SOFT-TISSUE RECONSTRUCTION USING BIOLOGIC TISSUE MATRIX: WHERE DO WE STAND?

EDITED BY: Ferdinand Köckerling
PUBLISHED IN: Frontiers in Surgery

frontiers Research Topics

frontiers

ISSN 1664-8714
ISBN 978-2-88945-503-4
DOI 10.3389/978-2-88945-503-4

About Frontiers

Frontiers is more than just an open-access publisher of scholarly articles: it is a pioneering approach to the world of academia, radically improving the way scholarly research is managed. The grand vision of Frontiers is a world where all people have an equal opportunity to seek, share and generate knowledge. Frontiers provides immediate and permanent online open access to all its publications, but this alone is not enough to realize our grand goals.

Frontiers Journal Series

The Frontiers Journal Series is a multi-tier and interdisciplinary set of open-access, online journals, promising a paradigm shift from the current review, selection and dissemination processes in academic publishing. All Frontiers journals are driven by researchers for researchers; therefore, they constitute a service to the scholarly community. At the same time, the Frontiers Journal Series operates on a revolutionary invention, the tiered publishing system, initially addressing specific communities of scholars, and gradually climbing up to broader public understanding, thus serving the interests of the lay society, too.

Dedication to quality

Each Frontiers article is a landmark of the highest quality, thanks to genuinely collaborative interactions between authors and review editors, who include some of the world's best academicians. Research must be certified by peers before entering a stream of knowledge that may eventually reach the public - and shape society; therefore, Frontiers only applies the most rigorous and unbiased reviews.
Frontiers revolutionizes research publishing by freely delivering the most outstanding research, evaluated with no bias from both the academic and social point of view. By applying the most advanced information technologies, Frontiers is catapulting scholarly publishing into a new generation.

What are Frontiers Research Topics?

Frontiers Research Topics are very popular trademarks of the Frontiers Journals Series: they are collections of at least ten articles, all centered on a particular subject. With their unique mix of varied contributions from Original Research to Review Articles, Frontiers Research Topics unify the most influential researchers, the latest key findings and historical advances in a hot research area! Find out more on how to host your own Frontiers Research Topic or contribute to one as an author by contacting the Frontiers Editorial Office: researchtopics@frontiersin.org

SOFT-TISSUE RECONSTRUCTION USING BIOLOGIC TISSUE MATRIX: WHERE DO WE STAND?

Topic Editor:
Ferdinand Köckerling, Academic Teaching Hospital of Charité Medical School, Germany

Soft-tissue reconstruction for a variety of surgical conditions, such as abdominal wall hernia, hiatal hernia, stomal hernia, anal fistula and pelvic floor replacement remains a challenge. There is an insufficient level of high-quality evidence in the literature on the value of bioprosthetics for soft-tissue reconstruction. An expanded knowledge about their clinical efficacy is urgently needed.

Citation: Köckerling, F., ed. (2018). Soft-Tissue Reconstruction Using Biologic Tissue Matrix: Where Do We Stand?. Lausanne: Frontiers Media. doi: 10.3389/978-2-88945-503-4

Table of Contents

frontiers in Surgery

REVIEW
published: 26 September 2016
doi: 10.3389/fsurg.2016.00053

Prevention of Incisional Hernias with Biological Mesh: A Systematic Review of the Literature

Filip E. Muysoms[1†], An Jairam[2†], Manuel López-Cano[3], Maciej Śmietański[4,5], Guido Woeste[6], Iris Kyle-Leinhase[1], Stavros A. Antoniou[7,8], Ferdinand Köckerling[9] and BioMesh Study Group[‡]*

[1] Department of Surgery, Maria Middelares, Gent, Belgium, [2] Erasmus University Medical Center, Rotterdam, Netherlands, [3] Vall'd Hebron Hospital, Universidad Autónoma de Barcelona, Barcelona, Spain, [4] Department of Surgery, District Hospital in Puck, Puck, Poland, [5] Department of Radiology, Medical University of Gdansk, Gdansk, Poland, [6] Klinikum der Johann Wolfgang Goethe-Universität, Frankfurt am Main, Germany, [7] Center for Minimally Invasive Surgery, Hospital Neuwerk, Mönchengladbach, Germany, [8] Department of General Surgery, University of Heraklion, Crete, Greece, [9] Vivantes Hospital, Berlin, Germany

OPEN ACCESS

Edited by:
Vincenzo Neri,
University of Foggia, Italy

Reviewed by:
Gabriel Sandblom,
Karolinska Institutet, Sweden
Piero Chirletti,
Sapienza University of Rome, Italy

***Correspondence:**
Filip E. Muysoms
filip.muysoms@azmmsj.be

[†]Dr. Filip E. Muysoms and Dr. An Jairam have contributed equally to this study.

[‡]The members of the BioMesh Study Group are listed at the end of the article.

Specialty section:
This article was submitted to Visceral Surgery, a section of the journal Frontiers in Surgery

Received: *30 July 2016*
Accepted: *09 September 2016*
Published: *26 September 2016*

Citation:
Muysoms FE, Jairam A, López-Cano M, Śmietański M, Woeste G, Kyle-Leinhase I, Antoniou SA, Köckerling F and BioMesh Study Group (2016) Prevention of Incisional Hernias with Biological Mesh: A Systematic Review of the Literature. Front. Surg. 3:53. doi: 10.3389/fsurg.2016.00053

Background: Prophylactic mesh-augmented reinforcement during closure of abdominal wall incisions has been proposed in patients with increased risk for development of incisional hernias (IHs). As part of the BioMesh consensus project, a systematic literature review has been performed to detect those studies where MAR was performed with a non-permanent absorbable mesh (biological or biosynthetic).

Methods: A computerized search was performed within 12 databases (Embase, Medline, Web-of-Science, Scopus, Cochrane, CINAHL, Pubmed publisher, Lilacs, Scielo, ScienceDirect, ProQuest, Google Scholar) with appropriate search terms. Qualitative evaluation was performed using the MINORS score for cohort studies and the Jadad score for randomized clinical trials (RCTs).

Results: For midline laparotomy incisions and stoma reversal wounds, two RCTs, two case–control studies, and two case series were identified. The studies were very heterogeneous in terms of mesh configuration (cross linked versus non-cross linked), mesh position (intraperitoneal versus retro-muscular versus onlay), surgical indication (gastric bypass versus aortic aneurysm), outcome results (effective versus non-effective). After qualitative assessment, we have to conclude that the level of evidence on the efficacy and safety of biological meshes for prevention of IHs is *very low*. No comparative studies were found comparing biological mesh with synthetic non-absorbable meshes for the prevention of IHs.

Conclusion: There is no evidence supporting the use of non-permanent absorbable mesh (biological or biosynthetic) for prevention of IHs when closing a laparotomy in high-risk patients or in stoma reversal wounds. There is no evidence that a non-permanent absorbable mesh should be preferred to synthetic non-absorbable mesh, both in clean or clean-contaminated surgery.

Keywords: incisional hernia, prevention, prophylaxis, biological mesh, bio-absorbable mesh, systematic review

INTRODUCTION

Prophylactic mesh-augmented reinforcement during closure of abdominal wall incisions has been proposed in patients at high risk for incisional hernia (IH). Several randomized clinical trials (RCTs) have been published on the use of prophylactic mesh in patients undergoing aortic aneurysm surgery (1–4), obesity surgery (3, 5–7), stoma creation (8–14), in colorectal cancer patients (15, 16), or other high-risk patients (17, 18). The recently published guidelines of the European Hernia Society have provided the following *weak* recommendation: *"Prophylactic mesh augmentation for an elective midline laparotomy in high-risk patients in order to reduce the risk of incisional hernias is suggested."* Due to the lack of sufficient data, no recommendations on the type of mesh, the optimal mesh position, or the optimal mesh fixation technique could be made (19). Although prophylactic mesh-augmented reinforcement has been performed safely in clean-contaminated setting, one concern is the potential short- or long-term harms by implantation of a permanent mesh (20). Application of a non-permanent absorbable for prophylactic mesh-augmented reinforcement might therefore hold some benefit if these meshes will be as effective as permanent meshes.

A systematic literature review has been performed to detect those studies where prophylactic mesh-augmented reinforcement was performed with a non-permanent absorbable biological or biosynthetic mesh and provide guidance for future research on the use of biological or biosynthetic meshes.

METHODS

Protocol

The systematic search was part of the BioMesh consensus project. This project, initiated by Ferdinand Köckerling, gathered surgical expertise in a working group to provide a summary on the use of non-permanent absorbable biological or biosynthetic meshes in different indications. During a consensus meeting in Berlin on January 27, 2016, the working group decided in consensus on the statements and conclusions derived from the level of evidence for each indication. This manuscript reports on the review of the use of non-permanent absorbable biological or biosynthetic meshes for the prevention of IHs.

Eligibility Criteria

Inclusion criteria: because of the paucity of available studies on prophylactic mesh-augmented reinforcement with biological or biosynthetic mesh for the prevention of IHs, no limitation, to the study design, length of follow-up, or number of included patients, was used.

Exclusion criteria: prevention of parastomal hernias were excluded because this was part of a separate search within the BioMesh study group (21).

Information Sources

A computerized search was performed within 12 databases (Embase, Medline, Web-of-Science, Scopus, Cochrane, CINAHL, Pubmed publisher, Lilacs, Scielo, ScienceDirect, ProQuest, Google Scholar) on June 25, 2015.

Search

The biomedical librarian of the Erasmus University Medical Centre, Rotterdam, The Netherlands performed the search, and the search strategy is provided in Section "Addendum 1" in Appendix.

Study Selection

From the search, only the studies reporting on the use of a non-permanent absorbable biological or biosynthetic mesh were retained. Studies written in English, Dutch, French, and Spanish were considered.

Data Collection Process

Two authors (Filip Etienne Muysoms and An Jairam) independently screened all records retrieved upon application of the search strategy by title and abstract. The full text of all retained records was screened for eligibility. The references of all review articles found were cross-checked for additional eligible records.

Data Items

The following data were extracted by two authors independently and cross-checked: type of study, number of patients included, patient characteristics, indication for surgery, type of biological mesh, position of the mesh, method of mesh fixation, length of follow-up, and outcome measures (hernias, seroma, wound infections, burst abdomen). Primary outcome was IH incidence, and secondary outcomes were postoperative seroma, wound infection, and burst abdomen.

Quality Assessment of Individual Studies

Qualitative evaluation was performed using the MINORS score for non-randomized studies (22) and the Jadad score for RCTs (23). Additionally, the quality of evidence across the RCTs was done using the GRADE Pro software.[1]

Statistical Analysis

A meta-analysis of the outcome from the RCTs detected was performed for relevant outcomes: IH, seroma, wound infections, and burst abdomen. Meta-analysis was performed using the Review Manager 5.3 software (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2013). Our outcomes were expressed as risk ratios (RRs) with 95% confidence intervals (CIs) to estimate the pooled effect size and p-value. All tests were two-sided.

RESULTS

Study Selection

The PRISMA flow diagram of our search is illustrated in **Figure 1**. Six studies were retained after the screening and sift for eligibility. Four studies included patients with *midline laparotomy* (2, 7, 24, 25), and two studies investigated the prevention of IHs after *stoma reversal* (26, 27).

[1] www.gradepro.org

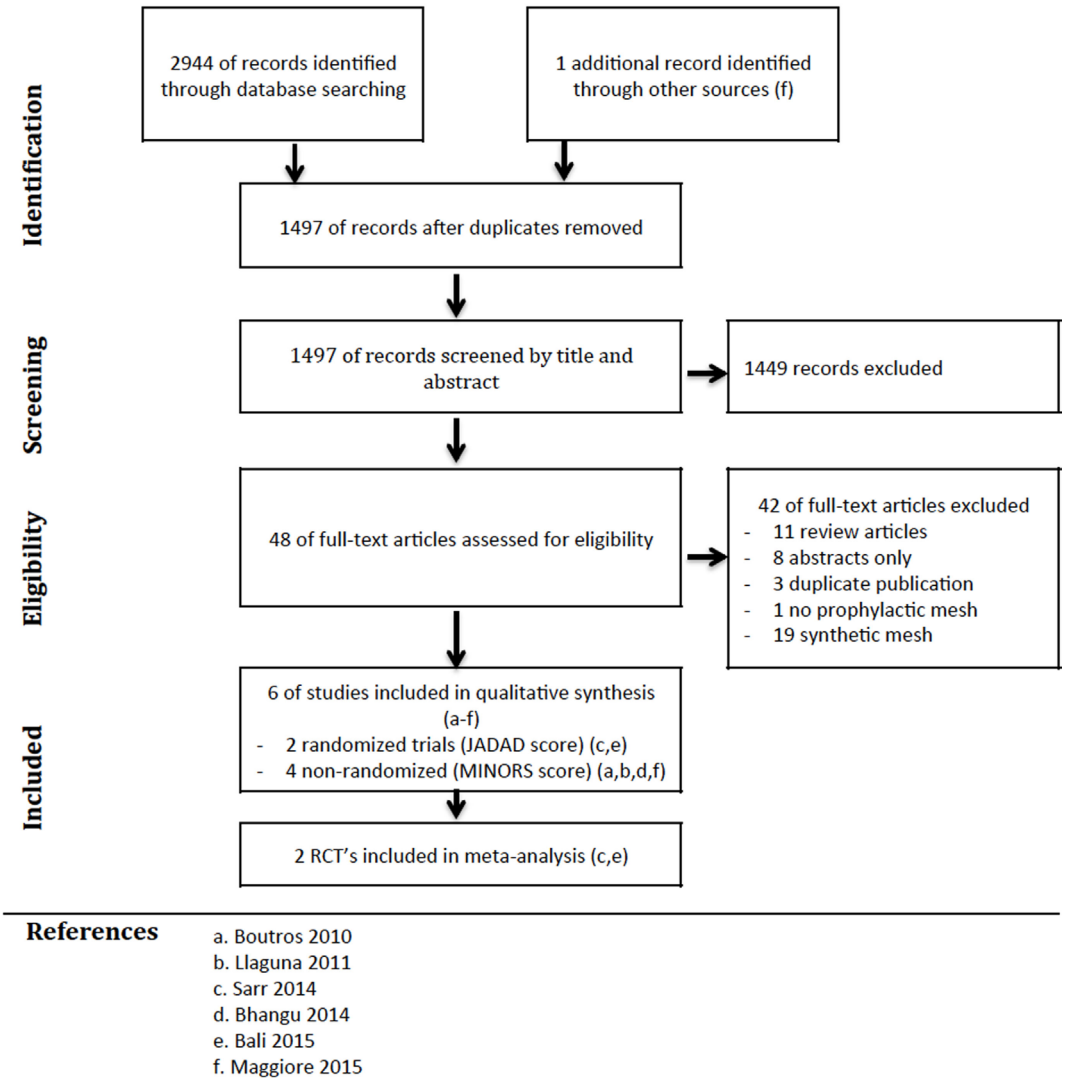

FIGURE 1 | **PRISMA flow diagram of a systematic review on the use of biological mesh for prevention of incisional hernias**.

Study Characteristics

Midline Laparotomy

Our literature review revealed four studies where a biological mesh was used to prevent IHs in high-risk patients. Details of the study characteristics and quality assessment (MINORS score, Jadad score) are shown in the summary of evidence table (**Table 1**). A small cohort study on eight patients that underwent a midline laparotomy for cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) described short-term outcome using an intraperitoneal biological mesh (24). In a prospective non-randomized case–control study, obese patients operated for a gastric bypass through a midline laparotomy were either treated with an intraperitoneal biological mesh ($n = 59$) or primary suture closure ($n = 75$). A significant reduction in the number of IHs by prophylactic mesh was reported [2.3% (90% CI: 2.31–6.86) versus 17.7% (90% CI: 7.92–27.52), $p = 0.014$] (25). In an RCT in obese patients undergoing a gastric bypass operation through a midline laparotomy, patients were randomized between an intraperitoneal biological mesh ($n = 185$) and primary suture closure ($n = 195$). This adequately powered RCT, did not show any benefit for prophylactic mesh concerning the risk for IH at 24 months (17.3 versus 19.5%, $p = 0.60$), but did show a significant higher number of wound infections and wound seroma in the mesh group (7). In an RCT of aortic aneurysm patients, midline laparotomy closure with an onlay biologic mesh ($n = 20$) was compared to primary suture closure ($n = 20$) (2). The study was not powered with a sample size calculation, but the follow up was adequate in length (36 months) and methodology (systematic CT

TABLE 1 | Summary of evidence table of a systematic review on the use of biological mesh for the prevention of incisional hernias after midline laparotomy.

Reference	Study type	Quality assessment	*N* (mesh/ no mesh)	Patient characteristics	Intervention	Comparison	Length of follow-up (months)	Outcome measure
Boutros et al. (24)	Non-comparative case series	MINORS score 5/16	8/–	Midline laparotomy for cytoreductive surgery and HIPEC in peritoneal carcinoma patients	Intraperitoneal Surgisis 20 cm × 20 cm fixed with PDS sutures	–	Mean 6.3	Seven patients had no abdominal wall morbidity. One patient had an incisional hernia and entero-cutaneous fistula following re-laparotomy 2 weeks after the primary operation
General comments: very low MINORS score of this case series. Follow-up inadequate to make conclusion about incisional hernia rate Funding: no direct funding; speakers fee from Cook Study registration: no								
Llaguna et al. (25)	Prospective case–control study	MINORS score 19/24	134 (59/75)	Patients undergoing gastric bypass surgery with midline laparotomy	Intraperitoneal Alloderm 16-cm long and 6-cm wide, fixed with PDS sutures	Sutured with PDS no 1, running suture	Mean 17.3	Incisional hernia: mesh: 1/44 (2%); no mesh: 11/62 (18%); $p = 0.014$ (OR 0.06)
General comments: prospective single surgeon non-randomized study, with adequate follow-up. Statistical significant differences on the number of patients with some confounding factors were seen: prior abdominal surgery, postoperative BMI Funding: not mentioned Study registration: no								
Sarr et al. (7)	RCT	JADAD score 2/5	402 (185/195)	Patients undergoing gastric bypass surgery with midline laparotomy	Intraperitoneal Surgisis 8-cm wide fixed with PDS sutures	Suture non-absorbable and absorbable, running suture	24	Incisional hernia: mesh: 32/185 (17.3%); no mesh: 38/195 (19.5%); $p = 0.60$; wound infections: 11.9% versus 3.6% ($p < 0.003$); wound seroma: 4.9% versus 0.5% ($p < 0.01$)
General comments: open label RCT with adequate sample calculation and power. Showed no difference in incisional hernia rate. The number of clinically relevant wound infections and wound seroma was significant higher in the Mesh group Funding: industry-funded study (Cook Biotech, Inc., West Lafayette, IN, USA) Study registration: www.ClinicalTrials.gov NCT00274625								
Bali et al. (2)	RCT	JADAD score 1/5	40 (20/20)	Elective midline laparotomy for AAA repair	Onlay periguard 8-cm wide fixed with non-absorbable sutures	Sutured with PDS no 1, running suture	36	Incisional hernia: mesh: 0/20 (0%); no mesh: 6/20 (32%); estimate freedom of incisional hernia was significantly higher for the mesh group ($p < 0.008$)
General comments: small open label RCT, no sample size calculation. Prophylactic mesh was effective and safe Funding: not mentioned Study registration: no								

TABLE 2 | Summary of evidence table of a systematic review on the use of biological mesh for prevention of incisional hernias after stoma reversal.

Reference	Study type	Quality assessment	*N* (mesh/no mesh)	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measure
Bhangu et al. (26)	Non-comparative case series	MINORS score 4/16	7/–	Patients with a temporary ileostomy needing stoma closure	Intraperitoneal Strattice 3-cm overlap fixed with PDS sutures	–	30 days	One superficial wound infection. No early hernias
General comments: very low MINORS score of this case series. Follow-up inadequate to make conclusion about incisional hernia rate. This study is a pilot study on the safety of the technique, before starting a large RCT Funding: industry-funded study Study registration: part of the ROCCS study: www.ClinicalTrials.gov NCT02238964								
Maggiori et al. (27)	Matched case–control study	MINORS score 15/24	94 (30/64)	Closure of a diverting ileostomy following rectal cancer resection	Retro-muscular Meccellis mesh 10 cm × 10 cm, fixed with prolene sutures	Two layer continuous suture of anterior and posterior fascia with Vicryl 1	1 year	Radiological incisional hernia rate mesh: 1/30 (3%); no mesh: 12/64 (19%) $p = 0.043$
General comments: Significant reduction of the number of incisional hernias at the stoma wound diagnosed with CT scan. No difference in morbidity Funding: industry-funded study Study registration: no								

scan evaluation). A highly significant protective effect of the mesh was shown, with no hernias in the mesh group and 32% in the non-mesh group [cumulative freedom of IH at 36 months was 100 versus 74.4% ($p < 0.008$)] (2).

Stoma Reversal Wound

Our literature review revealed two studies in which a biological mesh was used to prevent IHs after reversal of a temporary ileostomy. Details of the studies are shown in the summary of evidence table (**Table 2**). In a pilot study with a limited patient population ($n = 7$), the feasibility of an intraperitoneal prophylactic mesh was investigated in terms of safety in the short term (27). The second report was a matched case–control study of 30 patients that received a retro-muscular prophylactic biological mesh, compared to 64 matched patients with suture closure of the stoma wound. At 1-year follow-up with CT scan, the number of patients with IH was significantly lower for the mesh group ($p = 0.043$).

