (26.0%), onlay in eight patients (10.4%), inlay in three patients (3.9%), and in 15 patients (19.5%) it remained unclear in which anatomical plane the mesh was placed. Component separation was performed in 26 patients. There were also 26 patients in which the fascia defect could not be closed tension-free. In these cases mesh bridging was performed.

3.2. Postoperative outcomes

Postoperative complications occurred in 30 patients (39%). The most frequent complication after X-PADM implantation was wound infection (n = 21; 27.3%). In five patients (6.5%) the mesh had to be removed due to mesh infection. The remaining 16 patients (20.8%) with wound infection could be treated conservatively by either use of antibiotics and/or the use of vacuum-assisted therapy. The incidence of wound infection was significantly correlated with a previous episode of mesh infection in the history of the patient, prior to the operation (not being the indication of the operation). Less frequent complications were enterocutaneous fistula (n = 4; 5.2%), skin necrosis (n = 3; 3.9%), and fascia dehiscence (n = 2; 2.6%). Although a high mortality in this series was observed, there was no evidence for mesh-related mortality. The group of deceased patients will be discussed separately.

3.3. Long term outcomes

Twenty-nine patients had no recurrence or bulging (37.7%). Twenty-two patients (28.6%) had a recurrence of abdominal wall hernia, of whom ten (13%) had undergone reoperation. Thirty-nine patients (50.6%) had bulging of the abdominal wall. A total of 15 patients suffered from both bulging and a recurrence (19.5%). Considering both recurrence and bulging as undesirable outcomes of treatment, a total of 46 patients (59.7%) had an unfavorable outcome.

No correlation was found between hernia recurrence and/or abdominal bulging and the anatomical plane in which the mesh was placed. Also bridging the hernia with mesh and VHWG Classification [2] were not significantly associated with recurrence and/or bulging. The results of physical examination were plotted in a Kaplan-Meier analysis (Fig. 2).

3.4. Quality-of-life parameters

Thirty-two patients (42%) were satisfied with the cosmetic result. Patients rated their scars with a mean of 6.0 ± 2.4 out of 10 points (10 being the best cosmetic outcome). Patients graded their general health at the moment of their visit to the outpatient clinic with a mean of 6.8 ± 1.8 out of 10 points (10 is the best health status).

When patients compared their postoperative general health status during their visit to the outpatient clinic with their health status a year before, it was graded “much better” in 20 patients (27.4%), and “somewhat better” in 13 patients (17.8%), which is an improvement in 45.2% of cases. In 26 patients (35.6%), the general health status was graded “about the same as one year ago”. In 14 patients a worsening occurred: in nine (12.3%) patients a small deterioration and in five patients (6.8%) a severe deterioration. In four patients, data were missing regarding the comparison between the current health status and the health status before.

Analysis of SF-36 questionnaires revealed that patients who had

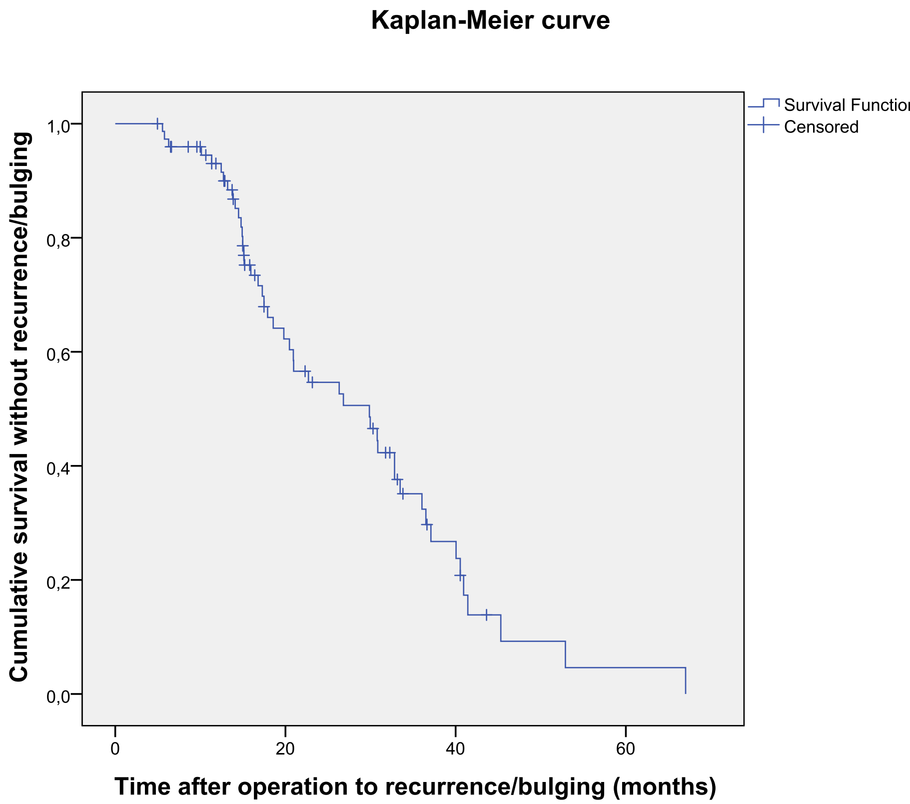

Fig. 2. Kaplan-Meier survival analysis (cumulative survival of patients without recurrence or bulging versus time of operation until recurrence or bulging (expressed in months)).

Table 3A
Quality-of-life analysis assessed with Short Form-36. The results of this cohort were compared with an incisional hernia population (Rickert, 2012) [9]. This incisional hernia population consists mainly of VHWG grade 1–2 patients.

Modality	X-PADM patient population Mean ± SD	Incisional hernia population Mean ± SD	Difference with incisional hernia population
Physical functioning	54.4 ± 28.7	80.2 ± 23.7	Significantly lower
Role physical	43.9 ± 44.3	69.6 ± 32.4	Significantly lower
Bodily Pain	54.4 ± 30.0	80.6 ± 20.6	Significantly lower
General health	49.0 ± 25.7	72.1 ± 19.5	Significantly lower
Vitality	57.5 ± 23.3	63.9 ± 17.0	Not significant
Social Functioning	67.3 ± 29.1	85.2 ± 20.4	Significantly lower
Role emotional	62.5 ± 46.1	78.2 ± 26.2	Significantly lower
Mental Health	75.9 ± 19.8	69.8 ± 13.7	Not significant

Table 3B
Quality-of-life analysis assessed with Short Form-36. The results of this cohort were compared with the Dutch validation sample of the SF-36 (Aaronson, 1998) [10]. This group consists of a random selection of the general Dutch population.

Modality	X-PADM patient population Mean ± SD	General Dutch population Mean ± SD	Difference with general Dutch population
Physical functioning	54.4 ± 28.7	76.8 ± 22.6	Significantly lower
Role physical	43.9 ± 44.3	70.8 ± 39.1	Significantly lower
Bodily Pain	54.4 ± 30.0	70.8 ± 24.2	Significantly lower
General health	49.0 ± 25.7	65.0 ± 19.7	Significantly lower
Vitality	57.5 ± 23.3	69.0 ± 18.9	Significantly lower
Social Functioning	67.3 ± 29.1	82.7 ± 22.5	Significantly lower
Role emotional	62.5 ± 46.1	82.4 ± 32.3	Significantly lower
Mental Health	75.9 ± 19.8	75.6 ± 17.8	Not significant

undergone CAWHR with X-PADM had a significantly lower score on six out of eight quality-of-life modalities, when compared with an incisional hernia population (VHWG grade1 and 2) [2]. The only two modalities that were not significantly different were the "mental health" status and "vitality" of both groups (Table 3A). When this cohort was compared to the general Dutch population, patients who had been treated for a complex abdominal wall hernia had a significantly lower score on seven out of eight quality-of-life modalities. The only modality that was not significantly different was the "mental health" status of both groups (Table 3B).

3.5. Deceased patients

The group of deceased patients consisted of 22 patients (18.6% of total cohort): 12 males (54.5%) and ten females (45.5%). The mean age at decease was 67.8 ± 11.8 years and the postoperative survival after X-PADM was 124.6 ± 159.5 days. Only two of the deceased patients (9.1%) survived more than one year after CAWHR. Causes for decease were formally unknown due to no autopsy in 15 patients (68.2%), abdominal sepsis/septic shock in three patients (13.6%), general clinical deterioration in two patients (9.1%), respiratory insufficiency in one patient (4.5%), and cardiac arrest in one patient (4.5%). Mortality seemed not associated with the mesh; all patients passed away due to a deterioration in general health caused by the underlying disease (abdominal sepsis in the majority of the cases). Fifteen patients (68.2%) passed away during admission in hospital, three patients (13.6%) deceased at home or in a nursing home, and in four patients (18.2%) it remained unknown where they passed away.

4. Discussion

Taking into account the complexity of potentially contaminated or infected ventral hernia, this Dutch cohort study demonstrates that repair of this category of abdominal wall hernia with X-PADM leads to disappointing results. There was bulging and recurrence in 59.7% of patients and infection rates were high. Quality-of-life questionnaires revealed that patients were satisfied with their general health, but scored significantly lower on most quality-of-life modalities of the Short Form-36 questionnaire.