Meta-analysis

The pooled analysis for the outcome IH showed no statistical differences between groups (RR 0.38, 95% CI 0.04–3.83; $p = 0.41$). The forest plots of the meta-analysis of the two RCTs on prevention of midline laparotomy IHs, and the secondary outcomes are shown in **Figure 2**.

DISCUSSION

Midline Laparotomy

Overall, the *Level of Evidence* on the efficacy of biological mesh to prevent IHs is *very low*. Moreover, the study with the highest level of evidence and lowest risk of bias did not show any advantage in reducing IHs by prophylactic intraperitoneal biological mesh in patients undergoing a midline laparotomy for performing gastric bypass surgery (7). On the contrary, it did show a higher number of wound complications after the use of the prophylactic mesh. Another study regarding gastric bypass patients did show a benefit, but this study was non-randomized and had a high risk of bias (25).

For aortic aneurysm patients, only one RCT is available, which showed a high efficacy with 3 years follow-up. However, this study was poorly powered, non-blinded, and scored low in the Jadad scale (2). Moreover, no information on sources of funding and protocol registration was provided, and therefore, the risk of bias cannot be assessed.

The currently available evidence is not strong enough to make any statements regarding the optimal mesh position (intraperitoneal, retro-muscular, or onlay) in case a prophylactic biological mesh is used. Also, the different meshes used in the studies (non-cross-linked human origin; non-cross-linked porcine small intestinal submucosa; cross-linked bovine pericardium) might have an important impact on the outcome.

On the contrary, the Level of Evidence on the efficacy of prophylactic synthetic non-absorbable mesh (all polypropylene) in high-risk patients currently is high, with 8 published RCTs encompassing 727 patients with a follow-up of at least 12 months (1, 4–6, 15–18). Moreover, the safety of prophylactic retro-muscular or onlay meshes in clean or clean-contaminated surgery is shown in 9 published RCTs encompassing 1207 patients (1, 3–6, 15–18).

No comparative studies were found comparing biological mesh with synthetic non-absorbable meshes for the prevention of IHs. There is a study ongoing at the Vall d'Hebron Hospital, Universidad Autónoma de Barcelona on the prevention of IHs from midline laparotomies using an absorbable synthetic mesh (Bio-A, WL Gore & Ass, USA), PREBIOUS trial.[2]

[2]www.ClinicalTrials.gov NCT02208557

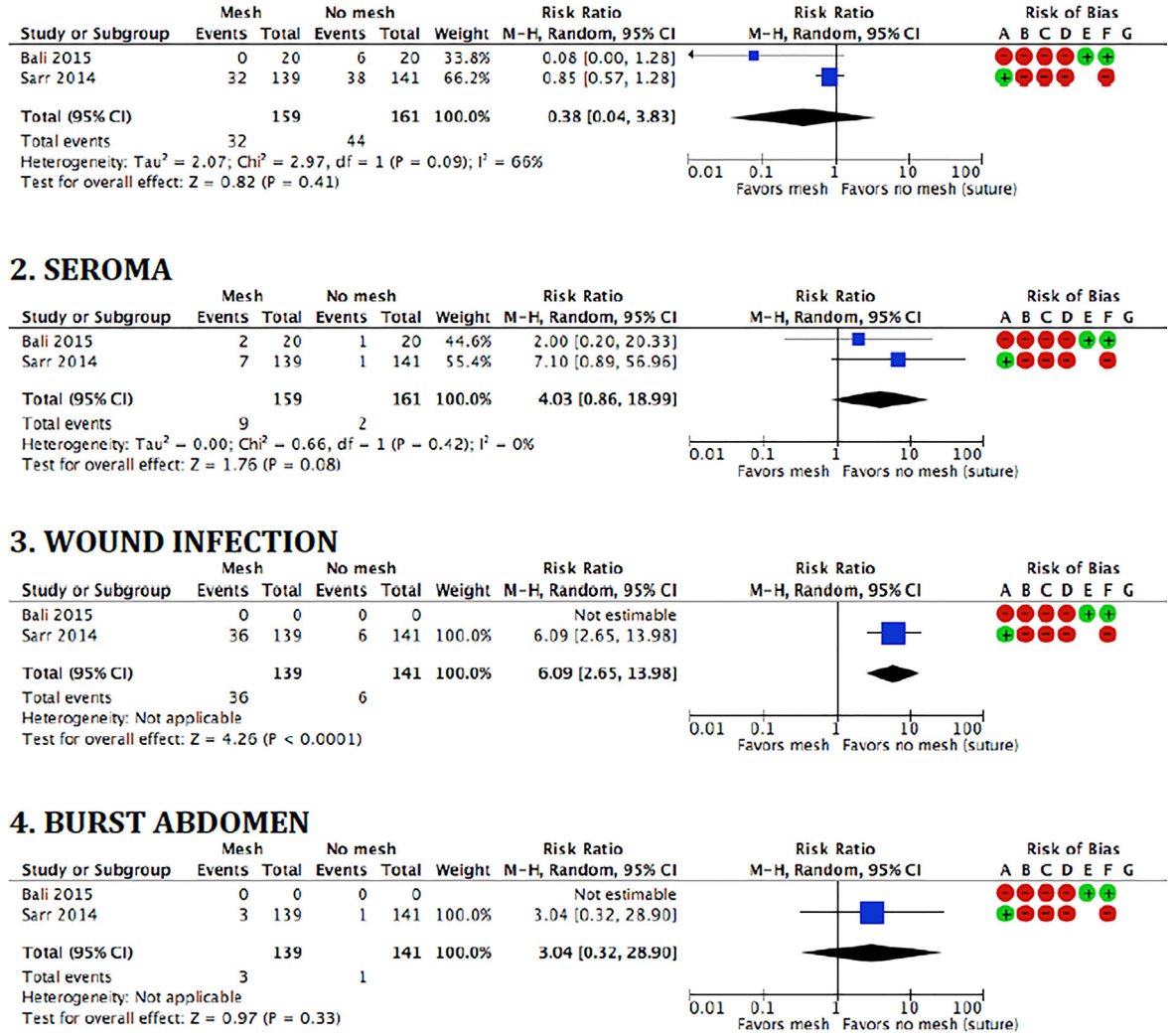

FIGURE 2 | Forest plots and risk of bias assessment of randomized studies on the prevention of incisional hernias by biological mesh reinforcement.

Stoma Reversal Wound

Overall, the *Level of Evidence* on the efficacy of biological mesh to prevent IHs of stoma reversal wounds is *very low*. Currently, the only study providing evidence is a matched case–control study, showing a lower IH rate at 1 year. This study is a pilot study for an RCT that is planned in France, the MEMBO trial[3] (27). The small pilot study by Banghu et al. is part of a large project, the ROCSS study, which is a properly powered multicenter RCT from

[3]www.ClinicalTrials.gov NCT02576184

the University of Birmingham[4] (26). This study compares the technique described in the pilot study with sutured closure of the stoma wound and has now included 790 patients, and the follow-up is ongoing. Furthermore, a study from the Vall d'Hebron Hospital (Universidad Autónoma de Barcelona), ILEOCLOSE study,[5] will investigate in a RCT the application of prophylactic mesh reinforcement of closure of temporary diverting ileostomy with an absorbable synthetic mesh (Bio-A) in 120 patients.

CONCLUSION

So far, there is no solid evidence on the effectiveness of prophylactic non-permanent absorbable biological or biosynthetic mesh for the closure of midline laparotomies or reinforcement of a stoma reversal site. There is no evidence that, in this setting, a non-permanent absorbable biological or biosynthetic mesh should be preferred to synthetic non-absorbable mesh, both in clean or clean-contaminated surgery.

PUBLICATION STATEMENT

This manuscript was written in accordance with the PRISMA statement: The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health-care interventions: guidelines for reporting parallel group randomized trials.[6]

AUTHOR CONTRIBUTIONS

All authors: initiation of the project, determination of search strategy, reviewing manuscript, and agreement. FM and AJ: systematic search at Erasmus University Rotterdam, the Netherlands, data collection process, and writing the manuscript. FM, AJ, FK, and IK-L: study selection from retrieved records. FM, AJ, ML-C, SA, MS, GW, and FK: qualitative evaluation of the retrieved records. FM, AJ, ML-C, and IK-L: quantitative evaluation of the retrieved records.

BioMESH STUDY GROUP

Ferdinand Köckerling (Chairman), Stavros Antoniou, René Fortelny, Frank A. Granderath, Markus Heiss, Franz Mayer, Marc Miserez, Agneta Montgomery, Salvador Morales-Conde, Filip Muysoms, Alexander Petter-Puchner, Rudolph Pointner, Neil Smart, Marciej Smietanski, and Bernd Stechemesser.

[4]www.ClinicalTrials.gov NCT02238964 and www.controlled-trials.com ISRCTN46330337

[5]www.ClinicalTrials.gov NCT02226887

[6]www.prisma-statement.org

REFERENCES

1. Bevis PM, Windhaber RAJ, Lear PA, Poskitt KR, Earnshaw JJ, Mitchell DC. Randomized clinical trial of mesh versus sutured wound closure after open abdominal aortic aneurysm surgery. *Br J Surg* (2010) 7:1497–502. doi:10.1002/bjs.7137
2. Bali C, Papakostas J, Georgiou G, Kouvelos G, Avgos S, Arnoutoglou E, et al. A comparative study of sutured versus bovine pericardium mesh abdominal closure after open abdominal aortic aneurysm repair. *Hernia* (2015) 19:267–71. doi:10.1007/s10029-014-1262-4
3. Timmermans L, Eker HH, Steyenberg EW, Jairam A, de Jong D, Pierik EG, et al. Short-term results of a randomized controlled trial comparing primary suture with primary glued mesh augmentation to prevent incisional hernia. *Ann Surg* (2015) 261:276–81. doi:10.1097/SLA.0000000000000798
4. Muysoms FE, Detry O, Vierendeels T, Huyghe M, Miserez M, Ruppert M, et al. Prevention if incisional hernia by prophylactic mesh-augmented reinforcement of midline laparotomies for abdominal aortic aneurysm treatment. *Ann Surg* (2016) 263:638–45. doi:10.1097/SLA.0000000000001369
5. Strzelczyk JM, Szymanski D, Nowicki ME, Wilczynski W, Gaszynski T, Czupryniak L. Randomized clinical trial of postoperative hernia prophylaxis in open bariatric surgery. *Br J Surg* (2006) 93:1347–50. doi:10.1002/bjs.5512
6. Abo-Ryia MH, El-Khadrawy OH, Abd-Allah HS. Prophylactic preperitoneal mesh placement in open bariatric surgery: a guard against incisional hernia development. *Obes Surg* (2013) 23:1571–4. doi:10.1007/s11695-013-0915-1
7. Sarr MG, Hutcher NE, Snyder S, Hodde J, Carmody B. A prospective, randomized, multicenter trial of Surgisis Gold, a biologic prosthetic, as a sublay reinforcement of the fascial closure after open bariatric surgery. *Surgery* (2014) 156:902–9. doi:10.1016/j.surg.2014.06.022
8. Hammond TM, Huang A, Prosser K, Frye JN, Williams NS. Parastomal hernia prevention using a novel collagen implant: a randomised controlled phase 1 study. *Hernia* (2008) 12:475–81. doi:10.1007/s10029-008-0383-z
9. Jänes A, Cengiz Y, Israelsson LA. Preventing parastomal hernia with a prosthetic mesh: a 5-year follow-up of a randomised study. *World J Surg* (2009) 33:118–23. doi:10.1007/s00268-008-9785-4
10. Serra-Aracil X, Bombardo-Junca J, Moreno-Matias J, Darnell A, Mora-Lopez L, Alcantara-Moral M, et al. Randomized, controlled, prospective trial of the use of a mesh to prevent parastomal hernia. *Ann Surg* (2009) 249:583–7. doi:10.1097/SLA.0b013e31819ec809
11. López-Cano M, Lozoya-Trujillo R, Quiroga S, Sanchez JL, Vallribera F, Marti M, et al. Use of a prosthetic mesh to prevent parastomal hernia during laparoscopic abdominoperineal resection: a randomized controlled trial. *Hernia* (2012) 16:661–7. doi:10.1007/s10029-012-0952-z
12. Fleshman JW, Beck DE, Hyman N, Wexner SD, Bauer J, George V, et al. A prospective, multicenter, randomized, controlled study of non-cross-linked porcine acellular dermal matrix fascial sublay for parastomal reinforcement in patients undergoing surgery for permanent abdominal wall ostomies. *Dis Colon Rectum* (2014) 57:623–31. doi:10.1097/DCR.0000000000000106
13. Lambrecht JR, Larsen SG, Reiertsen O, Vaktskjold A, Julsrud L, Flatmark K. Prophylactic mesh at end-colostomy construction reduces parastomal hernia rate: a randomized trial. *Colorectal Dis* (2015) 17:O191–7. doi:10.1111/codi.13065
14. Vierimaa M, Klintrup K, Biancari F, Victorzon M, Carpelan-Holmstrom M, Kossi J, et al. Prospective, randomized study on the use of a prosthetic mesh for prevention of parastomal hernia of permanent colostomy. *Dis Colon Rectum* (2015) 58:943–9. doi:10.1097/DCR.0000000000000443
15. Caro-Tarrago A, Olona Casas C, Jimenez Salido A, Duque Guillera E, Moreno Fernadez F, Vicente Guillen V. Prevention of incisional hernia in midline laparotomy with an onlay mesh: a randomized clinical trial. *World J Surg* (2014) 38:2223–30. doi:10.1007/s00268-014-2510-6
16. Garcia-Urena MA, Lopez-Monclus J, Blazquez Hernando LA, Melero Montes D, Valle de Lersundi RA, Pavon CC, et al. Randomized controlled trial of the use of a large-pore polypropylene mesh to prevent incisional hernia in colorectal surgery. *Ann Surg* (2015) 261:876–81. doi:10.1097/SLA.0000000000001116
17. Gutierrez de la Pena C, Medina Achirica C, Dominguez-Adame E, Medin Diez J. Primary closure of laparotomies with high risk of incisional hernia using prosthetic material: analysis of usefulness. *Hernia* (2003) 7:134–6. doi:10.1007/s10029-003-0124-2

18. El-Khadrawy OH, Moussa G, Mansour O, Hashish MS. Prophylactic prosthetic reinforcement of midline abdominal incisions in high-risk patients. *Hernia* (2009) 13:267–74. doi:10.1007/s10029-009-0484-3
19. Muysoms FE, Antoniou SA, Bury K, Campanelli G, Conze J, Cuccurullo D, et al. European Hernia Society guidelines on the closure of abdominal wall incisions. *Hernia* (2015) 19:1–24. doi:10.1007/s10029-009-0484-3
20. Herbert GS, Tausch TJ, Carter PL. Prophylactic mesh to prevent incisional hernia: a note of caution. *Am J Surg* (2009) 197:595–8. doi:10.1016/j.amjsurg.2009.01.002
21. Fortelny RH, Hofman A, May C, Köckerling F; BioMesh Study Group. Prevention of a parastomal hernia by biological mesh reinforcement. *Front Surg* (2015) 2:53. doi:10.3389/fsurg.2015.00053
22. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (minors): development and validation of a new instrument. *ANZ J Surg* (2003) 73:712–6. doi:10.1046/j.1445-2197.2003.02748.x
23. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials* (1996) 17:1–12. doi:10.1016/0197-2456(95)00134-4
24. Boutros C, Somasundar P, Espat NJ. Early results on the use of biomaterials as adjuvant to abdominal wall closure following cytoreduction and hyperthermic intraperitoneal chemotherapy. *World J Surg Oncol* (2010) 8:72. doi:10.1186/1477-7819-8-72
25. Llaguna OH, Avgerinos DV, Nagda P, Elfant D, Leitman IM, Goodman E. Does prophylactic biologic mesh placement protect against the development of incisional hernia in high-risk patients? *World J Surg* (2011) 35:1651–5. doi:10.1007/s00268-011-1131-6
26. Bhangu A, Futaba K, Patel A, Pinkney T, Morton D. Reinforcement of closure of stoma site using a biological mesh. *Tech Coloproctol* (2014) 18:305–8. doi:10.1007/s10151-013-1001-3
27. Maggiori L, Moszkowicz D, Zappa M, Mongin C, Panis Y. Bioprosthetic mesh reinforcement during temporary stoma closure decreases the rate of incisional hernia: a blinded, case-matched study in 94 patients with rectal cancer. *Surgery* (2015) 158:1651–7. doi:10.1016/j.surg.2015.07.004

Conflict of Interest Statement: Dr. FM reports grants and personal fees from Covidien, grants and personal fees from Johnson & Johnson, personal fees from WL Gore & Ass, personal fees from Bard Davol, grants and non-financial support from FEG DynaMesh, grants and personal fees from B. Braun, outside the submitted work; Dr. AJ reports no conflict of interest concerning the work. Dr. ML-C has received honoraria for consultancy and lectures from Ethicon, Johnson & Johnson, personal fees from Bard Davol, and grants from WL Gore & Ass, outside the submitted work. Dr. IK-L reports no conflict of interest concerning the work. Dr. MS reports fees for teaching and learning from Medtronic, Bard Davol, B. Braun, and Ehticon, outside of the submitted work. Dr. GW reports grants and consulting fees from Acelity, B. Braun, and Bard Davol, outside the submitted work. Dr. SA reports absence of any commercial or financial relationships that could be construed as a potential conflict of interest. Dr. FK reports no conflict of interest concerning the work.

APPENDIX

Addendum 1

Search strategy used for a systematic literature review on prevention of incisional hernias with mesh. A computerized search was performed within 12 databases (Embase, Medline, Web-of-Science, Scopus, Cochrane, Cinahl, Pubmed publisher, Lilacs, Scielo, ScienceDirect, ProQuest, Google scholar) on June 25th 2015.

Embase.com 839

('surgical mesh'/exp OR (mesh* OR 4DDOME OR AIGISRx OR AlloDerm OR AlloMax OR 'Bard Composix EX' OR 'BIO-A Tissue Reinforcement prosthesis' OR CollaMend OR DermaMatrix OR DualMesh OR 'Evolution P3EM' OR FasLata OR FlexHD OR FortaGen OR 'IntePro Lite' OR InteXen OR NEOVEIL OR 'Parietex composite' OR Pelvicol OR Pelvisoft OR Pelvitex OR PerFix OR 'Peri-Strips Dry' OR PeriGuard OR Permacol OR Physiomesh OR SeamGuard OR Strattice OR Surgisis OR 'TiLoop Bra' OR Timesh OR Tutomesh OR Tutopatch OR Ultrapro OR Ventralex OR Veritas OR Vivosorb OR Vypro OR X-Repair OR XenMatrix):ab,ti) AND (prevention/exp OR prevention:lnk OR (prevent* OR protect* OR prophyla*):ab,ti) AND ('incisional hernia'/exp OR 'abdominal wall hernia'/de OR 'abdominal wall defect'/de OR 'abdominal surgery'/de OR 'abdominal wall closure'/de OR laparotomy/exp OR 'abdominal wall'/de OR (((incision* OR cicatri* OR scar* OR ventral*) NEAR/3 (herni*)) OR ((abdominal* OR transabdominal*) NEAR/3 (surger* OR clos* OR defect* OR wall*)) OR laparotom* OR (midline NEAR/3 incision*)):ab,ti) NOT ([animals]/lim NOT [humans]/lim)

Medline (ovid) 490

("surgical mesh"/OR (mesh* OR 4DDOME OR AIGISRx OR AlloDerm OR AlloMax OR "Bard Composix EX" OR "BIO-A Tissue Reinforcement prosthesis" OR CollaMend OR DermaMatrix OR DualMesh OR "Evolution P3EM" OR FasLata OR FlexHD OR FortaGen OR "IntePro Lite" OR InteXen OR NEOVEIL OR "Parietex composite" OR Pelvicol OR Pelvisoft OR Pelvitex OR PerFix OR "Peri-Strips Dry" OR PeriGuard OR Permacol OR Physiomesh OR SeamGuard OR Strattice OR Surgisis OR "TiLoop Bra" OR Timesh OR Tutomesh OR Tutopatch OR Ultrapro OR Ventralex OR Veritas OR Vivosorb OR Vypro OR X-Repair OR XenMatrix).ab,ti.) AND ("Primary Prevention"/OR "prevention and control".xs. OR (prevent* OR protect* OR prophyla*).ab,ti.) AND ("Hernia, Ventral"/OR "Hernia, Abdominal"/OR abdomen/su OR laparotomy/OR "abdominal wall"/OR (((incision* OR cicatri* OR scar* OR ventral*) ADJ3 (herni*)) OR ((abdominal* OR transabdominal*) ADJ3 (surger* OR clos* OR defect* OR wall*)) OR laparotom* OR (midline ADJ3 incision*)).ab,ti.) NOT (exp animals/NOT humans/)