4.1. Study approach

Since treatment of complex abdominal wall hernia with a biological mesh is relatively new, there are only a few studies comparable to ours with respect to characteristics and methodology. The RICH study, in which the results of Strattice™ mesh (Acelity™, non-cross-linked, acellular porcine dermis) were analyzed, seems to have the most similarities in methodological approach [14]. Also a recently published study of Nockolds et al. has a comparable methodological approach but had different inclusion criteria, leading to a quite heterogeneous patient group [15]. Most other studies differ with regard to the following characteristics: they were either single-center studies [15,16], presented retrospective data [17,18], involved small patient samples [15,19] analyzed heterogeneous patient groups (i.e. different types of hernias, repairs or meshes in one study [15,20]), used different surgical techniques, had a different follow-up period (9.1 months in Diaz et al. [17] to 24.0 months in Itani et al. [14]), applied the Ventral Hernia Working Group grading system less stringently [21,22], had a different patient population, or analyzed a different biological mesh prosthesis [14,17,18]. The current study is a multicenter cohort study, with a carefully selected patient group, of whom cross-sectional data were collected. In addition, quality of life was also assessed. This is an important but rarely studied item in CAWHR research. To our knowledge, other studies with quality-of-life assessment in this specific patient group have not been published yet. Therefore, the current study gives a more complete impression of the efficacy of X-PADM in the treatment of potentially contaminated and infected ventral hernia (VHWG grade 3–4) [2].

After completion of the study, two new classifications for complex abdominal wall hernia were proposed. In this study, the VHWG classification was used to classify the severity of the complex abdominal wall hernias [2]. Later in 2012 the modified VHWG classification was proposed [23]. The modified VHWG classification was divided into grade 1 to 3 (grade 1: low risk, grade 2: co-morbid, grade 3A: clean-contaminated, grade 3B: contaminated, and grade 3C: dirty) instead of grade 1 to 4 in the VHWG classification [2]. The aim of Kanters et al. was to propose a new classification to improve the accuracy of predicting surgical site occurrences after complex abdominal wall hernia repair [23]. Reclassifying this patient cohort could lead to a shift of patients from VHWG classification grade 3 and 4 into modified VHWG classification grade 3B of grade 3C. Another classification for complex abdominal wall hernia was proposed by Slater et al. [24]. This new classification takes more different factors into account. This new classification is – compared with the VHWG classification [2] – extended with the categories “size and location” (of hernia) and ”clinical scenario” (of patient). Another difference, is the subdivision of the group complex abdominal wall hernia into the severity classes minor, moderate and major. In this new classification, most of our patients would be scored as “complex abdominal wall hernia, severity grade major”. This could lead to a shift of patients from VHWG classification grade 3 into the group of complex abdominal wall hernia, severity major [24].

4.2. Patient group

In this study, patients were enrolled belonging to a very difficult treatment group. All patients had a potentially contaminated or infected ventral hernia i.e. grade 3 to 4 hernia according to the VHWG classification [2]. Moreover, two-third of this cohort consisted of patients with an infected hernia (VHWG classification grade 4). In addition to a complex abdominal wall hernia, most patients suffered from multiple comorbidities and risk factors which increased the risk of postoperative complications such as wound infection and hernia recurrence.

Risk factors seen in the underlying cohort study included smoking, preoperative wound infection, and COPD. Other risk factors mentioned in literature are age, pre-existent disease (obesity, diabetes, hypertension, American Society of Anesthesiologists (ASA) score > 3), operation setting (emergency presentation and operation, duration of operation, fistula at the time of operation, defect size > 30 cm^2), and hospital stay over 14 days [25,26]. In other studies these risk factors are associated with more postoperative wound infections [25,26]. In this study the incidence of postoperative wound infection was significantly correlated with a previous episode of mesh infection. This episode of mesh infection was defined as an episode some time before the operation with X-PADM, not representing the actual indication for this operation. To our knowledge, this finding was not reported in other studies. A hypothesis could be that there is some ongoing state of infection, there might be a spill of encapsulated bacterial material during the operation, or that patients have a poor immune response to invasion of bacteria. However, the exact mechanism is unclear. We did not find this correlation with postoperative wound infection for other patient characteristics and risk factors.

A history of burst abdomen was significantly correlated with bulging. Burst abdomen can lead to loss of domain of the abdominal wall. To achieve a tension-free closure of the abdominal wall, surgeons use in some patients the technique of component separation [27]. Thereafter, a relative weakness of the abdominal wall can occur, due to separation of different components in the abdominal wall. This could lead to an increasing risk for bulging. Progressive bulging might be the result of failure of the mesh implant due to elongation [28].

Both length of the patient and other abdominal wall hernias in history were significantly correlated with recurrence. The correlation with the length of the patient could be a coincidence. Since we found no other studies reporting this correlation, we can only hypothesize what the cause can be. One could consider a longer abdominal wall and therefore a larger force on a mesh prosthesis when implanted in a longer/larger abdominal wall. About one-fifth of these patients had a hernia in their history (not being the indication for X-PADM placement). Since we investigated CAWHR, many patients had a hernia in history or a hernia as indication for X-PADM placement. Therefore this correlation is not a “true” correlation. Other risk factor or patient characteristics were not significantly correlated to either bulging or recurrence.

4.3. Long-term postoperative results

The hernia recurrence rate found in this study (28.6%) was similar to that seen in the RICH study. This study evaluated patients treated with Strattice™ mesh for contaminated incisional hernia two years after their operation and had a recurrence rate of 28%. Rosen et al. had a much higher recurrence rate of over 50% after three years follow-up [16]. This high recurrence rate could possibly be explained by the use of a different mesh (non-cross-linked biological mesh) and a longer follow-up. Only ten out of 77 patients in this study underwent reoperation to treat hernia recurrence, which is relatively low in comparison with other studies published in literature [16,17]. Despite the relatively low rate of hernia recurrence in this study, a high rate of abdominal wall bulging was observed in more than half of all patients. This finding was also seen in other studies, but these studies displayed a lower percentage of bulging than the present study [29,30]. An explanation for this difference could be that larger hernia defects were included in this study in which patients had a higher VHWG classification.

The high rate of abdominal wall bulging could also be secondary to an intense inflammatory response to X-PADM without (or with insufficient) xenograft remodeling. The inflammatory response on X-PADM in experimental animal models is ranging from mild/low [31] to moderate [32]. Due to the variety in animal species, it is difficult to extrapolate these results to the human situation. There is a recent publication available with X-PADM meshes that were explanted from humans [33]. In this study, the authors examined seven explanted X-PADM meshes and analyzed these histologically. Their conclusion was that the explants lacked identifiable biologic behavior; i.e. absence of xenograft remodeling and a large variety in histological response. However, these conclusions are based on only seven X-PADM explants.

In another attempt to acquire data for the human situation, Grotenhuis et al. [34] performed an in vitro study in which was shown that X-PADM in a human macrophage culture model led to mild local inflammation. The latter study implies that local inflammation in X-PADM might not be the explanation for the large amount of patients suffering from bulging. However, evidence is not strong yet and partly contradictory.

4.4. Operation techniques and plane of mesh placement

It is generally assumed, that complete fascial closure is the preferred method in CAWHR, and that the bridging technique increases the risk for recurrence and bulging. In spite of these assumptions, we found no significant association between hernia recurrence and/or abdominal bulging and the anatomical plane in which the mesh was placed. Also bridging was not significantly associated with recurrence and/or bulging. These results are confirmed by studies of Iacco et al. [3] and Sbitany et al. [35]. However, Lupinacci et al. did find a significant association between bridging and recurrence in a smaller group of patients [21].

4.5. Postoperative complications

Since two-third of the patients in this cohort had an infected hernia, one could expect that there would be a higher incidence of postoperative wound infections than in other studies in literature [14,17,18]. Against our expectation, we found less surgical site infections (27.3%) than found in the RICH study [14] (35%) and the study by Diaz et al. [17] (33% infections). The infection rates as observed are similar to those found by Helton et al. [18] (23%). This is an interesting finding, because the other studies mainly included patients with VHWG grade 2–3. Therefore, the results in this study with mainly VHWG grade 4 patients are still high, though comparable with other studies.

Although 21 patients in this study suffered from wound infection, many of these infections could be treated conservatively. The mesh removal rate following a wound infection was 6.5% in the current study, a rate similar to that seen in the study of Diaz et al. [17] but lower than that seen by Helton et al. [18] and Rosen et al. [16]. Rosen et al. investigated a large group of CAWHR patients and found a wound complication rate of 47.7%. Despite this high number of wound complications, Rosen et al. found no long-term infectious complications related to the biological mesh [16].