Cochrane 30

((mesh* OR 4DDOME OR AIGISRx OR AlloDerm OR AlloMax OR 'Bard Composix EX' OR 'BIO-A Tissue Reinforcement prosthesis' OR CollaMend OR DermaMatrix OR DualMesh OR 'Evolution P3EM' OR FasLata OR FlexHD OR FortaGen OR 'IntePro Lite' OR InteXen OR NEOVEIL OR 'Parietex composite' OR Pelvicol OR Pelvisoft OR Pelvitex OR PerFix OR 'Peri-Strips Dry' OR PeriGuard OR Permacol OR Physiomesh OR SeamGuard OR Strattice OR Surgisis OR 'TiLoop Bra' OR Timesh OR Tutomesh OR Tutopatch OR Ultrapro OR Ventralex OR Veritas OR Vivosorb OR Vypro OR X-Repair OR XenMatrix):ab,ti) AND ((prevent* OR protect* OR prophyla*):ab,ti) AND ((((incision* OR cicatri* OR scar* OR ventral*) NEAR/3 (herni*)) OR ((abdominal* OR transabdominal*) NEAR/3 (surger* OR clos* OR defect* OR wall*)) OR laparotom* OR (midline NEAR/3 incision*)):ab,ti)

Web-of-science 474

TS = (((mesh* OR 4DDOME OR AIGISRx OR AlloDerm OR AlloMax OR "Bard Composix EX" OR "BIO-A Tissue Reinforcement prosthesis" OR CollaMend OR DermaMatrix OR DualMesh OR "Evolution P3EM" OR FasLata OR FlexHD OR FortaGen OR "IntePro Lite" OR InteXen OR NEOVEIL OR "Parietex composite" OR Pelvicol OR Pelvisoft OR Pelvitex OR PerFix OR "Peri-Strips Dry" OR PeriGuard OR Permacol OR Physiomesh OR SeamGuard OR Strattice OR Surgisis OR "TiLoop Bra" OR Timesh OR Tutomesh OR Tutopatch OR Ultrapro OR Ventralex OR Veritas OR Vivosorb OR Vypro OR X-Repair OR XenMatrix)) AND ((prevent* OR protect* OR prophyla*)) AND ((((incision* OR cicatri* OR scar* OR ventral*) NEAR/3 (herni*)) OR ((abdominal* OR transabdominal*) NEAR/3 (surger* OR clos* OR defect* OR wall*)) OR laparotom* OR (midline NEAR/3 incision*))) NOT ((animal* OR rat OR rats OR mouse OR mice OR murine OR rabbit* OR rodent* OR pig OR sus OR swine* OR porcine OR monkey* OR dog OR sheep OR ovine) NOT (human* OR patient*)))

Scopus 697

TITLE-ABS-KEY(((mesh* OR 4DDOME OR AIGISRx OR AlloDerm OR AlloMax OR "Bard Composix EX" OR "BIO-A Tissue Reinforcement prosthesis" OR CollaMend OR DermaMatrix OR DualMesh OR "Evolution P3EM" OR FasLata OR FlexHD OR FortaGen OR "IntePro Lite" OR InteXen OR NEOVEIL OR "Parietex composite" OR Pelvicol OR Pelvisoft OR Pelvitex OR PerFix OR "Peri-Strips Dry" OR PeriGuard OR Permacol OR Physiomesh OR SeamGuard OR Strattice OR Surgisis OR "TiLoop Bra" OR Timesh OR Tutomesh OR Tutopatch OR Ultrapro OR Ventralex OR Veritas OR Vivosorb OR Vypro OR X-Repair OR XenMatrix)) AND ((prevent* OR protect* OR prophyla*)) AND ((((incision* OR cicatri* OR scar* OR ventral*) W/3 (herni*)) OR ((abdominal* OR transabdominal*) W/3 (surger* OR clos* OR defect* OR wall*)) OR laparotom* OR (midline W/3 incision*))) AND NOT ((animal* OR rat OR rats OR mouse OR mice OR murine OR rabbit* OR rodent* OR pig OR sus OR swine* OR porcine OR monkey* OR dog OR sheep OR ovine) AND NOT (human* OR patient*)))

cinahl (ebsco) 23

(MH "surgical mesh + " OR (mesh* OR 4DDOME OR AIGISRx OR AlloDerm OR AlloMax OR "Bard Composix EX" OR

"BIO-A Tissue Reinforcement prosthesis" OR CollaMend OR DermaMatrix OR DualMesh OR "Evolution P3EM" OR FasLata OR FlexHD OR FortaGen OR "IntePro Lite" OR InteXen OR NEOVEIL OR "Parietex composite" OR Pelvicol OR Pelvisoft OR Pelvitex OR PerFix OR "Peri-Strips Dry" OR PeriGuard OR Permacol OR Physiomesh OR SeamGuard OR Strattice OR Surgisis OR "TiLoop Bra" OR Timesh OR Tutomesh OR Tutopatch OR Ultrapro OR Ventralex OR Veritas OR Vivosorb OR Vypro OR X-Repair OR XenMatrix)) AND (MH "Preventive Health Care" OR MW prevention OR (prevent* OR protect* OR prophyla*)) AND (MH "Hernia, Abdominal" OR MH abdomen/su OR MH laparotomy OR (((incision* OR cicatri* OR scar* OR ventral*) N3 (herni*)) OR ((abdominal* OR transabdominal*) N3 (surger* OR clos* OR defect* OR wall*)) OR laparotom* OR (midline N3 incision*))) NOT (MH animals + NOT humans +)

Pubmed publisher 14

("surgical mesh"[mh] OR (mesh*[tiab] OR 4DDOME OR AIGISRx OR AlloDerm OR AlloMax OR "Bard Composix EX" OR "BIO-A Tissue Reinforcement prosthesis" OR CollaMend OR DermaMatrix OR DualMesh OR "Evolution P3EM" OR FasLata OR FlexHD OR FortaGen OR "IntePro Lite" OR InteXen OR NEOVEIL OR "Parietex composite" OR Pelvicol OR Pelvisoft OR Pelvitex OR PerFix OR "Peri-Strips Dry" OR PeriGuard OR Permacol OR Physiomesh OR SeamGuard OR Strattice OR Surgisis OR "TiLoop Bra" OR Timesh OR Tutomesh OR Tutopatch OR Ultrapro OR Ventralex OR Veritas OR Vivosorb OR Vypro OR X-Repair OR XenMatrix)) AND ("Primary Prevention"[mh] OR "prevention and control"[sh] OR (prevent*[tiab] OR protect*[tiab] OR prophyla*[tiab])) AND ("Hernia, Ventral"[mh] OR "Hernia, Abdominal"[mh] OR abdomen/su[mh] OR laparotomy[mh] OR "abdominal wall"[mh] OR (((incision*[tiab] OR cicatri*[tiab] OR scar*[tiab] OR ventral*[tiab]) AND (herni*[tiab])) OR ((abdominal*[tiab] OR transabdominal*[tiab]) AND (surger*[tiab] OR clos*[tiab] OR defect*[tiab] OR wall*[tiab])) OR laparotom*[tiab] OR (midline AND incision*[tiab]))) NOT (animals[mh] NOT humans[mh]) AND publisher[sb]

Google scholar

Mesh|meshes prevention|preventive|protective|protection|prophylactic|prophylaxis"incisioal|cicatrical|scar|ventralhernia"|"abdominal|transabdominal surgery|closure|defect|wall"|laparotomy|"midline incision" -animal -animals -rats -mice

Lilacs 18

Scielo 8

(Mesh*) AND (prevent* OR protect* OR prophyla*) AND ("incisional hernia" OR "cicatrical hernia" OR "scar hernia" OR " ventral hernia" OR "abdominal hernia" OR "abdominal surgery" OR "abdominal closure" OR "abdominal defect" OR "abdominal wall" OR laparotom* OR "midline incision")

ScienceDirect 92

(Mesh*) AND (prevent* OR protect* OR prophyla*) AND ("incisional hernia" OR "cicatrical hernia" OR "scar hernia" OR " ventral hernia" OR "abdominal hernia" OR "abdominal surgery" OR "abdominal closure" OR "abdominal defect" OR "abdominal wall" OR laparotom* OR "midline incision") AND TOPIC (incisional hernia)

ProQuest 9

(ti(Mesh*) OR ab(Mesh*)) AND (ti(prevent* OR protect* OR prophyla*) OR ab(prevent* OR protect* OR prophyla*)) AND (ti("incisional hernia" OR "cicatrical hernia" OR "scar hernia" OR " ventral hernia" OR "abdominal hernia" OR "abdominal surgery" OR "abdominal closure" OR "abdominal defect" OR "abdominal wall" OR laparotom* OR "midline incision") OR ab("incisional hernia" OR "cicatrical hernia" OR "scar hernia" OR " ventral hernia" OR "abdominal hernia" OR "abdominal surgery" OR "abdominal closure" OR "abdominal defect" OR "abdominal wall" OR laparotom* OR "midline incision"))

frontiers in Surgery

REVIEW
published: 21 October 2015
doi: 10.3389/fsurg.2015.00056

The use of biological meshes in diaphragmatic defects – an evidence-based review of the literature

Stavros A. Antoniou[1,2]*, *Rudolph Pointner*[3], *Frank-Alexander Granderath*[1] and *Ferdinand Köckerling*[4]

[1] Center for Minimally Invasive Surgery, Neuwerk Hospital, Mönchengladbach, Germany, [2] Department of General Surgery, University Hospital of Heraklion, Heraklion, Greece, [3] Department of General and Visceral Surgery, Hospital Zell am See, Zell am See, Austria, [4] Department of Surgery, Center for Minimally Invasive Surgery, Vivantes Hospital, Berlin, Germany

The widespread use of meshes for hiatal hernia repair has emerged in the era of laparoscopic surgery, although sporadic cases of mesh augmentation of traumatic diaphragmatic rupture have been reported. The indications for biologic meshes in diaphragmatic repair are ill defined. This systematic review aims to investigate the available evidence on the role of biologic meshes in diaphragmatic rupture and hiatal hernia repair. Limited data from sporadic case reports and case series have demonstrated that repair of traumatic diaphragmatic rupture with biologic mesh is safe technique in both the acute or chronic setting. High level evidence demonstrates short-term benefits of biologic mesh augmentation in hiatal hernia repair over primary repair, although adequate long-term data are not currently available. Long-term follow-up data suggest no benefit of hiatal hernia repair using porcine small intestine submucosa over suture repair. The effectiveness of different biologic mesh materials on hernia recurrence requires further investigation.

Keywords: biologic mesh, biologic graft, hiatal hernia, diaphragmatic rupture, paraesophageal hernia, fundoplication

OPEN ACCESS

Edited by:
Vincenzo Neri,
University of Foggia, Italy

Reviewed by:
Kun-Ming Chan,
Chang Gung Memorial Hospital at Linkou, Taiwan
Ulf Gunnarsson,
Karolinska Institutet, Sweden

***Correspondence:**
Stavros A. Antoniou
stavros.antoniou@hotmail.com

Specialty section:
This article was submitted to Visceral Surgery, a section of the journal Frontiers in Surgery

Received: *05 August 2015*
Accepted: *08 October 2015*
Published: *21 October 2015*

Citation:
Antoniou SA, Pointner R, Granderath F-A and Köckerling F (2015) The use of biological meshes in diaphragmatic defects – an evidence-based review of the literature. Front. Surg. 2:56. doi: 10.3389/fsurg.2015.00056

INTRODUCTION

Blunt or penetrating trauma of the abdomen and thorax may cause injury to the diaphragm (1). In the case of traumatic diaphragmatic rupture, abdominal organs such as the stomach, spleen, colon, or the liver may herniate into the thoracic cavity causing a wide range of symptoms, which may occur several years after the injury (2–5). Chest X-ray is often diagnostic, whereas computed tomography and magnetic resonance imaging provide detailed information about the herniated structures and the size of the defect (6, 7). There is no consensus on the absolute indications for surgery or the timing of surgical intervention. A traumatic rupture of the diaphragm is generally considered an indication for surgical repair, especially in the presence of symptoms.

Relevant literature evidence is limited, mainly due to the rarity of the condition. Primary suture repair or covering the defect with a synthetic mesh has been the standard of care during the past decades (8). Biologic meshes have been thought to be effective in closing the diaphragmatic defect, induce limited inflammatory response, and minimize adhesion formation.

In the presence of insufficient evidence, there is ongoing debate on the need of augmentation of the diaphragmatic hiatus during hernia repair (9). A number of randomized controlled trials (RCTs) and a meta-analysis have demonstrated lower recurrence rates after mesh repair; however, long-term data are not currently available (10). Several studies have reported complications, which has created skepticism with regard to the benefits of augmented hiatal hernia repair (11–13).Several biologic materials have been manufactured and are currently in use in surgical practice. Experimental data have shown biologic meshes to possess characteristics of an ideal mesh material, such as reduced adhesion formation, improved biocompatibility, decreased inflammatory response, and optimal neovascularization (14). Our objective was to review the evidence investigating the role of biologic meshes in traumatic repair of the diaphragm and in hiatal hernia repair.

MATERIALS AND METHODS

Repair of Traumatic Diaphragmatic Defects

Electronic searches of the Medline database were conducted using the PubMed search engine. The following combination of terms and keywords was applied: (trauma OR traumatic OR posttraumatic OR rupture*) AND (diaphragm* OR phren*) AND (mesh OR implant). The search returned 141 reports. The last search was run in November 2014. Titles and abstracts were interrogated and clinical reports on the use of biologic material for closure of traumatic diaphragmatic defects were selected. The full texts of 17 articles were assessed for eligibility; three relevant reports were identified (15–17). The remaining 15 articles were excluded because they reported on the use of synthetic materials in diaphragmatic rupture repair or did not provide relevant outcomes. A summary of the study characteristics and outcomes is presented in **Table 1**.

Hiatal Hernia Repair with Mesh Augmentation

Similarly, Medline was searched to identify relevant clinical evidence using the PubMed interface up to November 2014. The keywords (hiat*) AND (hernia) AND (mesh OR implant) were used. Of a total of 309 records, 28 articles were selected for full text review based on relevant information from titles and abstracts. Twenty-two articles provided relevant outcome data on mesh-reinforced hiatal hernia repair with biologic meshes (18–39). The study characteristics and outcomes are listed in **Table 2**.

RESULTS

Repair of Traumatic Diaphragmatic Defects

Two case reports and one case series reported on the use of biologic meshes in traumatic diaphragmatic rupture. Four chronic traumatic defects and two acute ruptures were repaired laparoscopically, or with a laparotomy or a combined (thoracotomy and laparotomy) approach using human acellular cadaveric dermis (HACD) or porcine small intestine submucosa (SIS). Two of the repairs were performed in contaminated surgical fields, one due to inflammation of the herniated gallbladder and one due to pleural empyema. No septic complications requiring prolonged hospital stay or reintervention were reported. Chest X-ray in five of these cases did not reveal recurrence within a 6- to 24-month follow-up period.

Hiatal Hernia Repair with Mesh Augmentation

A plethora studies reporting use of biologic mesh augmentation of the esophageal hiatus have been published since 2003. Most of these are retrospective industry-sponsored cohort studies. Both

TABLE 1 | Characteristics and outcomes of studies reporting on repair of traumatic diaphragmatic rupture with the use of biologic mesh.

References	Study design	Patient characteristics	Mesh material	Intervention details	Follow up	Outcome	Conflict of interest	LoE[a]
Teicher et al. (15)	Case report	25 years old Acute case Grade IV left-sided diaphragm rupture	HADM	Open tension-free repair with a 4 cm × 4 cm mesh Anchorage with a 3–0 polydioxanone running suture	6 months Chest X-ray	No recurrence	NR	5
Pulido et al. (16)	Case report	70 years old Chronic case Accident 41 years before – no surgery Inflamed gallbladder and small bowel herniated	HADM	Laparoscopic cholecystectomy Anchorage with interrupted #0 polyethylene sutures	NR	Empyema, bile leak, and biliary effusion of the right pleura ERCP and VAT pleurodesis	NR	5
Al-Nouri et al. (17)	Case series	$n = 4$ 2 right-sided, 2 left-sided diaphragm ruptures 3 chronic cases, 1 acute case 1 case of concurrent pleural empyema	HADM/ SIS	Thoracotomy or thoracotomy/laparotomy repair Suture approximation and mesh reinforcement Pleurodesis in the case of pleural empyema	1–2 years Chest X-ray	No recurrence	NR	4

HADM, human acellular dermal matrix; SIS, small intestine submucosa; ERCP, endoscopic retrograde cholangiopancreatography; VAT, video-assisted thoracoscopy; LoE, level of evidence.

[a]*Based on the Oxford Centre for Evidence-based Medicine – Levels of Evidence (March 2009).*

TABLE 2 | Characteristics and outcomes of studies reporting on hiatal hernia repair with the use of biologic mesh.

References	Study design	Patient characteristics	Mesh material	Intervention details	Follow up	Outcome	Conflict of interest	LoE[a]
Oelschlager et al. (18)	Retrospective case series	$n = 9$ Type III hernia, $n = 8$ Type II hernia, $n = 1$ Median age 63 years (range 47–80)	SIS	Keyhole or *U*-shaped SIS 7 cm × 10 cm mesh anchored with interrupted silk sutures Nissen fundoplication and gastropexy	3–16 months UGIS ± UGIE	1 recurrence 1 need for dilatation for mild persistent dysphagia	Yes	4
Strange (19)	Retrospective case series	$n = 12$ Patients with "large hiatal defects" Median age: 66 years	SIS	Suture repair Keyhole mesh, circular portion 2.5–3 cm anchored with #2–0 non-absorbable sutures fixed to the esophagus	Median 11 months UGIS	No recurrence	NR	4
Johnson et al. (20)	Case report	Type III, 82 years old Type IV, 62 years old Second recurrence, 53 years old	HACD	Suture repair with interrupted non-absorbable sutures Onlay mesh placement Nissen fundoplication	UGIS in the early postoperative period Symptom outcome at 8–10 months	No early recurrence Lack of symptoms at follow up	NR	5
Oelschlager et al. (21–23)	Assessor-blinded RCT	$n = 108$ Symptomatic paraesophageal hernia size >5 cm	SIS	Suture repair with interrupted #2–0 or #0, $n = 57$ U-shaped 7 cm × 10 cm mesh anchored with interrupted sutures, additionally to the suture repair, $n = 51$ Nissen fundoplication	Short term: 6 months Long-term: median 58 months (range, 40–78) UGIS	Short-term recurrence(10% attrition): 24 vs. 9% (sutured vs. mesh) Long-term recurrence (44% attrition): 59 vs. 54% (sutured vs. mesh)	Yes	1b 2b
Ringley et al. (24)	Prospective case–control	$n = 44$ Size of hiatal defect ≥5 cm BMI significantly higher in the HACD group	HACD	Suture repair with #0 silk sutures, $n = 22$ U-shaped 4 cm × 8 cm mesh anchored with #2–0 silk sutures Nissen fundoplication	12 months UGIS	9 vs. 0% recurrence in favor of HACD 100% (suture repair) vs. 68% (mesh repair) of patients subjected to UGIS Duration of follow up 9.5 months (suture repair) vs. 6.7 months (mesh repair)	Yes	4
Wisbach et al. (25)	Retrospective case series	$n = 11$ Median age 41 years (range 26–60) Hiatal defect >5 cm Recurrent, $n = 7$	HADM	Suture repair with interrupted #0 polyethylene Y-shape mesh sutured with #2–0 polyethylene sutures and tacks Additionally square piece of mesh sutured onto the Y-shaped piece Nissen fundoplication	Median 1 year (range 8–19 months) UGIS	Follow up, $n = 8$ One recurrence	None	4
Jacobs et al. (26)	Retrospective case series	$n = 127$	SIS	Suture repair with interrupted #0 non-absorbable sutures Tension-free repair mesh repair, anchored with interrupted #2–0 non-absorbable sutures Nissen fundoplication, $n = 102$ Toupet fundoplication, $n = 19$ No fundoplication, $n = 6$	Median 3.2 years UGIS and/or UGIE	Three recurrences (65% attrition)	NR	4
Lee et al. (27)	Retrospective case series	$n = 17$ Mean age 65 ± 12 years Mean BMI 31 ± 4 kg/m^2 Large hiatal hernias (4–7 cm) Revisional repairs, $n = 4$	HACD	Suture repair with interrupted #0 polyethylene sutures U-shaped 4 cm × 7 cm mesh anchored with staples and #0 polyethylene sutures Nissen fundoplication Collis gastroplasty, $n = 1$ Wedge fundectomy, $n = 3$	Mean 14.4 ± 4.4 months (range 5–22) UGIS	Two recurrences	Yes	4

(Continued)

TABLE 2 | Continued

References	Study design	Patient characteristics	Mesh material	Intervention details	Follow up	Outcome	Conflict of interest	LoE[a]
St Peter et al. (28)	Retrospective case–control	$n = 21$ Pediatric patients with hernia recurrence	SIS	Sutured repair with # 2–0 silk sutures and esophagopexy with 4 #3–0 silk sutures, $n = 13$ Pantaloon shaped mesh anchored to the diaphragm and the esophagus with #3–0 silk sutures, $n = 18$ With or without fundoplication	Unclear	Recurrence 4/13 vs. 0/18	NR	4
Fumagalli et al. (29)	Prospective case series	$n = 6$ Median age 65 years Primary or recurrent hernia type II-IV and weak crura	SIS	Suture repair with interrupted #2–0 silk sutures U-shaped mesh anchored with staples Nissen fundoplication	12 months UGIS	Three recurrences		4
Lee et al. (30)	Retrospective case series	$n = 52$ Mean age 56.7 years (range 34–74) Mean size of hernia 7.75 cm (range 5–10)	HACD	Suture repair U-shaped mesh 4 cm × 7cm anchored with 4–6 #2–0 silk sutures Nissen fundoplication	Median 16 months (range 12–24) UGIS	Two recurrences	Yes	4
Varela and Jacks (31)	Retrospective case series	$n = 5$ Mean age 65 ± 7 Years Large type III hernia, mean size 5 cm ± 1	HACD	Suture repair with 5 interrupted non-absorbable sutures Circular 4 cm × 8 cm mesh anchored with four non-absorbable sutures to the crura Nissen fundoplication	NR	No short-term mesh-related complications	NR	4
Diaz and Roth (32)	Retrospective case series	$n = 46$ Mean age 60.3 ± 13.9 Mean BMI 30.3 ± 5.3 Hernia size ≥5 cm on UGIS or UGIE	HACD	Suture repair with interrupted non-absorbable sutures U-shaped 5 cm × 8 cm mesh Tension-free, $n = 3$ Collis gastroplasty, $n = 2$ Nissen fundoplication Selectively gastrostomy	Mean 3.6 months UGIS	Two recurrences (44% attrition) One gastric perforation 30 days post surgery Dysphagia for solids 13%	NR	4
Goers et al. (33)	Retrospective case–control	$n = 89$ Mesh repair: type II-IV hernias with thin crura Suture repair: type III hernias	Biologic NS	Suture repair with pledgeted polyester #0 matress sutures, $n = 33$ Pledgeted polyester #0 matress sutures incorporating the mesh, $n = 56$	NR	Residual resting LESP and mean amplitude higher for mesh repair Similar incidence of dysphagia	NR	4
Alicuben et al. (34)	Retrospective case series	$n = 82$ Median age 63 years Type I hernia, $n = 35$ Type II–IV hernia, $n = 47$ Revisional repair, $n = 6$	HACD	Suture repair with pledgeted #0 polyethylene sutures ± relaxing incision ($n = 10$), ±Collis gastroplasty ($n = 23$) U-shaped mesh anchored with #2–0 silk sutures, tacks or fibrin sealant	5–12 months UGIS or UGIE	Three recurrences (16% attrition)	Yes	4
Molena et al. (35)	Case series	$n = 18$ Mean age 68.2 (range 47–76) Mean BMI 29.2 (range 19–44) Type III, $n = 7$ Type IV, $n = 11$ Revision surgery, $n = 6$	Biologic NS	VATS dissection Suture repair with interrupted non-absorbable sutures *U*-shaped biological mesh anchored with fibrin glue and interrupted sutures Nissen or Toupet and gastropexy Sleeve gastrectomy, $n = 1$ Planned laparotomy, $n = 2$	NR	NR	None	4
Schmidt et al. (36)	Retrospective case–control	$n = 70$ Hernia size 1–5 cm in UGIS or UGIE	HACD	Suture repair with #0 silk sutures, $n = 32$ U-shaped mesh anchored with 4–6 #2–0 silk sutures, $n = 38$	12 months UGIS or UGIE	16 vs. 0% recurrence in favor of HACD 0% dysphagia in the mesh group	NR	4

(Continued)

TABLE 2 | Continued

References	Study design	Patient characteristics	Mesh material	Intervention details	Follow up	Outcome	Conflict of interest	LoE[a]
Sharp et al. (37)	Retrospective case–control	$n = 52$ Pediatric patients with hernia recurrence	SIS or HACD	Suture repair, $n = 26$ Mesh repair, $n = 25$	NA	23.1% (suture) vs. 56% (mesh) of patients presented fever, $p = 0.02$ Mean max temperature 37.8 ± 0.7 (suture) vs. 38.6 ± 0.9 (mesh), $p = 0.002$	None	4
Ward et al. (38)	Prospective case series	$n = 54$ Sliding, $n = 14$ Paraesophageal, $n = 40$ Recurrent, $n = 3$	HACD	Suture repair with #0 polyethylene sutures U-shaped 4 cm × 7 cm mesh anchored with 8–10 #2–0 polyethylene sutures	Min. 6 months UGIS	7.4% recurrence 13% attrition	Yes	4
Watson et al. (39)	Double blind RCT	$n = 126$ Herniation of $\geq$50% of the stomach	SIS	Suture repair, $n = 43$ Ti-mesh, $n = 42$ SIS, $n = 41$ Granderath buttress technique 2–3 cm × 4–5 cm mesh posterior repair anchored with sutures or tacks	6 months UGIE ± UGIS 12-month symptom outcome	Similar dysphagia rates 7.9% (suture) vs. 5.9% (SIS) vs. 0% (Ti-mesh) recurrence (non-significant)	No	2b

UGIS, barium contrast upper gastrointestinal series; UGIE, upper gastrointestinal endoscopy; LoE, level of evidence; RCT, randomized controlled trial; SIS, small intestine submucosa, HACD, human acellular cadaveric dermis; LESP, lower esophageal sphincter pressure; BMI, body mass index; VATS, video-assisted thoracoscopic surgery.
[a]*Based on the Oxford Centre for Evidence-based Medicine – Levels of Evidence (March 2009).*

HACD and SIS meshes have been used, most commonly in a U-shape or a pantaloon fashion, placed in a retroesophageal position with the limbs of the mesh encircling the esophagus. The graft is anchored to the diaphragm and, in some cases, to the esophagus with non-absorbable sutures, tacks, or fibrin sealant, most commonly following suture repair of the crura or in a tension-free bridging fashion. A Collis gastroplasty has also been reported as a lengthening procedure in cases of a short esophagus (27, 32). Although no adverse effects associated with allografts or xenografts have been reported, in a chart review of 51 pediatric patients, Sharp and colleagues found that fever occurred more frequently after mesh repair and this group of subjects presented with a higher mean temperature during their hospital stay (37).

The best available evidence is provided by two well-designed RCTs (21–23, 39). In an industry-sponsored trial, Oelschlager and colleagues assigned 108 patients with paraesophageal hernia to receive either U-shaped SIS or suture repair. The authors found a significant reduction in the incidence of hernia recurrence (24 vs. 9%) at 6 months (21); however, long-term follow-up data (median 58 months, range 40–78) demonstrated no such benefit (22). Although this outcome may be biased by significant attrition (exceeding 20%), the reported recurrence rate for the mesh group remains unacceptably high.

In a recent double blind RCT that was sponsored by a national authority, suture mesh repair was compared with SIS or collagen-coated titanium mesh augmentation of the hiatus(39); similar recurrence rates at 6 months (7.9 vs. 5.9%, respectively) were found in the suture and biologic mesh repair groups, whereas no recurrence occurred in the synthetic mesh group. This finding, however, should be cautiously interpreted in the presence of wide confidence interval (95% confidence interval, 0.24–9.78). Long-term follow-up data of this trial are pending.

Most authors have focused their interest on potential beneficial effects of biologic grafts in paraesophageal hernia. In a cohort study, Schmidt and colleagues compared suture repair and mesh augmentation with HACD in small hernias (1–5 cm as assessed by barium upper gastrointestinal series or esophagogastroscopy) (36). A benefit of mesh repair was demonstrated, as indicated by a reduced recurrence rate (16 vs. 0%) at 1 year and improvement of symptoms of dysphagia.

DISCUSSION

Limited evidence exists investigating the role of biologic meshes in traumatic diaphragmatic repair. Low quality evidence (Level 4) suggests that this approach is feasible, at least in chronic cases. Biologic meshes have also been used in contaminated surgical fields with favorable results (Level 5). Because of the difficulties randomizing patients in the acute setting and the rarity of this condition, clinicians should be encouraged to publish their experience with biologic meshes in traumatic diaphragmatic rupture.

Level 1b data currently support lower recurrence rates for biologic mesh repair in the setting of paraesophageal hernia in the short term with conflicting evidence, whereas level 2b data support that this outcome benefit is lost in the long term. In a recent systematic review and meta-analysis of randomized and observational studies conducted by our research group, we found a beneficial short-term effect of mesh augmentation of the hiatus using biologic mesh (odds ratio 3.74, 95% confidence interval 0.92–8.98, $p = 0.003$) (40). However, no long-term outcome data were available for meta-analysis. Low quality data (level 4) suggest

that patients with hiatal hernia measuring between 1 and 5 cm may benefit from biologic mesh augmentation. Nevertheless, cost-benefit assessment is lacking and the available evidence favoring biologic over synthetic meshes is insufficient.

The impact of type of biologic graft on hernia recurrence remains to be investigated. Further experimental and clinical research is required to assess new biologic implants in hiatal hernia repair. Although current data have shown SIS implants to be associated with high recurrence rates, other biologic materials have not been adequately investigated. Considering the rarity of cases with traumatic diaphragmatic defects, the effectiveness of biologic implants in such situations may be extrapolated from evidence derived from hiatal hernia repair. Future RCTs are required to investigate the role of biologic meshes in both paraesophageal and small hiatal hernias and evaluate their comparative efficacy to synthetic meshes.

AUTHOR CONTRIBUTIONS

Conception and design: SA, FK. Acquisition and interpretation of data: SA, FG, RP. Drafting the work or revision for important intellectual content: SA, FG, RP, FK. Final approval: SA, FG, RP, FK. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: SA, FG, RP, FK.

REFERENCES

1. Morgan BS, Watcyn-Jones T, Garner JP. Traumatic diaphragmatic injury. *J R Army Med Corps* (2010) **156**:139–44. doi:10.1136/jramc-156-03-02
2. Disler DG, Deluca SA. Traumatic rupture of the diaphragm and herniation of the liver. *Am Fam Physician* (1992) **46**:453–6.
3. Barbiera F, Nicastro N, Finazzo M, Lo Casto A, Runza G, Bartolotta TV, et al. The role of MRI in traumatic rupture of the diaphragm. Our experience in three cases and review of the literature. *Radiol Med* (2003) **105**:188–94.
4. Zarzavadjian Le Bian A, Costi R, Smadja C. Delayed right-sided diaphragmatic rupture and laparoscopic repair with mesh fixation. *Ann Thorac Cardiovasc Surg* (2014) **20 Suppl**:550–3. doi:10.5761/atcs.cr.12.02065
5. Matz A, Landau O, Alis M, Charuzi I, Kyzer S. The role of laparoscopy in the diagnosis and treatment of missed diaphragmatic rupture. *Surg Endosc* (2000) **14**:537–9. doi:10.1007/s004640000362
6. Desir A, Ghaye B. CT of blunt diaphragmatic rupture. *Radiographics* (2012) **32**:477–98. doi:10.1148/rg.322115082
7. Sliker CW. Imaging of diaphragm injuries. *Radiol Clin North Am* (2006) **44**:199–211. doi:10.1016/j.rcl.2005.10.003
8. Haciibrahimoglu G, Solak O, Olcmen A, Bedirhan MA, Solmazer N, Gurses A. Management of traumatic diaphragmatic rupture. *Surg Today* (2004) **34**:111–4. doi:10.1007/s00595-003-2662-8
9. Furnée E, Hazebroek E. Mesh in laparoscopic large hiatal hernia repair: a systematic review of the literature. *Surg Endosc* (2013) **27**:3998–4008. doi:10.1007/s00464-013-3036-y
10. Antoniou SA, Antoniou GA, Koch OO, Pointner R, Granderath FA. Lower recurrence rates after mesh-reinforced versus simple hiatal hernia repair: a meta-analysis of randomized trials. *Surg Laparosc Endosc Percutan Tech* (2012) **22**:498–502. doi:10.1097/SLE.0b013e3182747ac2
11. Stadlhuber RJ, Sherif AE, Mittal SK, Fitzgibbons RJ Jr, Michael Brunt L, Hunter JG, et al. Mesh complications after prosthetic reinforcement of hiatal closure: a 28-case series. *Surg Endosc* (2009) **23**:1219–26. doi:10.1007/s00464-008-0205-5
12. Parker M, Bowers SP, Bray JM, Harris AS, Belli EV, Pfluke JM, et al. Hiatal mesh is associated with major resection at revisional operation. *Surg Endosc* (2010) **24**:3095–101. doi:10.1007/s00464-010-1095-x
13. Antoniou SA, Koch OO, Antoniou GA, Pointner R, Granderath FA. Mesh-reinforced hiatal hernia repair: a review on the effect on postoperative dysphagia and recurrence. *Langenbecks Arch Surg* (2012) **397**:19–27. doi:10.1007/s00423-011-0829-0
14. Antoniou SA, Pointner R, Granderath FA. Hiatal hernia repair with the use of biologic meshes: a literature review. *Surg Laparosc Endosc Percutan Tech* (2011) **21**:1–9. doi:10.1097/SLE.0b013e31820ad56c
15. Teicher EJ, Madbak FG, Dangleben DA, Pasquale MD. Human acellular dermal matrix as a prosthesis for repair of a traumatic diaphragm rupture. *Am Surg* (2010) **76**:231–2.
16. Pulido J, Reitz S, Gozdanovic S, Price P. Laparoscopic repair of chronic traumatic diaphragmatic hernia using biologic mesh with cholecystectomy for intrathoracic gallbladder. *Int J Surg Case Rep* (2012) **3**:349–53. doi:10.4293/108680811X13176785204472
17. Al-Nouri O, Hartman B, Freedman R, Thomas C, Esposito T. Diaphragmatic rupture: is management with biological mesh feasible? *JSLS* (2011) **15**:546–9. doi:10.1016/j.ijscr.2012.04.011
18. Oelschlager BK, Barreca M, Chang L, Pellegrini CA. The use of small intestine submucosa in the repair of paraesophageal hernias: initial observations of a new technique. *Am J Surg* (2003) **186**:4–8. doi:10.1016/S0002-9610(03)00114-4
19. Strange PS. Small intestinal submucosa for laparoscopic repair of large paraesophageal hiatal hernias: a preliminary report. *Surg Technol Int* (2003) **11**:141–3.
20. Johnson JM, Carmody BJ, Jamal MK, DeMaria EJ. Onlay hiatal reinforcement utilizing human acellular dermal matrix: three case series. *Surg Innov* (2005) **12**:239–41. doi:10.1177/155335060501200309
21. Oelschlager BK, Pellegrini CA, Hunter J, Soper N, Brunt M, Sheppard B, et al. Biologic prosthesis reduces recurrence after laparoscopic paraesophageal hernia repair: a multicenter, prospective, randomized trial. *Ann Surg* (2006) **244**:481–90. doi:10.1097/01.sla.0000237759.42831.03
22. Oelschlager BK, Pellegrini CA, Hunter JG, Brunt ML, Soper NJ, Sheppard BC, et al. Biologic prosthesis to prevent recurrence after laparoscopic paraesophageal hernia repair: long-term follow-up from a multicenter, prospective, randomized trial. *J Am Coll Surg* (2011) **213**:461–8. doi:10.1016/j.jamcollsurg.2011.05.017
23. Oelschlager BK, Petersen RP, Brunt LM, Soper NJ, Sheppard BC, Mitsumori L, et al. Laparoscopic paraesophageal hernia repair: defining long-term clinical and anatomic outcomes. *J Gastrointest Surg* (2012) **16**:453–9. doi:10.1007/s11605-011-1743-z
24. Ringley CD, Bochkarev V, Ahmed SI, Vitamvas ML, Oleynikov D. Laparoscopic hiatal hernia repair with human acellular dermal matrix patch: our initial experience. *Am J Surg* (2006) **192**:767–72. doi:10.1016/j.amjsurg.2006.08.042
25. Wisbach G, Peterson T, Thoman D. Early results of the use of acellular dermal allograft in type III paraesophageal hernia repair. *JSLS* (2006) **10**:184–7.
26. Jacobs M, Gomez E, Plasencia G, Lopez-Penalver C, Lujan H, Velarde D, et al. Use of surgisis mesh in laparoscopic repair of hiatal hernias. *Surg Laparosc Endosc Percutan Tech* (2007) **17**:365–8. doi:10.1097/SLE.0b013e318123fc49
27. Lee E, Frisella MM, Matthews BD, Brunt LM. Evaluation of acellular human dermis reinforcement of the crural closure in patients with difficult hiatal hernias. *Surg Endosc* (2007) **21**:641–5. doi:10.1007/s00464-006-9117-4
28. St Peter SD, Ostlie DJ, Holcomb GW III. The use of biosynthetic mesh to enhance hiatal repair at the time of redo Nissen fundoplication. *J Pediatr Surg* (2007) **42**:1298–301. doi:10.1016/j.jpedsurg.2007.03.040
29. Fumagalli U, Bona S, Caputo M, Elmore U, Battafarano F, Pestalozza A, et al. Are surgisisbiomeshes effective in reducing recurrences after laparoscopic repair of large hiatal hernias? *Surg Laparosc Endosc Percutan Tech* (2008) **18**:433–6. doi:10.1097/SLE.0b013e3181802ca7
30. Lee YK, James E, Bochkarev V, Vitamvas M, Oleynikov D. Long-term outcome of cruroplasty reinforcement with human acellular dermal matrix in large paraesophageal hiatal hernia. *J Gastrointest Surg* (2008) **12**:811–5. doi:10.1007/s11605-007-0463-x
31. Varela JE, Jacks SP. Laparoscopic circular biomeshhiatoplasty during paraesophageal hernia repair. *Surg Innov* (2009) **16**:124–8. doi:10.1177/1553350609336420

32. Diaz DF, Roth JS. Laparoscopic paraesophageal hernia repair with acellulardermal matrix cruroplasty. *JSLS* (2011) **15**:355–60. doi:10.4293/108680811X13125733356594
33. Goers TA, Cassera MA, Dunst CM, Swanström LL. Paraesophageal hernia repair with biomesh does not increase postoperative dysphagia. *J Gastrointest Surg* (2011) **15**:1743–9. doi:10.1007/s11605-011-1596-5
34. Alicuben ET, Worrell SG, DeMeester SR. Impact of crural relaxing incisions, collis gastroplasty, and non-cross-linked human dermal mesh crural reinforcement on early hiatal hernia recurrence rates. *J Am Coll Surg* (2014) **219**:988–92. doi:10.1016/j.jamcollsurg.2014.07.937
35. Molena D, Mungo B, Stem M, Lidor AO. Novel combined VATS/laparoscopic approach for giant and complicated paraesophageal hernia repair: description of technique and early results. *Surg Endosc* (2015) **29**:185–91. doi:10.1007/s00464-014-3662-z
36. Schmidt E, Shaligram A, Reynoso JF, Kothari V, Oleynikov D. Hiatal hernia repair with biologic mesh reinforcement reduces recurrence rate in small hiatal hernias. *Dis Esophagus* (2014) **27**:13–7. doi:10.1111/dote.12042
37. Sharp NE, Alemayehu H, Desai A, Holcomb GW III, St Peter SD. Fever after redo Nissen fundoplication with hiatal hernia repair. *J Surg Res* (2014) **190**:594–7. doi:10.1016/j.jss.2014.05.021
38. Ward KC, Costello KP, Baalman S, Pierce RA, Deeken CR, Frisella MM, et al. Effect of acellular human dermis buttress on laparoscopic hiatal hernia repair. *Surg Endosc* (2015) **29**:2291–7. doi:10.1007/s00464-014-3946-3
39. Watson DI, Thompson SK, Devitt PG, Smith L, Woods SD, Aly A, et al. Laparoscopic repair of very large hiatus hernia with sutures versus absorbable mesh versus nonabsorbable mesh: a randomized controlled trial. *Ann Surg* (2015) **261**:282–9. doi:10.1097/SLA.0000000000000842
40. Antoniou SA, Müller-Stich BP, Antoniou GA, Köhler G, Luketina RR, Koch OO, et al. Laparoscopic augmentation of the diaphragmatic hiatus with biologic mesh versus suture repair: a systematic review and meta-analysis. *Langenbecks Arch Surg* (2015) **400**:577–83. doi:10.1007/s00423-015-1312-0

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

APPENDIX

BioMesh Study Group

Ferdinand Köckerling (Chairman), Stavros A. Antoniou, René Fortelny, Frank A. Granderath, Markus Heiss, Franz Mayer, Marc Miserez, Agneta Montgomery, Salvador Morales-Conde, Filip Muysoms, Alexander Petter-Puchner, Rudolph Pointner, Neil Smart, MarciejSmietanski, Bernd Stechemesser undertaken by the BioMesh Study Group.

AIM

The BioMesh Study Group has set itself the task of identifying how best to use biological meshes for the various indications. The first step toward achieving that goal is to compile systematic reviews of the different indications on the basis of the existing literature. The available literature sources will be evaluated in accordance with the Oxford Centre for Evidence-based Medicine-Levels of Evidence (March 2009). Next, based on the review findings corresponding Statements and Recommendations are to be formulated in a Consensus Conference for the use of biological meshes for the different indications. The findings of the Consensus Conference are then to be summarized for a joint publication. This present publication is part of the project undertaken by the BioMesh Study Group.

frontiers in Surgery

ORIGINAL RESEARCH
published: 09 March 2016
doi: 10.3389/fsurg.2016.00016

Functional Results after Repair of Large Hiatal Hernia by Use of a Biologic Mesh

Filimon Antonakis[1], Ferdinand Köckerling[2] and Friedrich Kallinowski[1]*

[1] Department of General and Visceral Surgery, Asklepios Klinikum Harburg, Hamburg, Germany, [2] Department of General, Visceral and Vascular Surgery, Vivantes Klinikum Spandau, Berlin, Germany

Background: The aim of this observational study is to analyze the results of patients with large hiatal hernia and upside-down stomach after surgical closure with a biological mesh (Permacol®, Covidien, Neustadt an der Donau, Germany). Biological mesh is used to prevent long-term detrimental effects of artificial meshes and to reduce recurrence rates.