Recent studies about X-PADM by Giordano et al. [36] and Doussot et al. [37] concluded that X-PADM is safe and effective for complex abdominal wall hernia. Giordano et al. assessed a group of 109 patients and found that the recurrence rates at one and two years were 9.2 and 18.3%, respectively, and were higher in cases without fascial closure. Doussot et al. assessed the short-term and long-term outcomes of a group of 250 patients undergoing abdominal wall hernia repair with X-PADM [37]. They found a one-year, two-year, and three-year recurrence-free survival of 90%, 74% and 57%, respectively. They concluded that single-stage abdominal wall hernia repair is feasible using X-PADM. However, mortality and complication rates are high due to patients' comorbidities and the degree of contamination of the operative field. An important disclaimer is that given the observed recurrence rate, the benefit of biological meshes remains to be ascertained.

Sainfort et al. assessed the literature regarding all available biological abdominal wall implants [38]. They concluded that in the current state of knowledge, there are no high-level evidence data on the therapeutic contribution of biological meshes that allow prioritization of the various biological meshes according to their characteristics or their different manufacturing processes. Tripolli et al. [39] also assessed the available literature regarding five biological meshes (Permacol™, Strattice™, Surgisis®, Tutomesh™, and XenMatrix™). They found 11 studies of a poor methodological quality. A significantly lower rate of recurrence at 12 months was found for Permacol™ compared with Strattice™. They concluded that the different types of meshes showed a marked statistical variability in the clinical outcomes.

4.6. Financial implications

Biological meshes are expensive and rarely used [5]. In this study no cost analysis was performed. A previous study by Byrge et al. compared head-to-head the costs of using Permacol™ and Strattice™ meshes in a similar patient group. The costs of the mesh were significantly higher for Strattice™ (median cost $8940) compared to Permacol™ (median costs $1600). The use of Permacol™ resulted in a savings of $181,320 with similar clinical outcomes when compared with Strattice™ [40]. Another alternative could be found in the use of biosynthetic meshes (i.e. slowly resorbable synthetic meshes like Phasix™ Mesh (poly-4-hydroxybutyrate), GORE® BIO-A® Mesh (poly(glycolide:trimethylene carbonate) copolyme), and TIGR® Matrix Surgical mesh (fast-resorbing fiber: copolymer of glycolide, lactide, and trimethylene carbonate (40% of weight) and a slow resorbing fiber: copolymer of lactide, and trimethylene carbonate (60% of weight)). In a recent consensus review by Köckerling et al., all available literature about these meshes was assessed, but concluded was that there is lack of studies comparing the use of biological or biosynthetic versus synthetic meshes in complex abdominal wall hernia [41].

4.7. Mortality

A mortality of 22 patients (18.6%) was observed in this cohort. Reported mortality in other studies varied between 2.4% [35] and 15–22% [3]. Reported mortality rates strongly depend on the inclusion criteria in these studies. Mortality is not only depending on the design of the study (retrospective, cross-sectional, or prospective analyses), but also on the inclusion criteria (type of abdominal wall hernia, VHWG classification, analysis of living patients only). The design of this study and its results are comparable to the study of Iacco et al. [3]. We possibly found a relatively high mortality due to high number of VHWG grade 3–4 patients in this initial cohort.

4.8. Limitations

The outcome of this study may have been influenced by the small numbers, the heterogeneity, and the high mortality in this study. There is also another methodological limitation: the current study was designed as a cohort study assessing cross-sectional data (partly retrospective, partly prospective). A well-performed full prospective trial would improve our knowledge on biological meshes even more. We also have to take into account that there might be a difference in clinical outcomes between cross-linked and non-cross-linked collagen mesh prostheses. Since convincing evidence is lacking and no head-to-head studies were performed, the impact of cross-linking on the outcome cannot be judged. Further studies on this topic are required.

5. Conclusion

Our results of repair of potentially contaminated and infected complex abdominal wall hernias with Permacol™ show that bulging and recurrence are frequently observed (59.7% of patients). Infection rates were high (27.3%), but comparable with similar patient cohorts. Quality-of-life questionnaires revealed that patients were satisfied with their general health, but scored significantly lower on most quality-of-life modalities of the Short Form-36 questionnaire. Until now no ideal mesh has been identified for complex abdominal wall hernia repair. Therefore future studies are required.

Ethical approval

This cohort study was ethically approved by the Ethics Board of the Erasmus University Medical Center in Rotterdam, the Netherlands. After ethical approval in the Erasmus University Medical Center, ethical approval from all ethical comities in all participating hospitals was achieved. There is no Judgement's reference number (study is registered by name: The Permacol Dutch Cohort study).