Methods: A total of 13 patients with a large hiatal hernia and endothoracic stomach, who underwent surgery between 2010 and 2014, were included. Interviews and upper endoscopy were conducted to determine recurrences, lifestyle restrictions, and current complaints.

Results: After a mean follow-up of 26 ± 18 months (range: 3–58 months), 10 patients (3 men, mean age 73 ± 13, range: 26–81 years) were evaluated. A small recurrent axial hernia was found in one patient postoperatively. Dysphagia was the most common complaint (four cases); while in one case, the problem was solved after endoscopic dilatation. In three cases, bloat and postprandial pain were documented. In one case, an explantation of the mesh was necessary due to mesh migration and painful adhesions. In one further case with gastroparesis, pyloroplasty was performed without success. The data are compared to the available literature. It was found that dysphagia and recurrence rates are unrelated both in biological and in synthetic meshes if the esophagus is encircled. In series preserving the esophagus at least partially uncoated, recurrences after the use of biological meshes relieve dysphagia. After the application of synthetic meshes, dysphagia is aggravated by recurrences.

Conclusion: Recurrence is rare after encircling hiatal hernia repair with the biological mesh Permacol®. Dysphagia, gas bloat, and intra-abdominal pain are frequent complaints. Despite the small number of patients, it can be concluded that a biological mesh may be an alternative to synthetic meshes to reduce recurrences at least for up to 2 years. Our study demonstrates that local fibrosis and thickening of the mesh can affect the outcome being associated with abdominal discomfort despite a successful repair. The review of the literature indicates comparable results after 2 years with both biologic and synthetic meshes embracing the esophagus. At the same point in time, reconstruction with synthetic and biologic materials differs when the esophagus is not or only partially encircled in the repair. This is important since encircling artificial meshes can erode the esophagus after 5–10 years.

Keywords: hiatal hernia repair, recurrence, dysphagia, biologic mesh, complications

OPEN ACCESS

Edited by:
Hubert Scheuerlein, University Hospital Jena, Germany

Reviewed by:
Abdulzahra Hussain, South London NHS Trust, UK
Michael Ardelt, University Hospital Jena, Germany
Juan Manuel Suárez-Grau, Hospital General Básico de Riotinto, Spain

****Correspondence:***
Filimon Antonakis
filimonantonakis@gmail.com

Specialty section:
This article was submitted to Visceral Surgery, a section of the journal Frontiers in Surgery

Received: *14 January 2016*
Accepted: *25 February 2016*
Published: *09 March 2016*

Citation:
Antonakis F, Köckerling F and Kallinowski F (2016) Functional Results after Repair of Large Hiatal Hernia by Use of a Biologic Mesh. Front. Surg. 3:16. doi: 10.3389/fsurg.2016.00016

INTRODUCTION

Surgery for hiatal hernia has gone through many developmental stages after the first repair was reported by Soresi in 1926 (1). The therapy of a large hiatal hernia is far from being established due to the complexity of the anatomical region and the need for improvement of some current methods. In analogy to hernia repair of the abdominal wall, synthetic materials were used to repair hiatal hernia to reduce the risk for hernia recurrence (2). Despite the lower recurrence rates in comparison to direct suture (3), there were significant long-term complications due to local fibrosis, stricture formation around the prosthetic material, esophageal erosion, mesh migration, and late dysphagia (4). To solve these problems, biological meshes from human acellular cadaveric dermis (HACD), porcine small intestine submucosa (SIS), porcine dermal collagen (PDC), or bovine pericardium were developed. HACD and SIS have been utilized as mesh grafts for hiatal hernia repair (5). It is assumed that the natural tissue texture of the biologic mesh results in less esophageal erosions and lowers the risk of complications. Less inflammation and reduced fibrotic tissue changes at the hiatus should lead to a better quality of life, specifically lower dysphagia rates (6).

This study aims to assess the clinical result of patients with large hiatal hernia after repair with a biologic mesh.

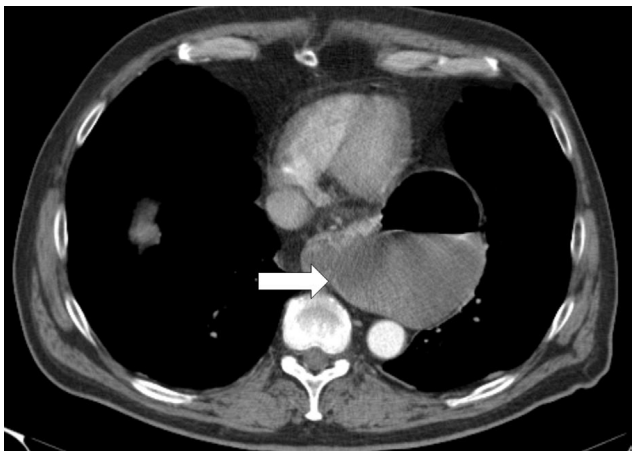

FIGURE 1 | Preoperative computed tomography of the upside-down stomach of a 73-year-old male with the gastroesophageal junction being fully dislocated into the thoracic cavity (arrow).

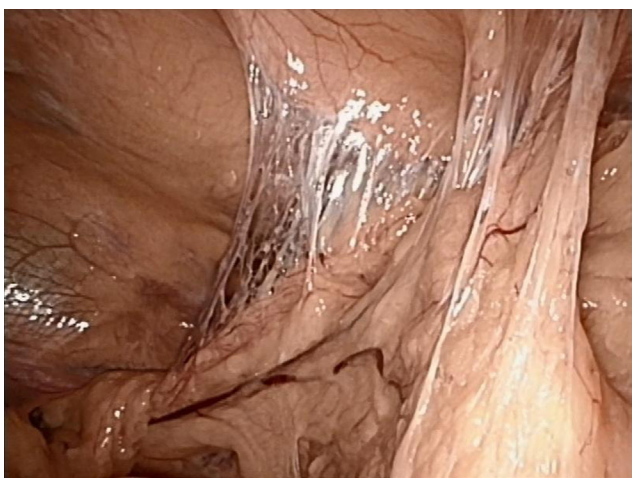

FIGURE 2 | Situs of a large hiatal hernia in this 72-year-old male operated on 2 years ago. The upside-down stomach is fully encased in both loose and dense adhesions.

PATIENTS AND METHODS

A consecutive number of patients, who were diagnosed with large hiatal hernia and thoracic stomach, underwent surgery between 2010 and 2014. Pre- and postoperative work-up included symptoms assessment, barium swallow, endosopy, and CT scan. The large hiatal hernias were anatomically classified as types III and IV and clinically as type 2dII according to Koch et al. (7). Using the formula given by Granderath (8), the hiatal surface area was calculated intraoperatively as 13.5 ± 4.5 cm^2, which is well in the range of large mixed-type hiatal hernia (9).

The CT scan in **Figure 1** and the intraoperative picture in **Figure 2** demonstrate a representative finding of a large hiatal hernia with an upside-down stomach.

Surgery was conducted in the Asklepios Klinikum Harburg in Hamburg, a teaching hospital of the University of Hamburg, and the Asklepios Medical School. All patients complained of unbearable mass reflux with regurgitation of acid material preoperatively. Eight patients complained of the inability to sustain their weight due to dysphagia. Five patients were subsequently unable to conduct routine daily life, such as gardening, wiping of the floor, cycling, etc. One patient suffered from chronic obstructive airway disease and another patient from recurrent pneumonia due to silent aspiration. All hernias were surgically treated by a sutured hiatal repair reinforced with a cross-linked biologic mesh of a porcine acellular dermal collagen matrix (Permacol®, Covidien) under general anesthesia. The mesh was placed to circularly enclose the esophagus with an opening of at least 15 mm in diameter. All patients were included prospectively into an inhospital registry. Data including demographics, prior history, and individualized surgical technique were obtained from the patients' charts and surgical reports. The postoperative progress, the patients' complaints, and the recurrence status were recorded at regular intervals of maximally 1 year. All case notes were reviewed to determine follow-up and to check specifically whether a recurrence occurred or any further unplanned surgery or endoscopy was required. The current status to date was supplemented by a telephone interview.

Surgical Procedures

Both laparoscopic and conventional methods were used. The principle was the same: the closure of the paraesophageal hernia using a 10 cm × 10 cm and 1-mm thick biologic mesh of a porcine

acellular dermal collagen matrix (Permacol® and Covidien). The surgical technique has previously been described (10). Briefly, the hiatal hernia repair involves the preparation and resection of the sac and reduction and retention of the hernia contents intra-abdominally (**Figure 3**). The reposition of the stomach back to the abdominal cavity was followed by a wide mediastinal mobilization of the distal esophagus to ensure appropriate intra-abdominal length to prevent the stomach from sliding back up. Retention was achieved with a posterior hiatoplasty (**Figure 4**) using non-absorbable sutures (Ethibond 0, Ethicon, Norderstedt, Germany). Additionally, a short floppy Nissen's fundoplication was executed and sutured in place again using Ethibond 0 as three interrupted stitches encircling the intra-abdominal esophagus for 25 mm (**Figure 5**). The closure of the hiatus was supported with the quadratic biologic mesh. The mesh was tailored to the individual anatomy by rounding the edges, placed on the diaphragmal crura from the abdominal side, sutured into place with at least four non-absorbable sutures (Ethibond 0), and reinforced with fibrin sealant (Evicel®, Ethicon®, Norderstedt, Germany) (**Figure 6**).

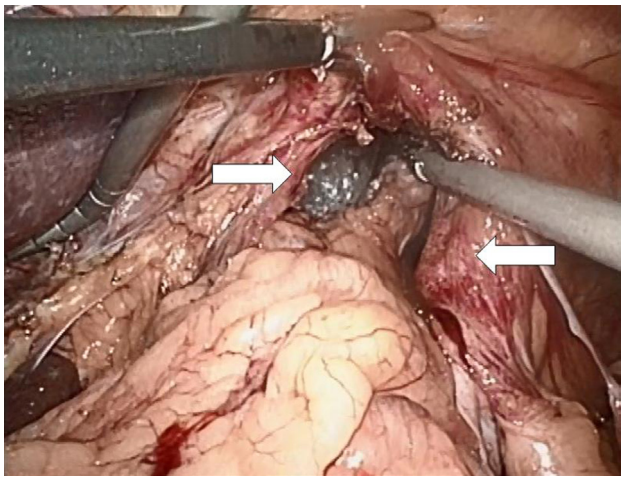

FIGURE 3 | Preparation of the hiatal sac with the right and the left crus of the diaphragm prepared in their ventral aspect (arrows).

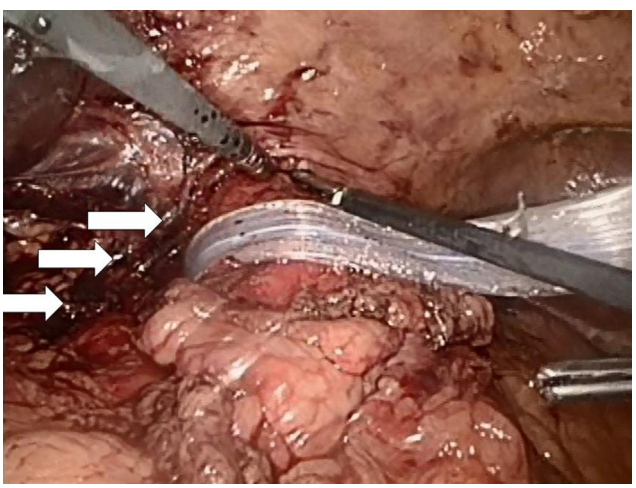

FIGURE 4 | A hiatoplasty is formed with three evenly spaced non-absorbable sutures (Ethibond 0, Ethicon, Norderstedt, Germany, arrows). The distal esophagus is encircled with a silastic band and held to the left. At this point of time, a 54-Ch Rüsch tube is passed through the esophagogastric junction and a 5-mm instrument is additionally placed from the left into the newly formed hiatus in order to ensure sufficient space for the passage of food. A similar instrument is placed at the low left corner of the picture for comparison of sizes. Another 5-mm instrument is inserted from the right in order to lift the ventral crural junction to facilitate instrumentation.

RESULTS

During the study period, 13 patients were surgically treated for a thoracic stomach. Among them one patient passed away in the meantime from coronary heart disease. Additionally, two patients were lost to follow-up by moving to an unknown destination – they could not be located either by searching their medical records or by contacting their primary care physicians, leaving a total of 10 patients for further study. There were three (30%)

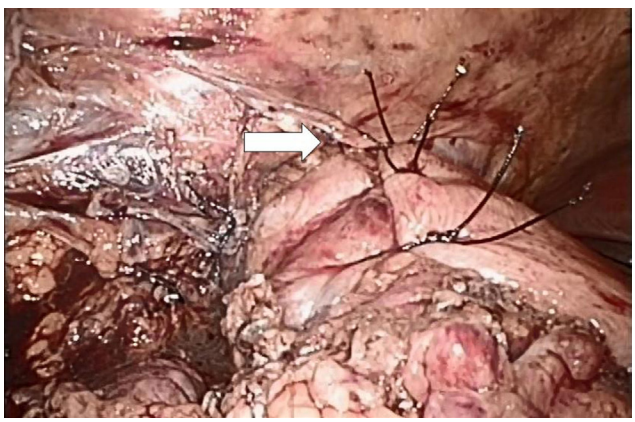

FIGURE 5 | Short floppy Nissen's fundoplication in place with the top suture fixing the stomach, esophagus, and right hiatal leg (white arrow).

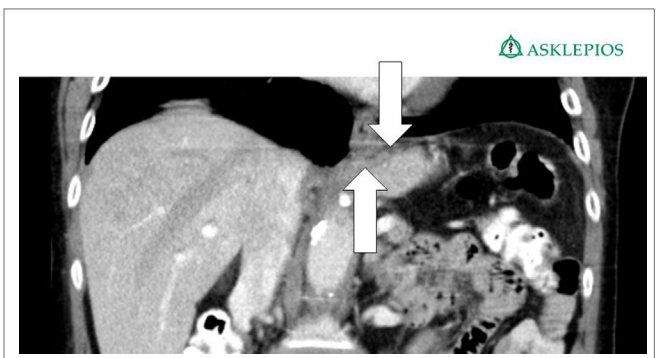

FIGURE 6 | Hiatal region of a 75-year-old female patient 1 year after implantation of the Permacol® mesh as described above. The arrows show the position of the mesh. An upper endoscopy showed a mild gastritis without signs of esophageal reflux at this time.

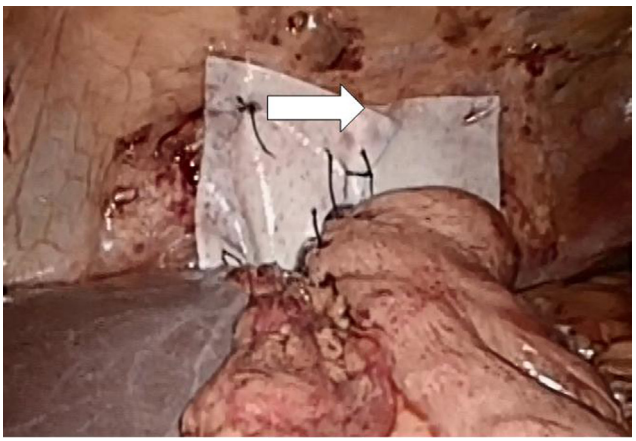

FIGURE 7 | Permacol® reinforment of the hiatoplasty shown above. The Permacol® is secured with non-absorbable interrupted stitches and additionally fastened with fibrin glue (Evicell®) in critical areas (white arrow).

men and seven (70%) women with a median age of 73 ± 13 years (range: 26–81).

The mean follow-up was 27 ± 18 months (range: 3–58). The patients underwent in four cases an open procedure twice due to respiratory and once due to cardiocirculatory instability upon laparoscopy. In one case, the laparoscopic approach had to be converted to a combined laparotomy and left-sided thoracotomy due to the inability to reduce the completely intrathoracic stomach in the abdominal cavity. In six cases, a laparoscopic procedure was performed as described above. A total of 20% (2 of 10) underwent one further, unplanned surgery after the prior therapy; in one case, the mesh was explantated because of dysphagia and pain due to dense fibrosis surrounding the mesh. In the other case, pain due to peritoneal adhesions was found unrelated to the sufficient hiatoplasty with mesh enforcement. In the latter case, first, a gastritis was found on repeat gastrocopy, and later, a Herpes zoster infection was elucidated. On an intercurrent computed tomography scan, the mesh was found in place but appears thickened (arrows in **Figure 7** below). Measuring the mesh from the scans, a 5-mm plate resulted from the 1-mm mesh in this case.

In this case, a pyloroplasty was performed because of gastroparesis without complete relief of symptoms. Since the patient can keep a normal weight, she is reluctant to any further surgical treatment. There were no other major complications. A total of six patients underwent upper endoscopy because of various complaints, such as burning, intra-abdominal pain, regurgitation, and dysphagia. Except for one case with a stenosis bettered by balloon dilatation and the one reported with a small recurrence, there were no pathological findings related to the hiatal repair.

Four patients (40%) complained about dysphagia postoperatively. In one case, the symptoms declined spontaneously within 6 months. Another patient successfully underwent esophageal dilatation of a stenosis 2 months postoperatively. Up to this date, two patients (20%) still report mild dysphagia but maintain normal body weight. Four cases report persistent intra-abdominal discomfort without weight loss. Three patients experienced bloating, while another patient reported reflux. In another case, regurgitation was described by the patient without abnormal endoscopic findings. The symptoms are summarized in **Table 1**.

TABLE 1 | Summary of the status after 2 years (multiple declarations possible).

Symptom	Cases% (*n*)
Pain	30 (3)
Bloating	30 (3)
Dysphagia	20 (2)
Gastroparesis	10 (1)
Reflux with recurrence	10 (1)
Regurgitation	10 (1)

DISCUSSION

The treatment of large and giant hiatal hernias has been a challenge, since it is both technically more difficult and has always substantially elevated recurrence rates (10–12). Laparoscopic hiatal hernia repair for larger hernias seem to have even higher recurrence rates leading to revision surgery (13). Primary suture hiatoplasty without reinforcement is associated with high recurrence rates, so that a variety of meshes has been developed to reduce the risk of recurrence (11). The main concern using a synthetic mesh is the risk of specific complications through the local erosion into the stomach, fibrosis, mesh contraction, and esophageal stenosis, which are thought to cause higher dysphagia rates (4, 14–19). Synthetic meshes are associated with a higher risk of esophageal resection at revision surgery (4, 20). In order to minimize these side effects, biologic meshes from human cadaveric dermis and SIS have been developed. A mild inflammatory response and neovascularization were reported for the biologic grafts (21–23). It is believed that a limited foreign body reaction at the hiatus due to their biocompatibility minimizes the risk of postoperative dysphagia (24).

Among the US surgeons who use mesh to repair the hiatal hernia, 67% prefer biologic mesh (25). The recurrence rates following a biological mesh hiatoplasty can vary in the literature between 0 and 54%, with a median value of 10% (**Table 2**). These recurrence rates are almost identical to those found after hiatal repair using synthetic meshes (range: 0–35, median 7%). In this study, large hiatal hernias were repaired using a cross-linked collagen matrix derived from pig tissue.

According to a retrospective analysis of hiatal revisions following synthetic or biologic mesh application, there were no significant differences in terms of blood loss, duration of surgery, morbidity, and need for esophageal reconstruction (17). The recurrence rate can be significantly reduced from 16 to 0% with the use of an absorbable mesh for the repair of small hiatal hernia (23). In a study of 108 patients, the recurrence rate was reduced from 24 to 9% with the laparoscopic use of a biologic mesh compared to the suture of the hiatus (7). A new meta-analysis confirmed the lower recurrence rates for the biologic mesh in the short-term, but the long-term benefit remains unclear (24). The repair of large hiatal hernias with biologic mesh may be associated

with a lower risk for short-term recurrence compared to primary suture repair. Short-term recurrence rates for suture repair and biologic mesh repair ranged in a meta-analysis between 16.6 and 3.5%, respectively. The same study showed that the long-term recurrence based on data provided by one trial only was 51.3 and 42.4%, respectively (25). In our study, the recurrence rate was 10% after a median time of 27 months. The recurrence rate after the use of SIS can be up to 9% (26). Another large study with 92 patients treated with SIS achieved a recurrence rate of 3.3% and a dysphagia rate of 8.6% in a median follow-up of 3.3 years (27). The incidence of postoperative dysphagia in 22 patients after treatment with human acellular dermal matrix was 4.5% (28). In our study, 40% of the patients complaint postoperatively about dysphagia. Up to now and after successful endoscopic dilatation in one case, 20% of the patients still have the sensation of dysphagia but keep their weight.