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. A list with anonymized operation dates was disclosed to the research group by Covidien, Mansfield MA, USA. The company was not involved in the design of the study, the conduct of the study, the analysis of the results, or the preparation of the manuscript.

Author contribution

R. Kaufmann: study design, data collections, data analysis, writing.
L. Timmermans: study design, data collections, data analysis, writing.
Y.T. van Loon: data collections, writing.
J.P.A.M. Vroemen: data collections, data analysis, writing.
J. Jeekel: study design, data analysis, writing.
J.F. Lange: study design, data analysis, writing.

Conflicts of interest

R. Kaufmann declares no conflict of interest.
L. Timmermans declares no conflict of interest.
Y.T. van Loon declares no conflict of interest.
J.P.A.M. Vroemen declares no conflict of interest.
J. Jeekel declares no conflict of interest.
J.F. Lange declares conflict of interest not directly related to the submitted work (grants from Covidien/Medtronic for different studies).

Trial registry number

The study was registered at ClinicalTrials.gov with Identifier NCT02166112.
The study was registered at Research Registry with UIN Research Registry 4713.

Guarantor

R. Kaufmann and J.F. Lange.

Provenance and peer review

Not commissioned, externally peer-reviewed.

CRediT authorship contribution statement

Ruth Kaufmann: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Writing - original draft. **Lucas Timmermans:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Writing - review & editing. **Yu T. van Loon:** Data curation, Investigation, Writing - review & editing. **Joseph P.A.M. Vroemen:** Data curation, Investigation, Writing - review & editing. **Johannes Jeekel:** Conceptualization, Investigation, Methodology, Supervision, Validation. **Johan F. Lange:** Conceptualization, Investigation, Methodology, Supervision, Validation.

Acknowledgement

The authors would like to thank all patients and hospitals that participated in this study.

Appendix ASupplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijsu.2019.03.023.

References

[1] J.W. Burger, R.W. Luijendijk, W.C. Hop, J.A. Halm, E.G. Verdaasdonk, J. Jeekel, Long-term follow-up of a randomized controlled trial of suture versus mesh repair of incisional hernia, Ann. Surg. 240 (4) (2004) 578–583 discussion 83-5.
[2] Ventral Hernia Working Group, K. Breuing, C.E. Butler, S. Ferzoco, M. Franz, C.S. Hultman, et al., Incisional ventral hernias: review of the literature and recommendations regarding the grading and technique of repair, Surgery 148 (3) (2010) 544–558.
[3] A. Iacco, A. Adeyemo, T. Riggs, R. Janczyk, Single institutional experience using biological mesh for abdominal wall reconstruction, Am. J. Surg. 208 (3) (2014 Sep) 480–484, https://doi.org/10.1016/j.amjsurg.2013.09.020 discussion 483-4, Epub 2013 Dec 25.
[4] M.M. Abdelfatah, N. Rostambeigi, E. Podgaetz, M.G. Sarr, Long-term outcomes (> 5-year follow-up) with porcine acellular dermal matrix (Permacol) in incisional hernias at risk for infection, Hernia 19 (1) (2015 Feb) 135–140, https://doi.org/10.1007/s10029-013-1165-9 Epub 2013 Oct 16.
[5] A. Darehzereshki, M. Goldfarb, J. Zehetner, A. Moazzez, J.C. Lipham, R.J. Mason, et al., Biologic versus nonbiologic mesh in ventral hernia repair: a systematic review and meta-analysis, World J. Surg. 38 (1) (2014) 40–50.
[6] B. Chand, M. Indeck, B. Needleman, M. Finnegan, K.R. Van Sickle, B. Ystgaard, et al., A retrospective study evaluating the use of Permacol surgical implant in incisional and ventral hernia repair, Int. J. Surg. 12 (4) (2014) 296–303.
[7] R.A. Agha, M.R. Borrelli, M. Vella-Baldacchino, R. Thavayogan, D.P. Orgill, for the STROCSS Group, The STROCSS statement: strengthening the reporting of cohort studies in surgery, Int. J. Surg. 46 (2017) 198–202.
[8] M. Korenkov, A. Paul, S. Sauerland, E. Neugebauer, M. Arndt, J.P. Chevrel, et al., Classification and surgical treatment of incisional hernia. Results of an experts' meeting, Langenbeck's Arch. Surg. 386 (1) (2001) 65–73.
[9] J. Heisterkamp, P.T. den Hoed, J. Kluin, W.F. Weidema, C.J. van Steensel, Long-term results after modified Gallie technique for incisional hernia repair: results in 19 patients, Hernia 9 (1) (2005) 12–15.
[10] K. Mitura, M. Skolimowska-Rzewuska, K. Garnysz, Outcomes of bridging versus mesh augmentation in laparoscopic repair of small and medium midline ventral hernias, Surg. Endosc. 31 (1) (2017) 382–388.
[11] E.J. Schoenmaeckers, E.B. Wassenaar, J.T. Raymakers, S. Rakic, Bulging of the mesh after laparoscopic repair of ventral and incisional hernias, J. Soc. Laparoendosc. Surg. 14 (4) (2010) 541–546.
[12] A. Rickert, P. Kienle, A. Kuthe, P. Baumann, R. Engemann, J. Kuhlgatz, et al., A randomised, multi-centre, prospective, observer and patient blind study to evaluate a non-absorbable polypropylene mesh vs. a partly absorbable mesh in incisional hernia repair, Langenbeck's Arch. Surg. 397 (8) (2012) 1225–1234.
[13] N.K. Aaronson, M. Muller, P.D. Cohen, M.L. Essink-Bot, M. Fekkes, R. Sanderman, et al., Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations, J. Clin. Epidemiol. 51 (11) (1998) 1055–1068.
[14] K.M. Itani, M. Rosen, D. Vargo, S.S. Awad, G. Denoto 3rd, C.E. Butler, et al., Prospective study of single-stage repair of contaminated hernias using a biologic porcine tissue matrix: the RICH Study, Surgery 152 (3) (2012) 498–505.
[15] C.L. Nockolds, J.P. Hodde, P.S. Rooney, Abdominal wall reconstruction with components separation and mesh reinforcement in complex hernia repair, BMC Surg. 14 (1) (2014) 25.
[16] M.J. Rosen, D.M. Krpata, B. Ermlich, J.A. Blatnik, A 5-year clinical experience with single-staged repairs of infected and contaminated abdominal wall defects utilizing biologic mesh, Ann. Surg. 257 (6) (2013) 991–996.