Since dysphagia impairs the quality of life significantly, an attempt is made to further elucidate potential associations. In **Table 2**, data are accumulated from the available literature attempting an assessment at a certain postoperative period, namely, 1–2 years as observed in this manuscript. The data are divided in biological and synthetic meshes using techniques embracing the esophagus in order to reduced long-term recurrence rate or excluding the esophagus in an attempt to preserve its function. Since it cannot be assumed that the data are homogenously distributed, the Mann–Whitney *U*-test was used to evaluate group differences. Neither the preoperative dysphagia rate nor the placement of the mesh influences the dysphagia rate

TABLE 2 | Pre- and postoperative data from published hiatal repairs embracing the esophagus and reinforcing only the crural repair.

Author	Year	Mesh type	Patients	Hernia type	Dysphagia preoperatively (%)	Follow-up (months)	Recurrence (%)	Dysphagia 1–2 years postoperatively (%)
Mesh placement encircling the esophagus								
Hazebroek (26)	2008	TiMesh	18	II–IV	22	24	6	41
Carlson (27)	1999	PTFE	15	III–IV	na	30	0	na
Frantzides (28)	2002	PTFE	36	III–IV	na	30	0	na
Lubezky (29)	2007	PTFE/ePTFE	45	III–IV	17	28	13	20
Stavropoulos (30)	2012	ePTFE	38	II–IV	na	24	na	na
Zaninotto (31)	2007	Polypropylene/ePTFE	35	III	na	71	9	22
Gouvas (32)	2011	Polypropylene/PTFE	20	II–IV	84	36	15	19
Chilintseva (33)	2012	PTFE/polyester/polypropylene/ePTFE	45	I–IV	7	51	4	11
Oelschläger (34)	2003	SIS	9	II–III	33	8	0	13
Jacobs (35)	2007	SIS	92	I–III	na	38	3	11
Massullo (36)	2012	Polyglycolic:trimethylene	11	I–III	na	13	9	0
Present paper	2015	Cross-linked acellular pig dermis	10	III–IV	80	26	10	20
Mesh placement avoiding the esophagus								
Watson (37)	2015	TiMesh	42	III–IV	19	12	23	7
Gryska (38)	2005	PTFE	130	I–III	na	48	8	0
Hazebroek (26)	2009	ePTFE	14	II–III	16	34	29	27
Champion (39)	2003	Polypropylene	19	II–III	na	25	5	11
Leeder (40)	2003	Polypropylene	14	I–III	93	46	14	0
Horstmann (41)	2004	Polypropylene	16	II–III	31	14	0	na
Granderath (42)	2006	Polypropylene	150	II–IV	na	12	8	4
Turkcapar (43)	2007	Polypropylene	156	I–II	na	24	2	1
Soricelli (44)	2009	Polypropylene	91	II–III	na	69	2	0
Morino (45)	2006	Polypropylene/PTFE	37	I–III	na	36	35	0
Grubnik (46)	2013	Polypropylene-Monocryl	158	II–IV	na	28	5	2
Goers (47)	2011	Various biomeshes	40	II–IV	na	6	0	38
Molena (48)	2015	Various biomeshes	18	III–IV	na	na	na	na
Ringley (49)	2006	HACD	22	II–IV	0	7	0	6
Wisbach (50)	2006	HACD	11	III	55	24	11	18
Lee (51)	2007	HACD	17	I–III	na	14	12	6
Lee (52)	2008	HACD	52	na	44	24	4	na
Diaz (53)	2011	HACD	26	II–III	13	24	15	23
Alicuben (54)	2014	HACD	15	II–IV	na	12	20	13
Mesh placement avoiding the esophagus								
Jacobs (35)	2007	SIS	74	na	na	38	4	na
Fumagalli (55)	2008	SIS	6	na	na	12	50	13
Oelschlager (56)	2011	SIS	33	II–III	3	58	54	3
Wassenaar (57)	2012	SIS	31	I–IV	na	45	3	20
Watson (37)	2015	SIS	41	III–IV	27	12	23	9
Wang (58)	2015	SIS and alike	66	I–III	6	24	13	4

na, not available.

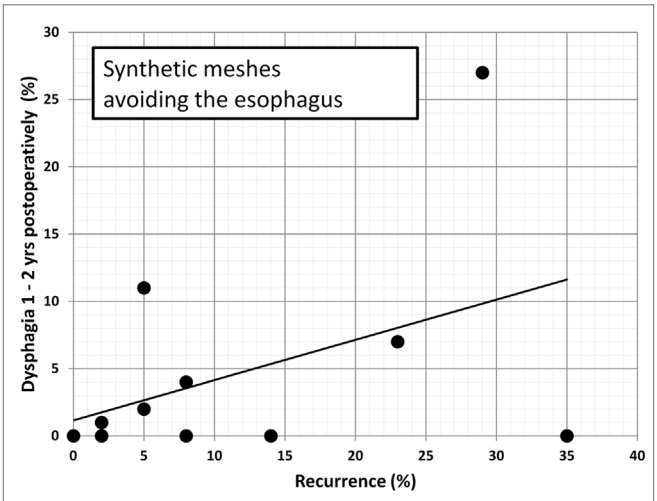

FIGURE 8 | Dysphagia rates as a function of recurring hiatal hernia after 1–2 years using synthetic meshes leaving at least half of the circumference of the esophagus to move freely (data from Table 2). The line indicates the trendline.

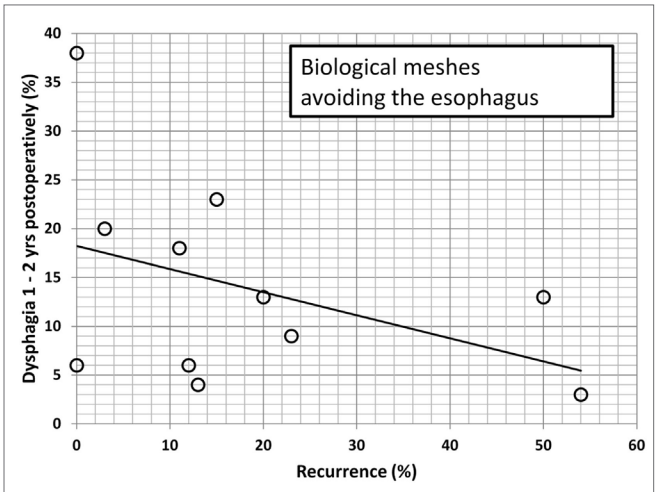

FIGURE 9 | Dysphagia rates as a function of recurring hiatal hernia after 1–2 years using biological meshes leaving at least half of the circumference of the esophagus to move freely (data from Table 2). The line indicates the trendline.

significantly although meshes encircling the esophagus tend to exhibit higher dysphagia rates (**Table 2**, $p = 0.126$). The length of the follow-up and the rate of recurrence or dysphagia are unrelated in all groups (**Table 2**, $p = 0.667$). In both synthetic and biological meshes embracing the esophagus, there is a trend toward elevated dysphagia rates with increasing recurrence rates (**Table 2**, $p = 0.021$). In reconstructions avoiding at least half of the circumference, synthetic meshes increase dysphagia as recurrences occur [**Table 2**; **Figure 8**, $r = 0.63$, small effect according to Thalheimer and Cook (59)]. In contrast, biological meshes decrease dysphagia rates as recurrences occur [**Table 2**; **Figure 9**, $r = -0.728$, intermediate effect according to Thalheimer and Cook (59)]. The results should be viewed with caution but can be interpreted that the integration of biological meshes in reconstructions avoiding the esophagus decreases dysphagia increasing recurrences within the first 2 years.

In a recent study with 49 patients, 8% required endoscopic dilatation with a successful resolution of the symptoms (60). Interestingly, hiatal hernia repair with biomesh fails to increase the postoperative dysphagia rate compared to suture repair alone (6). The reported rates of dysphagia with synthetic meshes vary between 0 and 41%, with a median of 15.5% [**Table 2** (24, 61–63)].

Most patients with a recurrent paraesophageal hernia still experience an improvement of clinical symptoms compared to the preoperative status (63, 64). Despite the high recurrence rate up to 54% after a laparoscopic repair of the hiatus with or without mesh, there can be a significant improvement in all parameters assessing the quality of life (10). This can be due to the smaller sac of the recurrent hernia compared to the original size with a diminished risk of volvulus, obstruction, and ischemia. Our findings demonstrate, in general, that gastrointestinal symptoms associated with big paraesophageal hernias and thoracic stomach, such as postprandial obstruction and pain, are significantly improved after a mesh repair up to 58 months following the surgical closure and reinforcement with the biomesh Permacol®. However, price and limited use, e.g., for religious reasons should be weighed against the potential of the biomesh.

Cross-linked collagen matrices have a more coordinated structure and therefore can sustain higher loads for longer times compared to non-cross-linked ones (60, 65). Several studies showed that cross-linking does not appear to affect the tissue integration in animal models or human (60, 65, 66). Mesh fibrosis may occur potentially increasing the stiffness of the repair (as demonstrated in a postoperative CT scan, **Figure 7**). Late onset dysphagia even in mesh positions avoiding the esophagus might be related to this scar formation (60). It remains unclear whether cross-linking contributes to fibrotic changes since we know that resorption is delayed. Permacol™ is a porcine-derived acellular dermal sheet, which is composed predominantly of type I collagen (93–95%). During the manufacturing process, the cellular components are removed and the collagen of the dermis is treated with hexamethylene diisocyanate (HMDI) to increase the degree of cross-linking. It is currently used for the repair of abdominal and thoracic wall defects and for hernias (60). To prevent mesh dislocation, meshes must be fixated (67). So far, little is known how to best fasten a hernia mesh in the hiatal position. There are many different ways to anchor a mesh, such as non-absorbable sutures, tacks, or fibrin sealant (61). We prefer a limited number of sutures and add fibrin glue as shown in **Figure 6** in order to achieve a maximal pliability still holding the mesh in place at the same time. Since the mesh can be placed in at least six different positions, the best placement is still unknown. Most surgeons place a mesh in a U-shape or a pantaloon collar in a retroesophageal position with the limbs of the mesh encircling the esophagus [**Table 2** (10–64)]. Data depicted in **Figures 8** and **9** indicate a different behavior of synthetic and biologic meshes when the esophagus is not fully

encircled. On the one hand, patients with smaller (up to 5 cm) hiatal hernias may benefit from the use of a biologic mesh for the repair (61, 64, 68). On the other hand, larger hernias are more prone to develop recurrences, even with mesh reinforcement (68). At this point of time, the preferred technique, the superior mesh position, or the outstanding material still awaits future investigation.

CONCLUSION

The principle of hiatal hernia repair aims to eliminate the hernia preserving the functionality of the gastroesophageal junction at the same time. The use of a biologic mesh to repair large hiatal hernias is an effective method with low recurrence rates. It can reduce the local inflammation and postoperative dysphagia compared to synthetic meshes. Our study demonstrates that local fibrosis and thickening of the mesh can affect the outcome being associated with abdominal discomfort despite a successful repair. The review of the literature indicates comparable results after 2 years with both biologic and synthetic meshes embracing the esophagus. At the same point of time, reconstruction with synthetic and biologic materials differs when the esophagus is not or only partially encircled in the repair.

ETHICS STATEMENT

Retrospective case series. No ethic committee approval necessary.

AUTHOR CONTRIBUTIONS

FA and FK have treated the patients in their hospital. The development of the study design and the follow-up of the patients have been also done by FA and FK. FA, FKö, and FK are responsible for the content of the manuscript.

REFERENCES

1. Stylopoulos N, Rattner DW. The history of hiatal hernia surgery: from Bowditch to laparoscopy. *Ann Surg* (2005) **2005**(241):185–93.
2. Kuster GG, Gilroy S. Laparoscopic technique for repair of paraesophageal hiatal hernias. *J Laparoendosc Surg* (1993) **3**:331–8. doi:10.1089/lps.1993.3.331
3. Antoniou SA, Antoniou GA, Koch OO, Pointner R, Granderath FA. Lower recurrence rates after mesh-reinforced versus simple hiatal hernia repair: a meta-analysis of randomized trials. *Surg Laparosc Endosc Percutan Tech* (2012) **22**:498–502. doi:10.1097/SLE.0b013e3182747ac2
4. Stadlhuber RJ, Sherif AE, Mittal SK, Fitzgibbons RJ Jr, Michael Brunt L, Hunter JG, et al. Mesh complications after prosthetic reinforcement of hiatal closure: a 28-case series. *Surg Endosc* (2009) **23**:1219–26. doi:10.1007/s00464-008-0205-5
5. Antoniou SA, Pointner R, Granderath FA. Hiatal hernia repair with the use of biologic meshes: a literature review. *Surg Laparosc Endosc Percutan Tech* (2011) **21**:1–9. doi:10.1097/SLE.0b013e31820ad56c
6. Goers TA, Cassera MA, Dunst CM, Swanström LL. Paraesophageal hernia repair with biomesh does not increase postoperative dysphagia. *J Gastrointest Surg* (2011) **15**:1743–9. doi:10.1007/s11605-011-1596-5
7. Koch O, Köhler G, Antoniou SA, Pointner R. Diagnosis and surgical therapy of hiatal hernia. *Zentralbl Chir* (2014) **139**:393–8. doi:10.1055/s-0033-1360294
8. Granderath FA. Measurement of the esophageal hiatus by calculation of the hiatal surface area (HSA). Why, when and how? *Surg Endosc* (2007) **21**:2224–5. doi:10.1007/s00464-007-9348-z
9. Ouyang W, Dass C, Zhao H, Kim C, Criner G; COPDGene Investigators. Multiplanar MDCT measurement of esophageal hiatus surface area: association with hiatal hernia and GERD. *Surg Endosc* (2015). doi:10.1007/s00464-015-4499-9
10. Oelschlager BK, Pellegrini CA, Hunter J, Soper N, Brunt M, Sheppard B, et al. Biologic prosthesis reduces recurrence after laparoscopic paraesophageal hernia repair: a multicenter, prospective, randomized trial. *Ann Surg* (2006) **244**:481–90. doi:10.1097/01.sla.0000237759.42831.03
11. Hashemi M, Peters JH, DeMeester TR, Huprich JE, Quek M, Hagen JA, et al. Laparoscopic repair of large type III hiatal hernia: objective followup reveals high recurrence rate. *J Am Coll Surg* (2000) **190**:553–60. doi:10.1016/S1072-7515(00)00260-X
12. Muller-Stich BP, Holzinger F, Kapp T, Klaiber C. Laparoscopic hiatal hernia repair: long-term outcome with the focus on the influence of mesh reinforcement. *Surg Endosc* (2006) **20**:380–4. doi:10.1007/s00464-004-2272-6
13. Mehta S, Boddy A, Rhodes M. Review of outcome after laparoscopic paraesophageal hiatal hernia repair. *Surg Laparosc Endosc Percutan Tech* (2006) **16**:301–6. doi:10.1097/01.sle.0000213700.48945.66
14. Yano F, El Sherif A, Filipi CJ, Mittal SK. Use of temporary esophageal stent in management of perforations after benign esophageal surgery. *Surg Laparosc Endosc Percutan Tech* (2008) **18**:283–5. doi:10.1097/SLE.0b013e31816b4bbd
15. Coluccio G, Ponzio S, Ambu V, Tramontano R, Cuomo G. [Dislocation into the cardial lumen of a PTFE prosthesis used in the treatment of voluminous hiatal sliding hernia, a case report]. *Minerva Chir* (2000) **2000**(55):341–5.
16. Dutta S. Prosthetic esophageal erosion after mesh hiatoplasty in a child, removed by transabdominal endogastric surgery. *J Pediatr Surg* (2007) **42**:252–6. doi:10.1016/j.jpedsurg.2006.09.043
17. Edelman DS. Laparoscopic paraesophageal hernia repair with mesh. *Surg Laparosc Endosc* (1995) **5**:32–7.
18. Gajbhiye R, Quraishi AH, Mahajan P, Warhadpande M. Dysphagia due to transmural migration of polypropylene mesh into esophagus. *Indian J Gastroenterol* (2005) **24**:226–7.
19. Griffith PS, Valenti V, Qurashi K, Martinez-Isla A. Rejection of goretex mesh used in prosthetic cruroplasty: a case series. *Int J Surg* (2008) **6**:106–9. doi:10.1016/j.ijsu.2007.12.004
20. Nandipati K, Bye M, Yamamoto SR, Pallati P, Lee T, Mittal SK. Reoperative intervention in patients with mesh at the hiatus is associated with high incidence of esophageal resection – a single-center experience. *J Gastrointest Surg* (2013) **17**:2039–44. doi:10.1007/s11605-013-2361-8
21. Kaleya RN. Evaluation of implant/host tissue interactions following intraperitoneal implantation of porcine dermal collagen prosthesis in the rat. *Hernia* (2005) **9**:269–76. doi:10.1007/s10029-005-0003-0
22. Zheng F, Verbeken E, de Ridder D, Deprest J. Improved surgical outcome by modification of porcine dermal collagen implant in abdominal wall reconstruction in rats. *Neurourol Urodyn* (2005) **24**:362–8. doi:10.1002/nau.20148
23. Ayubi FS, Armstrong PJ, Mattia MS, Parker DM. Abdominal wall hernia repair: a comparison of Permacol and Surgisis grafts in a rat hernia model. *Hernia* (2008) **12**:373–8. doi:10.1007/s10029-008-0359-z
24. Antoniou SA, Koch OO, Antoniou GA, Pointner R, Granderath FA. Mesh-reinforced hiatal hernia repair: a review on the effect on postoperative dysphagia and recurrence. *Langenbecks Arch Surg* (2012) **397**:19–27. doi:10.1007/s00423-011-0829-0
25. Ward KC, Costello KP, Baalman S, Pierce RA, Deeken CR, Frisella MM, et al. Effect of acellular human dermis buttress on laparoscopic hiatal hernia repair. *Surg Endosc* (2015) **29**:2291–7. doi:10.1007/s00464-014-3946-3
26. Hazebroek EJ, Ng A, Yong DH, Berry H, Leibman S, Smith GS. Evaluation of lightweight titanium-coated polypropylene mesh (TiMesh) for laparoscopic repair of large hiatal hernias. *Surg Endosc* (2008) **22**:2428–32.
27. Carlson MA, Richards CG, Frantzides CT. Laparoscopic prosthetic reinforcement of hiatal herniorrhaphy. *Dig Surg* (1999) **16**:407–10. doi:10.1159/000018756