[17] J.J. Diaz Jr., J. Guy, M.B. Berkes, O. Guillamondegui, R.S. Miller, Acellular dermal allograft for ventral hernia repair in the compromised surgical field, Am. Surg. 72 (12) (2006) 1181–1187 discussion 7-8.

[18] W.S. Helton, P.M. Fisichella, R. Berger, S. Horgan, N.J. Espat, H. Abcarian, Short-term outcomes with small intestinal submucosa for ventral abdominal hernia, Arch. Surg. 140 (6) (2005) 549–560 discussion 60-2.

[19] P. Gentile, G.M. Colicchia, F. Nicoli, G. Cervelli, C.B. Curcio, L. Brinci, et al., Complex Abdominal Wall Repair Using a Porcine Dermal Matrix, Surgical innovation, 2011.

[20] A.W. Cheng, M.A. Abbas, T. Tejirian, Outcome of abdominal wall hernia repair with Permacol biologic mesh, Am. Surg. 79 (10) (2013) 992–996.

[21] R.M. Lupinacci, A.S. Gizard, E. Rivkine, C. Debove, F. Menegaux, C. Barrat, et al., Use of a Bioprosthetic Mesh in Complex Hernia Repair: Early Results from a French Multicenter Pilot Study, Surgical innovation, 2014.

[22] T.S. Satterwhite, S. Miri, C. Chung, D.A. Spain, H.P. Lorenz, G.K. Lee, Abdominal wall reconstruction with dual layer cross-linked porcine dermal xenograft: the "Pork Sandwich" herniorraphy, J. Plast. Reconstr. Aesthet. Surg. 65 (3) (2012) 333–341.

[23] A.E. Kanters, D.M. Krpata, J.A. Blatnik, Y.M. Novitsky, M.J. Rosen, Modified hernia grading scale to stratify surgical site occurrence after open ventral hernia repairs, J. Am. Coll. Surg. 215 (6) (2012) 787–793.

[24] N.J. Slater, A. Montgomery, F. Berrevoet, A.M. Carbonell, A. Chang, M. Franklin, et al., Criteria for definition of a complex abdominal wall hernia, Hernia 18 (1) (2014) 7–17.

[25] M.N. Mavros, S. Athanasiou, V.G. Alexiou, P.K. Mitsikostas, G. Peppas, M.E. Falagas, Risk factors for mesh-related infections after hernia repair surgery: a meta-analysis of cohort studies, World J. Surg. 35 (11) (2011) 2389–2398.

[26] T.S. Satterwhite, S. Miri, C. Chung, D. Spain, H.P. Lorenz, G.K. Lee, Outcomes of complex abdominal herniorrhaphy: experience with 106 cases, Ann. Plast. Surg. 68 (4) (2012) 382–388.