28. Frantzides CT, Madan AK, Carlson MA, Stavropoulos GP. A prospective, randomized trial of laparoscopic polytetrafluoroethylene (PTFE) patch repair vs simple cruroplasty for large hiatal hernia. *Arch Surg* (2002) **137**:649–52. doi:10.1001/archsurg.137.6.649
29. Lubezky N, Sagie B, Keidar A, Szold A. Prosthetic mesh repair of large and recurrent diaphragmatic hernias. *Surg Endosc* (2007) **21**:737–41. doi:10.1007/s00464-007-9208-x
30. Stavropoulos G, Flessas II, Mariolis-Sapsakos T, Zagouri F, Theodoropoulos G, Toutouzas K, et al. Laparoscopic repair of giant paraesophageal hernia with synthetic mesh: 45 consecutive cases. *Am Surg* (2012) **78**:432–5.
31. Zaninotto G, Portale G, Costantini M, Fiamingo P, Rampado S, Guirroli E, et al. Objective follow-up after laparoscopic repair of large type III hiatal hernia. Assessment of safety and durability. *World J Surg* (2007) **31**:2177–83. doi:10.1007/s00268-007-9212-2
32. Gouvas N, Tsiaoussis J, Athanasakis E, Zervakis N, Pechlivanides G, Xynos E. Simple suture or prosthesis hiatal closure in laparoscopic repair of paraesophageal hernia: a retrospective cohort study. *Dis Esophagus* (2011) **24**:69–78. doi:10.1111/j.1442-2050.2010.01094.x
33. Chilintseva N, Brigand C, Meyer C, Rohr S. Laparoscopic prosthetic hiatal reinforcement for large hiatal hernia repair. *J Visc Surg* (2012) **149**:e215–20. doi:10.1016/j.jviscsurg.2012.01.006
34. Oelschlager BK, Barreca M, Chang L, Pellegrini CA. The use of small intestine submucosa in the repair of paraesophageal hernias: initial observations of a new technique. *Am J Surg* (2003) **186**:4–8. doi:10.1016/S0002-9610(03)00114-4
35. Jacobs M, Gomez E, Plasencia G, Lopez-Penalver C, Lujan H, Velarde D, et al. Use of surgisis mesh in laparoscopic repair of hiatal hernias. *Surg Laparosc Endosc Percutan Tech* (2007) **17**:365–8. doi:10.1097/SLE.0b013e318123fc49
36. Massullo JM, Tejinder PS, Dunnican WJ, Binetti BR. Preliminary study of hiatal hernia repair using polyglycolic acid: trimethylene carbonate mesh. *JSLS* (2012) **16**:55–9. doi:10.4293/108680812X13291597715943
37. Watson DI, Thompson SK, Devitt PG, Smith L, Woods SD, Aly A, et al. Laparoscopic repair of very large hiatus hernia with sutures versus absorbable mesh versus nonabsorbable mesh: a randomized controlled trial. *Ann Surg* (2015) **261**:282–9. doi:10.1097/SLA.0000000000000842
38. Gryska PV, Vernon JK. Tension-free repairof hiatal hernia during laparoscopic fundoplication: a ten-year experience. *Hernia* (2005) **9**:150–5. doi:10.1007/s10029-004-0312-8
39. Champion JK, Rock D. Laparoscopic mesh cruroplasty for large paraesophageal hernias. *Surg Endosc* (2003) **17**:551. doi:10.1007/s00464-002-8817-7
40. Leeder PC, Smith G, Dehn TC. Laparoscopic management of large paraesophageal hiatal hernia. *Surg Endosc* (2003) **17**:1372–5. doi:10.1007/s00464-002-9192-0
41. Horstmann R, Klotz A, Classen C, Palmes D. Feasibility of surgical technique and evaluation of postoperative quality of life after laparoscopic treatment of intrathoracic stomach. *Langenbecks Arch Surg* (2004) **389**:23–31. doi:10.1007/s00423-003-0437-8
42. Granderath FA, Carlson MA, Champion JK, Szold A, Basso N, Pointner R, et al. Prosthetic closure of the esophageal hiatus in large hiatal hernia repair and laparoscopicantireflux surgery. *Surg Endosc* (2006) **20**:367–79. doi:10.1007/s00464-005-0467-0
43. Turkcapar A, Kepenekci I, Mahmoud H, Tuzuner A. Laparoscopic fundoplication with prosthetic hiatal closure. *World J Surg* (2007) **31**:2169–76. doi:10.1007/s00268-007-9275-0
44. Soricelli E, Basso N, Genco A, Cipriano M. Long-term results of hiatal hernia mesh repair and antireflux laparoscopic surgery. *Surg Endosc* (2009) **23**:2499–504. doi:10.1007/s00464-009-0425-3
45. Morino M, Giaccone C, Pellegrino L, Rebecchi F. Laparoscopic management of giant hiatal hernia: factors influencing long-term outcome. *Surg Endosc* (2006) **20**:1011–6. doi:10.1007/s00464-005-0550-6
46. Grubnik VV, Malynovskyy AV. Laparoscopic repair of hiatal hernias: new classification supported by long-term results. *Surg Endosc* (2013) **27**:4337–46. doi:10.1007/s00464-013-3069-2
47. Goers TA, Cassera MA, Dunst CM, Swanstrom LL. Paraesophageal hernia repair with biomesh does not increase postoperative dysphagia. *J Gastrointest Surg* (2011) **15**:1743–9. doi:10.1007/s11605-011-1596-5
48. Molena D, Mungo B, Stem M, Lidor A. Novel combined VATS/laparoscopic approach for giant and complicated paraesophageal hernia repair: description of technique and early results. *Surg Endosc* (2015) **29**:185–91. doi:10.1007/s00464-014-3662-z
49. Ringley CD, Bochkarev V, Ahmed SI, Vitamvas ML, Oleynikov D. Laparoscopic hiatal hernia repair with human acellular dermal matrix patch: our initial experience. *Am J Surg* (2006) **192**:767–72. doi:10.1016/j.amjsurg.2006.08.042
50. Wisbach G, Peterson T, Thoman D. Early results of the use of acellular dermal allograft in type III paraesophageal hernia repair. *JSLS* (2006) **10**:184–7.
51. Lee E, Frisella MM, Matthews BD, Brunt LM. Evaluation of acellular human dermis reinforcement of the crural closure in patients with difficult hiatal hernias. *Surg Endosc* (2007) **21**:641–5. doi:10.1007/s00464-006-9117-4
52. Lee YK, James E, Bochkarev V, Vitamvas M, Oleynikov D. Long-term outcome of cruroplasty reinforcement with human acellular dermal matrix in large paraesophageal hiatal hernia. *J Gastrointest Surg* (2008) **12**:811–5. doi:10.1007/s11605-007-0463-x
53. Diaz DF, Roth JS. Laparoscopic paraesophageal hernia repair with acellular dermal matrix cruroplasty. *JSLS* (2011) **15**:355–60. doi:10.4293/108680811X13125733356594
54. Alicuben ET, Worrell SG, DeMeester SR. Impact of crural relaxing incisions, collis gastroplasty, and non-cross-linked human dermal mesh crural reinforcement on early hiatal hernia recurrence rates. *J Am Coll Surg* (2014) **219**:988–92. doi:10.1016/j.jamcollsurg.2014.07.937
55. Fumagalli U, Bona S, Caputo M, Elmore U, Battafarano F, Pestalozza A, et al. Are surgisis biomeshes effective in reducing recurrences after laparoscopic repair of large hiatal hernias? *Surg Laparosc Endosc Percutan Tech* (2008) **18**:433–6. doi:10.1097/SLE.0b013e3181802ca7
56. Oelschlager BK, Pellegrini CA, Hunter JG, Brunt ML, Soper NJ, Sheppard BC, et al. Biologic prosthesis to prevent recurrence after laparoscopic paraesophageal hernia repair: long-term follow-up from a multicenter, prospective, randomized trial. *J Am Coll Surg* (2011) **213**:461–8. doi:10.1016/j.jamcollsurg.2011.05.017
57. Wassenaar EB, Mier F, Sinan H, Petersen RP, Martin AV, Pellegrini CA, et al. The safety of biologic mesh for laparoscopic repair of large, complicated hiatal hernia. *Surg Endosc* (2012) **26**:1390–6. doi:10.1007/s00464-011-2045-y
58. Wang B, Zhang W, Shan CX, Liu S, Jiang ZG, Qiu M. Long-term outcomes of cruroplasty reinforcement with composite versus biologic mesh for gastroesophageal reflux disease. *Surg Endosc* (2015). doi:10.1007/s00464-015-4570-6
59. Thalheimer W, Cook S. *How to Calculate Effect Sizes from Published Research: A Simplified Methodology* (2002). Available from: http://www.bwgriffin.com/gsu/courses/edur9131/content/Effect_Sizes_pdf5.pdf as applied by Lenhard A (2015). Available from: http://www.psychometrica.de/effektstaerke.html#transform
60. Travers HC, Brewer JO, Smart NJ, Wajed SA. Diaphragmatic crural augmentation utilising cross-linked porcine dermal collagen biologic mesh (Permacol™) in the repair of large and complex para-oesophageal herniation: a retrospective cohort study. *Hernia* (2015). doi:10.1007/s10029-015-1390-5
61. Antoniou SA, Pointner R, Granderath FA, Köckerling F. The use of biological meshes in diaphragmatic defects – an evidence-based review of the literature. *Front Surg* (2015) **2**:56. doi:10.3389/fsurg.2015.00056
62. Antoniou SA, Müller-Stich BP, Antoniou GA, Köhler G, Luketina RR, Koch OO, et al. Laparoscopic augmentation of the diaphragmatic hiatus with biologic mesh versus suture repair: a systematic review and meta-analysis. *Langenbecks Arch Surg* (2015) **400**(5):577–83. doi:10.1007/s00423-015-1312-0
63. Oelschlager BK, Petersen RP, Brunt LM, Soper NJ, Sheppard BC, Mitsumori L, et al. Laparoscopic paraesophageal hernia repair: defining long-term clinical and anatomic outcomes. *J Gastrointest Surg* (2012) **16**(3):453–9. doi:10.1007/s11605-011-1743-z
64. Schmidt E, Shaligram A, Reynoso JF, Kothari V, Oleynikov D. Hiatal hernia repair with biologic mesh reinforcement reduces recurrence rate in small hiatal hernias. *Dis Esophagus* (2014) **27**(1):13–7. doi:10.1111/dote.12042
65. de Castro Brás LE, Shurey S, Sibbons PD. Evaluation of crosslinked and non-crosslinked biologic prostheses for abdominal hernia repair. *Hernia* (2012) **16**(1):77–89. doi:10.1007/s10029-011-0859-0

66. O'Brien JA, Ignotz R, Montilla R, Broderick GB, Christakis A, Dunn RM. Long-term histologic and mechanical results of a Permacol abdominal wall explant. *Hernia* (2011) **15**:211–5. doi:10.1007/s10029-010-0628-5
67. Kallinowski F, Baumann E, Harder F, Siassi M, Mahn A, Vollmer M, et al. Dynamic intermittent strain can rapidly impair ventral hernia repair. *J Biomech* (2015) **48**(15):4026–36. doi:10.1016/j.jbiomech.2015.09.045
68. Koch OO, Asche KU, Berger J, Weber E, Granderath FA, Pointner R. Influence of the size of the hiatus on the rate of reherniation after laparoscopic fundoplication and refundoplication with mesh hiatoplasty. *Surg Endosc* (2011) **25**:1024–30. doi:10.1007/s00464-010-1308-3

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

frontiers in Surgery

REVIEW
published: 25 February 2016
doi: 10.3389/fsurg.2016.00010

Open and Laparo-Endoscopic Repair of Incarcerated Abdominal Wall Hernias by the Use of Biological and Biosynthetic Meshes

René H. Fortelny[1], Anna Hofmann[1], Christopher May[1], Ferdinand Köckerling[2] and BioMesh Study Group[†]*

[1] Department of General, Visceral and Oncological Surgery, Wilhelminenspital, Vienna, Austria, [2] Department of Surgery, Center for Minimally Invasive Surgery, Vivantes Hospital, Berlin, Germany

Introduction: Although recently published guidelines recommend against the use of synthetic non-absorbable materials in cases of potentially contaminated or contaminated surgical fields due to the increased risk of infection (1, 2), the use of bio-prosthetic meshes for abdominal wall or ventral hernia repair is still controversially discussed in such cases. Bio-prosthetic meshes have been recommended due to less susceptibility for infection and the decreased risk of subsequent mesh explantation. The purpose of this review is to elucidate if there are any indications for the use of biological and biosynthetic meshes in incarcerated abdominal wall hernias based on the recently published literature.

Methods: A literature search of the Medline database using the PubMed search engine, using the keywords returned 486 articles up to June 2015. The full text of 486 articles was assessed and 13 relevant papers were identified including 5 retrospective case cohort studies, 2 case-controlled studies, and 6 case series.

Results: The results of Franklin et al. (3–5) included the highest number of biological mesh repairs (Surgisis®) by laparoscopic IPOM in infected fields, which demonstrated a very low incidence of infection and recurrence (0.7 and 5.2%). Han et al. (6) reported in his retrospective study, the highest number of treated patients due to incarcerated hernias by open approach using acellular dermal matrix (ADM®) with very low rate of infection as well as recurrences (1.6 and 15.9%). Both studies achieved acceptable outcome in a follow-up of at least 3.5 years compared to the use of synthetic mesh in this high-risk population (7).

Conclusion: Currently, there is a very limited evidence for the use of biological and biosynthetic meshes in strangulated hernias in either open or laparo-endoscopic repair. Finally, there is an urgent need to start with randomized controlled comparative trials as well as to support registries with data to achieve more knowledge for tailored indication for the use of biological meshes.

Keywords: incarceration, strangulation, groin hernia surgery, abdominal wall hernia, biological mesh, incisional hernia, ventral hernia, bio-resorbable mesh

OPEN ACCESS

Edited by:
Hakan Kulacoglu, Rize University, Turkey

Reviewed by:
Gabriel Sandblom, Karolinska University Hospital, Sweden
Premkumar Balachandran, Apollo Hospitals, India

****Correspondence:***
René H. Fortelny
rene.fortelny@wienkav.at

[†]Members of the BioMesh Study Group are listed at the end of the article.

Specialty section:
This article was submitted to Visceral Surgery, a section of the journal Frontiers in Surgery

Received: *15 January 2016*
Accepted: *05 February 2016*
Published: *25 February 2016*

Citation:
Fortelny RH, Hofmann A, May C, Köckerling F and BioMesh Study Group (2016) Open and Laparo-Endoscopic Repair of Incarcerated Abdominal Wall Hernias by the Use of Biological and Biosynthetic Meshes. Front. Surg. 3:10. doi: 10.3389/fsurg.2016.00010

INTRODUCTION

The BioMesh Study Group has set itself the task of identifying the best way to use biological meshes for various indications. The first step (toward achieving that goal) is to compile systematic reviews of different indications on the basis of the existing literature. The available literature sources will be evaluated in accordance with the Oxford Centre for Evidence-based Medicine-Levels of Evidence (March 2009). Next, based on the review findings, corresponding Statements and Recommendations are to be formulated in a Consensus Conference for the use of biological meshes regarding different indications. The findings of the Consensus Conference will then be summarized as a joint publication. This present publication is part of the project undertaken by the BioMesh Study Group.

Although recently published guidelines recommend against the use of synthetic non-absorbable materials in cases of potentially contaminated or contaminated surgical fields due to the increased risk of infection (1, 2), the use of bio-prosthetic meshes for abdominal wall or ventral hernia repair is still controversially discussed in such cases. Especially in these indications, bio-prosthetic meshes have been recommended due to less susceptibility for infection and the decreased risk of subsequent mesh explantation. The greatest drawback of bio-prosthetics is still the high cost in comparison to synthetic non-absorbable meshes (2). Above all, there is a lack of evidence concerning the clinical efficacy of biologic over synthetic non-absorbable meshes (7). In the literature, wound infection rates after the use of biological meshes even in clean-contaminated fields are reported up to 40% (8, 9) and hernia recurrence rates up to 30%, respectively (10). On the other hand, the reports of Zafar et al. (11) regarding emergency surgery of incarcerated incisional hernia with associated bowel obstructions enrolling 60 patients by the use of permanent prosthetic meshes revealed an almost identically high percentage (31%) of wound complications in a retrospective study. The purpose of this review is to elucidate if there are any indications for the use of biological and biosynthetic meshes in incarcerated abdominal wall hernias based on the recently published literature.

METHODS

A literature search of the Medline database using the PubMed search engine, using the keywords (incarcerated hernia OR strangulated hernia OR inguinal hernia OR Groin hernia OR inguinal hernia OR ventral hernia OR incisional hernia AND biological mesh OR Biomesh OR Biological OR biosynthetic mesh AND open repair OR laparoscopic repair OR endoscopic repair) returned 486 articles up to June 2015. Titles and abstracts were searched for the use of biologic meshes in open and laparo-endoscopic repair of incarcerated/strangulated abdominal wall hernias. The full text of 486 articles was assessed, and 13 relevant papers were identified including 5 retrospective case cohort studies (9, 12–14), 2 case-controlled studies (5, 15) and 6 case reports (16–21). A summary of study demographics and characteristics is presented in **Table 1** and the outcome data in **Table 2**. Qualitative assessment of all included studies was based on the Oxford Centre for Evidence-Based Medicine 2009 levels of evidence.

RESULTS

In the special case of an incarcerated recurrent Amyand's hernia, the only paper concerning the use of a biological mesh was published by Quartey et al. (16). After appendectomy in an open approach, an acellular hydrated dermis (Flex HD®) was implanted with an uneventful postoperative follow-up to 5 months. In a review regarding Amyand's hernia, Michalinos et al. (23) concluded that in case of proper treatment, including the use of meshes, the morbidity or mortality is not increased beyond that of a typical inguinal hernia repair. Similar conclusions can be found in the review of Köckerling et al. (24) with the statement: "The use of biological meshes in inguinal hernia repair especially in potentially contaminated fields is an alternative to the use of synthetic meshes with reasonable recurrence rates."

In the case cohort study of Ueno et al. (15) including 2 inguinal and 18 ventral hernias – 3 with incarceration – patients were treated with Surgisis® mesh implants. In a follow-up of 15.7 months, no infection or recurrence was detected.

TABLE 1 | Summary of study demographics and characteristics.

Reference	Study design	COI	Patient (*n*)	Mean age	Mean BMI	FU	LoE
Quartey et al. (16)	CR	NR	1	71	NR	5 months	4
Ueno et al. (15)	CCS	NR	20	60.1	NR	15.7 months	4
Xourafas et al. (12)	RCS	NR	51	59	29 > 30	22 months	3
Helton et al. (13)	RCS	NR	53	51	32	14 months	4
Giakoustidis et al. (17)	CR	No	1	53	NR	12 months	4
Shah et al. (9)	RCS	NR	58	57.2	33.8	12 months	4
Tsuda (22)	CR	No	1	33	38	6 weeks	4
Franklin et al. (5)	CCS	NR	116	58	NR	52 months	4
Han et al. (6)	RCS	No	63	57	29	43 months	4
Patton et al. (14)	RCS	NR	67	55	NR	10.6 months	4
Fallis et al. (18)	CR	NR	1	81	NR	6 months	4
Gooch et al. (19)	CR	No	1	38	NR	4 years	4
Pulido et al. (20)	CR	NR	1	70	NR	NR	4
Schiergens et al. (21)	CR	NR	1	32	NR	NR	4

n, number; RCS, Retrospective Cohort Study; CCS, Case–Control Study; CR, case report; COI, conflict of interest; NR, no report; LoE, level of evidence (based on the Oxford Centre for Levels of Evidence 2009).

TABLE 2 | Outcome data.

Reference	Mesh (*n*)	Meshtype	Meshposition	Fixation	Hernia type (*n*)	Incarceration/ strangulation	Resection (bowel)	Recurrence (%)	Wound infection (%)
Quartey et al. (16)	1	Flex-HD®	Inguinal	NR	Inguinal	1	1	0	0
Ueno et al. (15)	20	Surgisis®	Underlay (17) Onlay (3)	NR	Ventral (18) Inguinal (2)	3	NR	0	0
Xourafas et al. (12)	51	AlloDerm® (4) Surgisis® (1) Synthetic mesh (46)	Underlay	NR	Ventral	NR	51	22	22
Helton et al. (13)	53	Surgisis®	IPOM (2) Underlay (41) Onlay (3)	Sutures	Ventral	NR	13	17	24
Giakoustidis et al. (17)	1	NR	NR	NR	Incisional	1	0	0	0
Shah et al. (9)	58	AlloDerm® (29) Permacol® and CollaMend® (5) Surgisis® and Strattice® (24)	Onlay (10) Underlay (21) Bridging (27)	NR	Ventral	9	NR	27.9	19
Tsuda et al. (22)	1	Strattice®	IPOM	Sutures Titanium spiral tacks	Incisional	1	Omentum resection	0	0
Franklin et al. (5)	133	Surgisis®	IPOM	Tacks	Inguinal (29) Incisional (57) umbilical (38) Femoral (3) Parastomal (2) Spigelian (4)	32	17	5.2	0.7
Han et al. (6)	63	AlloDerm®	IPOM	Sutures	Ventral (45) Incisional (18)	63	33	15.9	1.5
Patton et al. (14)	67	AlloDerm®	Inlay (43) Interlay (28) Onlay (5)	Sutures	Ventral	10	NR	17.9	16
Fallis et al. (18)	1	Strattice®	Perineal bridge	Sutures	Perineal	1	1	0	NR
Gooch et al. (19)	1	Permacol®	Hiatal	Sutures	Hiatal	1	0	0	NR
Pulido et al. (20)	1	Flex HD®	Diaphragmatic	Sutures	Diaphragmatic	1	0	NR	NR
Schiergens et al. (21)	1	BioA®	Hiatal	NR	Diaphragmatic	1	0	0	0

n, number; NR, no report.

The retrospective case–control study of Xourafas et al. (12) regarding the use of meshes in incarcerated ventral hernia repair with a simultaneous bowel resection included five patients (out of 51 in the mesh group) with the implantation in underlay technique using Alloderm® in four cases and Surgisis® in one case, respectively. The overall infection and recurrence rate (synthetic and biological meshes) was 22% in a follow-up of 22 months. The result of an univariate and a multivariate analysis detected a significant risk of increased postoperative infection in the mesh group, without separation regarding the type of mesh.

Helton et al. (13) reported in a retrospective case–control study of 13 patients treated with bowel resection due to incarceration or strangulation in ventral hernia by the use of Surgisis Gold® in an open approach. The wound infection rate was 24% and the recurrence rate 17% in a follow-up of 14 months.

In a retrospective study of different bio-prosthetic materials in complex ventral hernia repair by Shah et al. (9) nine patients with incarceration (out of 58) were included. Different biological meshes were used (Alloderm®, CollaMend®, Permacol®, Surgisis®, and Strattice®). The overall recurrence rate was 27.9%, and surgical wound infections were detected in 19% in a follow-up of 1 year. The 17.2% of the meshes required explantation. Non-cross-linked porcine biologics were less likely to be explanted, but had higher recurrence rates compared to cross-linked porcine biologics and a higher infection rate compared to Alloderm® (non-cross-linked human dermis).

Franklin et al. published a case–control study using porcine small intestinal submucosa mesh (Surgisis®) for laparoscopic IPOM repair of hernias in infected fields in the years 2002, 2004, and 2008 (3–5). In summary, 133 procedures were performed

in 116 patients of which 17 (12.7%) required a bowel resection due to strangulated hernias with necrotic bowel. The overall recurrence rate was 5.2% and the infection rate 0.7% in a mean follow-up of 52 months.

Incarcerated abdominal wall hernias treated with the use of human dermal matrix (ADM®) in IPOM position by open approach in combination with vacuum wound drainage was reported by Han et al. (6) in a retrospective study. In 33 out of 63 incarcerated hernias, bowel resection was performed. In a follow-up of 43 months, 15.9% recurrences were detected and 1.6% suffered from a superficial wound infection. Multivariate analysis isolated BMI, defect size, and numbers of biological meshes used as risk factors to significantly affect recurrence rates.