[27] M.J. Rosen, J. Fatima, M.G. Sarr, Repair of abdominal wall hernias with restoration of abdominal wall function, J. Gastrointest. Surg. 14 (1) (2010) 175–185.

[28] E.B. Deerenberg, J. Verhelst, S.E.R. Hovius, J.F. Lange, Mesh expansion as the cause of bulging after abdominal wall hernia repair, Int. J. Surg. Case Rep. 28 (2016) 200–203.

[29] E.I. Lee, C.J. Chike-Obi, P. Gonzalez, R. Garza, M. Leong, A. Subramanian, et al., Abdominal wall repair using human acellular dermal matrix: a follow-up study, Am. J. Surg. 198 (5) (2009) 650–657.

[30] H.J. Lin, N. Spoerke, C. Deveney, R. Martindale, Reconstruction of complex abdominal wall hernias using acellular human dermal matrix: a single institution experience, Am. J. Surg. 197 (5) (2009) 599–603 (discussion).

[31] M.H. Schreinemacher, K.W. van Barneveld, R.E. Dikmans, M.J. Gijbels, J.W. Greve, N.D. Bouvy, Coated meshes for hernia repair provide comparable intraperitoneal adhesion prevention, Surg. Endosc. 27 (11) (2013) 4202–4209.

[32] M. Ditzel, E.B. Deerenberg, N. Grotenhuis, J.J. Harlaar, K. Monkhorst, Y.M. Bastiaansen-Jenniskens, et al., Biologic meshes are not superior to synthetic meshes in ventral hernia repair: an experimental study with long-term follow-up evaluation, Surg. Endosc. 27 (10) (2013) 3654–3662.

[33] G.S. De Silva, D.M. Krpata, Y. Gao, C.N. Criss, J.M. Anderson, H.T. Soltanian, et al., Lack of identifiable biologic behavior in a series of porcine mesh explants, Surgery 156 (1) (2014) 183–189.

[34] N. Grotenhuis, Y. Bayon, J.F. Lange, G.J. Van Osch, Y.M. Bastiaansen-Jenniskens, A culture model to analyze the acute biomaterial-dependent reaction of human primary macrophages, Biochem. Biophys. Res. Commun. 433 (1) (2013) 115–120.

[35] H. Sbitany, E. Kwon, H. Chern, E. Finlayson, M.G. Varma, S.L. Hansen, Outcomes analysis of biologic mesh use for abdominal wall reconstruction in clean-contaminated and contaminated ventral hernia repair, Ann. Plast. Surg. 75 (2) (2015 Aug) 201–204, https://doi.org/10.1097/SAP.0000000000000030.

[36] P. Giordano, R.D. Pullan, B. Ystgaard, F. Gossetti, M. Bradburn, A.J. McKinley, et al., The use of an acellular porcine dermal collagen implant in the repair of complex abdominal wall defects: a European multicentre retrospective study, Tech. Coloproctol. 19 (7) (2015) 411–417.

[37] A. Doussot, F. Abo-Alhassan, S. Derbal, I. Fournel, F. Kasereka-Kisenge, T. Codjia, et al., Indications and outcomes of a cross-linked porcine dermal collagen mesh (Permacol) for complex abdominal wall reconstruction: a multicenter audit, World J. Surg. 43 (3) (2019 Mar) 791–797, https://doi.org/10.1007/s00268-018-4853-x.

[38] A. Sainfort, I. Denis Hallouard, D. Hartmann, G. Aulagner, Y. Francois, O. Tiffet, et al., Xenograft biologic mesh in parietal and general surgery: technical assessment and review of clinical effectiveness and safety data, J. Vis. Surg. 153 (6) (2016) 403–417.

[39] S. Trippoli, E. Caccese, G. Tulli, P. Ipponi, C. Marinai, A. Messori, Biological meshes for abdominal hernia: lack of evidence-based recommendations for clinical use, Int. J. Surg. 52 (2018) 278–284.

[40] N. Byrge, M.C. Mone, D. Vargo, Hospital wide porcine mesh conversion results in cost savings with equivalent clinical outcomes, Am. J. Surg. 213 (6) (2017) 1042–1045.

[41] F. Kockerling, N.N. Alam, S.A. Antoniou, I.R. Daniels, F. Famiglietti, R.H. Fortelny, et al., What is the evidence for the use of biologic or biosynthetic meshes in abdominal wall reconstruction? Hernia 22 (2) (2018) 249–269.