Patton et al. (14) published a retrospective study of abdominal wall reconstructions with the use of acellular dermal matrix (ADM®) in complex and contaminated ventral hernias. In 51% of the repairs, the mesh was positioned as IPOM bridging with 3 cm overlap, 42% as an interlay, and 8% as an onlay. The 13 patients out of 89 were treated in case of incarcerated hernias. Overall, 16% developed wound infections, and in a follow-up of 10.6 months, 17.9% suffered from a recurrent hernia.

There are some single case reports like Giakoustidis et al. (17) reporting of a biological mesh used in an incarcerated recurrent incisional hernia as well as Tsuda (22) describing a laparoscopic repair of an incarcerated umbilical hernia using Strattice® and Fallis et al. (18) publishing an open mesh repair of a strangulated perineal hernia after abdominoperineal resection. Another single case was reported by Gooch et al. (19) concerning a transthoracic repair of an incarcerated diaphragmatic hernia with a cross-linked porcine dermal collagen (Permacol®) and finally Pulido et al. (20) who described a laparoscopic repair in a case of chronic traumatic diaphragmatic hernia containing an obstructed small bowel and gallbladder also used Permacol®.

Schiergens et al. (21) reported of an emergent laparoscopic fundoplication of acute upside-down stomach with incarceration using biocompatible gradually absorbable synthetic polymers (BioA®) in a 32-year-old male patient. The follow-up was uneventful.

DISCUSSION/SUMMARY

In summary, so far the data regarding the use of biological and biosynthetic meshes are very scarce and there is only one level 3 study published up to now. The results of this study of Xourafas et al. (12) comparing mesh versus mesh-free repair of ventral hernia with a simultaneous bowel resection obtained a significant risk factor for the mesh group concerning the development of an infection. On multivariate regression analysis, the risk was present irrespective of drain use, defect size, and type of bowel resection. However, the analysis of a subgroup of 10 patients treated with the use of biological meshes out of a total of 100, which underwent mesh repair, did not reveal a single infection, whereas the group of polypropylene meshes showed a 24% infection rate. There was no reported significant difference in the incidence of recurrences between the mesh- and the mesh-free group (22 versus 24%), but unfortunately no comparative analysis between synthetic and biological meshes was published.

The results of Franklin et al. (3–5) include the highest number of biological mesh repairs (Surgisis®) in infected fields by laparoscopic approach, which demonstrated a low ratio of required bowel resection (12.7%), furthermore the overall incidence of recurrence and infection was very low (5.2 and 0.7%) in a mean follow-up of 52 months. Han et al. (6) reported, in his retrospective study, the highest number of treated patients due to incarcerated hernias with bowel resection by open approach using acellular dermal matrix (ADM®) with very low rate of infection (1.6%) as well as recurrences (15.9%) in a follow-up of 43 months. Both studies achieved acceptable outcome in a follow-up of at least 3.5 years compared to the use of synthetic mesh in this high-risk population (7).

In the conclusion of a critical review of biologic mesh use in ventral hernia repairs under contaminated conditions by Primus and Harris (7) as well as in the systematic review by Lee et al. (25), a similar statement can be found: "The available evidence is limited, but does not support the superiority of biologic over synthetic non-absorbable prosthetics in contaminated fields. Due to a lack of scientific evidence concerning the use of biologic mesh in case of laparoscopic treatment in incarcerated/strangulated ventral hernias (in potentially contaminated field) no recommendation or suggestion can be stated."

Taking into account that there is a significantly increasing rate of emergent incisional hernia repair in the group of older men (>65 years) when analyzing the years 2001 to 2010 in the United States (26), the importance to treat this growing population with an appropriate method including the selection of mesh type and material should be addressed in further studies and registries. The results of a survey of practicing surgeons (members of American College of Surgeons) concerning the use of biological meshes in abdominal reconstructions (27) revealed a lack of consensus in terms of indication, surgical techniques, as well as type of biological mesh.

Looking to the different Guidelines based on consensus conferences of the European Association for Endoscopic Surgery (EAES), International Endo Hernia Society (IEHS), European Hernia Society (EHS), and the World Society of Emergency Surgery (WSES) (28–33), we can only find a recommendation of the WSES in terms of the question which kind of mesh should be used in incarcerated/strangulated hernia. The WSES guideline based on a Consensus Meeting in 2013 (29) recommends the use of biological meshes as a valid option in case of emergency hernia repair in potentially contaminated surgical field for patients with intestinal strangulation and/or concurrent bowel resection [grade 2C recommendation GRADE (34)]. In case of stable patients with strangulated obstruction and peritonitis by bowel perforation (contaminated-dirty surgical field), direct tissue suture is recommended when the hernia defect is small; in the events that direct tissue suture is not possible, biological mesh repair may be suggested (grade 2C recommendation). The choice between cross-linked and non-cross-linked biological mesh should be evaluated depending on the defect size and degree of contamination (grade 2C recommendation).

Without any doubt, currently there is a very limited evidence for the use of biological and biosynthetic meshes in strangulated hernias in open as well as in laparo-endoscopic repair. Finally, there is an urgent need to start with randomized controlled comparative trials as well as to support registries with data to achieve more knowledge for tailored indication for the use of biological meshes.

AUTHOR CONTRIBUTIONS

RF main authorship, corresponding author. AH support in selection of papers of the review, composing tables of the manuscript. CM support in composing of the manuscript, proof reading. FK final proof.

BioMesh Study Group

Ferdinand Köckerling (Chairman), Stavros Antoniou, René H Fortelny, Frank A. Granderath, Markus Heiss, Franz Mayer, Marc Miserez, Agneta Montgomery, Salvador Morales-Conde, Filip Muysoms, Alexander Petter-Puchner, Rudolph Pointner, Neil Smart, Marciej Smietanski, Bernd Stechemesser.

REFERENCES

1. Breuing K, Butler CE, Ferzoco S, Franz M, Hultman CS, Kilbridge JF, et al. Incisional ventral hernias: review of the literature and recommendations regarding the grading and technique of repair. *Surgery* (2010) **148**:544–58. doi:10.1016/j.surg.2010.01.008
2. Bachman S, Ramshaw B. Prosthetic material in ventral hernia repair: how do I choose? *Surg Clin North Am* (2008) **88**:101–12. doi:10.1016/j.suc.2007.11.001
3. Franklin ME Jr, Gonzalez JJ Jr, Michaelson RP, Glass JL, Chock DA. Preliminary experience with new bioactive prosthetic material for repair of hernias in infected fields. *Hernia* (2002) **6**(4):171–4. doi:10.1007/s10029-002-0078-9
4. Franklin ME Jr, Gonzalez JJ Jr, Glass JL. Use of porcine small intestinal submucosa as a prosthetic device for laparoscopic repair of hernias in contaminated fields: 2-year follow-up. *Hernia* (2004) **8**(3):186–9. doi:10.1007/s10029-004-0208-7
5. Franklin ME Jr, Treviño JM, Portillo G, Vela I, Glass JL, González JJ. The use of porcine small intestinal submucosa as a prosthetic material for laparoscopic hernia repair in infected and potentially contaminated fields: long-term follow-up. *Surg Endosc* (2008) **22**(9):1941–6. doi:10.1007/s00464-008-0005-y
6. Han JG, Pang GY, Wang ZJ, Zhao Q, Ma SZ. The combined application of human acellular dermal matrix and vacuum wound drainage on incarcerated abdominal wall hernias. *Int J Surg* (2014) **12**(5):452–6. doi:10.1016/j.ijsu.2014.03.019
7. Primus FE, Harris HW. A critical review of biologic mesh use in ventral hernia repairs under contaminated conditions. *Hernia* (2013) **17**:21–30. doi:10.1007/s10029-012-1037-8
8. Diaz JJ Jr, Conquest AM, Ferzoco SJ, Vargo D, Miller P, Wu YC, et al. Multiinstitutional experience using human acellular dermal matrix for ventral hernia repair in a compromised surgical field. *Arch Surg* (2009) **144**:209–15. doi:10.1001/archsurg.2009.12
9. Shah BC, Tiwari MM, Goede MR, Eichler MJ, Hollins RR, McBride CL, et al. Not all biologics are equal! *Hernia* (2011) **15**:165–71. doi:10.1007/s10029-010-0768-7
10. Rosen MJ, Krpata DM, Ermlich B, Blatnik JA. A 5-year clinical experience with single-staged repairs of infected and contaminated abdominal wall defects utilizing biologic mesh. *Ann Surg* (2013) **257**:991–6. doi:10.1097/SLA.0b013e3182849871
11. Zafar H, Zaidi M, Qadir I, Memon AA. Emergency incisional hernia repair: a difficult problem waiting for a solution. *Ann Surg Innov Res* (2012) **6**(1):1. doi:10.1186/1750-1164-6-1
12. Xourafas D, Lipsitz SR, Negro P, Ashley SW, Tavakkolizadeh A. Impact of mesh use on morbidity following ventral hernia repair with a simultaneous bowel resection. *Arch Surg* (2010) **145**(8):739–44. doi:10.1001/archsurg.2010.144
13. Helton WS, Fisichella PM, Berger R, Horgan S, Espat NJ, Abcarian H. Short-term outcomes with small intestinal submucosa for ventral abdominal hernia. *Arch Surg* (2005) **140**(6):549–60. doi:10.1001/archsurg.140.6.549
14. Patton JH Jr, Berry S, Kralovich KA. Use of human acellular dermal matrix in complex and contaminated abdominal wall reconstructions. *Am J Surg* (2007) **193**(3):360–3. doi:10.1016/j.amjsurg.2006.09.021
15. Ueno T, Pickett LC, de la Fuente SG, Lawson DC, Pappas TN. Clinical application of porcine small intestinal submucosa in the management of infected or potentially contaminated abdominal defects. *J Gastrointest Surg* (2004) **8**(1):109–12. doi:10.1016/j.gassur.2003.09.025
16. Quartey B, Ugochukwu O, Kuehn R, Ospina K. Incarcerated recurrent Amyand's hernia. *J Emerg Trauma Shock* (2012) **5**(4):344–6. doi:10.4103/0974-2700.102407
17. Giakoustidis A, Morrison D, Neofytou K, Giakoustidis D, Mudan S. Emergency open incarcerated hernia repair with a biological mesh in a patient with colorectal liver metastasis receiving chemotherapy and bevacizumab uncomplicated wound healing. *Case Rep Emerg Med* (2014) **2014**:848030. doi:10.1155/2014/848030
18. Fallis SA, Taylor LH, Tiramularaju RM. Biological mesh repair of a strangulated perineal hernia following abdominoperineal resection. *J Surg Case Rep* (2013) **2013**(4):ii:rjt023. doi:10.1093/jscr/rjt023
19. Gooch B, Smart N, Wajed S. Transthoracic repair of an incarcerated diaphragmatic hernia using hexamethylene diisocyanate cross-linked porcine dermal collagen (Permacol). *Gen Thorac Cardiovasc Surg* (2012) **60**(3):145–8. doi:10.1007/s11748-011-0786-0
20. Pulido J, Reitz S, Gozdanovic S, Price P. Laparoscopic repair of chronic traumatic diaphragmatic hernia using biologic mesh with cholecystectomy for intrathoracic gallbladder. *JSLS* (2011) **15**(4):546–9. doi:10.4293/108680811X13176785204472
21. Schiergens TS, Thomas MN, Hüttl TP, Thasler WE. Management of acute upside-down stomach. *BMC Surg* (2013) **13**:55. doi:10.1186/1471-2482-13-55
22. Tsuda S. Laparoscopic repair of complicated umbilical hernia with Strattice Laparoscopic– reconstructive tissue matrix. *Int J Surg Case Rep* (2014) **5**(12):1167–9. doi:10.1016/j.ijscr.2014.11.007
23. Michalinos A, Moris D, Vernadakis S. Amyand's hernia: a review. *Am J Surg* (2014) **207**(6):989–95. doi:10.1016/j.amjsurg.2013.07.043
24. Köckerling F, Alam NN, Narang SK, Daniels IR, Smart NJ. Biological meshes for inguinal hernia tepair – review of the literature. *Front Surg* (2015) **2**:48. doi:10.3389/fsurg.2015.00048
25. Lee L, Mata J, Landry T, Khwaja KA, Vassiliou MC, Fried GM, et al. A systematic review of synthetic and biologic materials for abdominal wall reinforcement in contaminated fields. *Surg Endosc* (2014) **28**(9):2531–46. doi:10.1007/s00464-014-3499-5
26. Beadles CA, Meagher AD, Charles AG. Trends in emergent hernia repair in the United States. *JAMA Surg* (2015) **150**(3):194–200. doi:10.1001/jamasurg.2014.1242
27. Harth KC, Krpata DM, Chawla A, Blatnik JA, Halaweish I, Rosen MJ. Biologic mesh use practice patterns in abdominal wall reconstruction: a lack of consensus among surgeons. *Hernia* (2013) **17**(1):13–20. doi:10.1007/s10029-012-1029-8
28. Agresta F, Ansaloni L, Baiocchi GL, Bergamini C, Campanile FC, Carlucci M, et al. Laparoscopic approach to acute abdomen from the Consensus Development Conference of the Società Italiana di Chirurgia Endoscopica e nuove tecnologie (SICE), Associazione Chirurghi Ospedalieri Italiani (ACOI), Società Italiana di Chirurgia (SIC), Società Italiana di Chirurgia d'Urgenza e del Trauma (SICUT), Società Italiana di Chirurgia nell'Ospedalità Privata (SICOP), and the European Association for Endoscopic Surgery (EAES). *Surg Endosc* (2012) **26**(8):2134–64. doi:10.1007/s00464-012-2331-3
29. Sartelli M, Coccolini F, van Ramshorst GH, Campanelli G, Mandalà V, Ansaloni L, et al. WSES guidelines for emergency repair of complicated abdominal wall hernias. *World J Emerg Surg* (2013) **8**(1):50. doi:10.1186/1749-7922-8-50

30. Bittner R, Arregui ME, Bisgaard T, Dudai M, Ferzli GS, Fitzgibbons RJ, et al. Guidelines for laparoscopic (TAPP) and endoscopic (TEP) treatment of inguinal hernia [International Endohernia Society (IEHS)]. *Surg Endosc* (2011) **25**(9):2773–843. doi:10.1007/s00464-011-1799-6
31. Bittner R, Montgomery MA, Arregui E, Bansal V, Bingener J, Bisgaard T, et al. Update of guidelines on laparoscopic (TAPP) and endoscopic (TEP) treatment of inguinal hernia (International Endohernia Society). *Surg Endosc* (2015) **29**(2):289–321. doi:10.1007/s00464-014-3917-8
32. Simons MP, Aufenacker T, Bay-Nielsen M, Bouillot JL, Campanelli G, Conze J, et al. European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. *Hernia* (2009) **13**(4):343–403. doi:10.1007/s10029-009-0529-7
33. Miserez M, Peeters E, Aufenacker T, Bouillot JL, Campanelli G, Conze J, et al. Update with level 1 studies of the European Hernia Society guidelines on the treatment of inguinal hernia in adult patients. *Hernia* (2014) **18**(2):151–63. doi:10.1007/s10029-014-1236-6
34. Guyatt G, Gutterman D, Baumann MH, Addrizzo-Harris D, Hylek EM, Phillips B, et al. Grading strength of recommendations and quality of evidence in clinical guidelines: report from an american college of chest physicians task force. *Chest* (2006) **129**(1):174–81. doi:10.1378/chest.129.1.174

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

frontiers in Surgery

MINI REVIEW
published: 08 January 2016
doi: 10.3389/fsurg.2015.00067

Evidence for Replacement of an Infected Synthetic by a Biological Mesh in Abdominal Wall Hernia Repair

Agneta Montgomery[1], Friedrich Kallinowski[2] and Ferdinand Köckerling[3]*

[1] Department of Surgery, Skane University Hospital, Malmö, Sweden, [2] Department of Surgery, Asklepios Hospital Harburg, Hamburg, Germany, [3] Department of Surgery, Centre for Minimally Invasive Surgery, Vivantes Hospital Berlin, Academic Teaching Hospital of Charité Medical School, Berlin, Germany

Introduction: The incidence of deep infection using a synthetic mesh in inguinal hernia repair is low and reported to be well below 1%. This is in contrast to incisional hernia surgery where the reported incidence is 3% respective 13% comparing laparoscopic to open mesh repair reported in a Cochrane review. Main risk factors were long operation time, surgical site contamination, and early wound complications. An infected mesh can be preserved using conservative treatment were negative pressure wound therapy (VAC®) could play an important role. If strategy fails, the mesh needs to be removed. This review aims to look at evidence for situations were a biological mesh would work as a replacement of a removed infected synthetic mesh.

Materials and methods: A literature search of the Medline database was performed using the PubMed search engine. Twenty publications were found relevant for this review.

Results: For studies reviewed three options are presented: removal of the infected synthetic mesh alone, replacement with either a new synthetic or a new biological mesh. Operations were all performed at specialist centers. Removal of the mesh alone was an option limited to inguinal hernias. In ventral/incisional hernias, the use of a biological mesh for replacement resulted in a very high recurrence rate, if bridging was required. Either a synthetic or a biological mesh seems to work as a replacement when fascial closure can be achieved. Evidence is though very low.

Conclusion: When required, either a synthetic or a biological mesh seems to work as a replacement for an infected synthetic mesh if the defect can be closed. It is, however, not recommended to use a biological mesh for bridging. Mesh replacement surgery is demanding and is recommended to be performed in a specialist center.

Keywords: hernia, mesh infection, biological mesh, mesh replacement, mesh complication

OPEN ACCESS

Edited by:
Vincenzo Neri,
University of Foggia, Italy

Reviewed by:
Jose M. Ramia,
SESCAM Regional Public Health System of Castilla La Mancha, Spain
Mirela Patricia Sirbu Boeti,
"Carol Davila" University of Medicine and Pharmacy, Romania
Juan Manuel Suárez-Grau,
General Hospital of Riotinto, Spain

****Correspondence:***
Agneta Montgomery
agneta.montgomery@skane.se

Specialty section:
This article was submitted to Visceral Surgery, a section of the journal Frontiers in Surgery

Received: *17 November 2015*
Accepted: *17 December 2015*
Published: *08 January 2016*

Citation:
Montgomery A, Kallinowski F and Köckerling F (2016) Evidence for Replacement of an Infected Synthetic by a Biological Mesh in Abdominal Wall Hernia Repair. Front. Surg. 2:67. doi: 10.3389/fsurg.2015.00067

INTRODUCTION

Reduced recurrence rates can be achieved by using standardized surgical techniques for mesh reinforcement in hernia surgery (1–3). Accordingly, several different types of meshes are used worldwide in hernia surgery. In the US alone, some 800,000 inguinal hernia (4) and 400,000 ventral hernia, including primary and incisional (5), operations are performed annually. In Sweden, 16,000 inguinal

and 7,000 ventral hernias are reported on an annual basis in the national registers. In Germany, 275,000 inguinal and 100,000 ventral hernia operations are carried out annually.

In a review (6), the reported incidence of mesh-related infections following hernia repair was between 1 and 8% in different series. The incidence was influenced by the underlying comorbidities, type of mesh, surgical technique, and the strategy used to prevent infections. Risk factors to determine the onset of mesh infection were a prolonged operation time (7, 8), the extent of contamination of the surgical site (9), and early complications of the wound (seroma, hematoma, and infection) (8). In the Cochrane review of laparoscopic versus open surgical techniques for ventral or incisional hernia repairs, the overall infection rate was 13% after open and 3% after laparoscopic mesh repair (10).

Prevention of mesh infections continues to be the best strategy (11). Not all infections necessitate mesh removal. In the Cochrane review, only 3.3% of meshes had to be removed following open and 0.7% following laparoscopic ventral and incisional hernia repairs (10). It was possible to preserve 17 (55%) of meshes through conservative treatment in a case series of 31 infected meshes after incisional hernias repair (7). In a study on in ventral hernia repairs by Liang et al., a total of 30 out of 407 (7.4%) were re-operated due to an infection and the mesh could be saved in 10 out of these 30 (33%) (9). Reoperations were performed evenly spread from operation up to 10 years after the primary operation. In another series, it was possible to preserve 12 out of 13 (92%) were VAC® was used in addition in 11 patients (12). The rate of mesh removal due to infection following inguinal hernia repairs was reported to be 0.13% (13). The interval between hernia operation and mesh removal could be up to 10 years or longer.

In a review by Darehzereshki et al. including eight retrospective studies, with a total of 1,229 patients comparing different biological to synthetic mesh repair in ventral and incisional hernias. It was demonstrated that biological grafts were associated with significantly fewer wound infections ($p < 0.00001$) but with no difference in recurrence rate (14).

The aim to look at evidence for situations were a biological mesh would work as a replacement of a removed infected synthetic mesh.

MATERIALS AND METHODS

A literature search of the Medline database was performed using the PubMed search engine. The following key words were used: biological mesh, replacement of infected mesh, ventral hernia AND infected mesh, inguinal hernia AND infected mesh, mesh infection AND biological mesh, infected synthetic mesh AND biological mesh. Two thousand five hundred one citations were found. After checking the title and abstracts, 20 publications remained included in this study. Seven of these publications, four case series and three case reports, do report on the replacement of a synthetic by a biological mesh (**Table 1**).

TABLE 1 | Characteristics and outcomes of studies reporting on replacement of infected synthetic meshes with either a synthetic or biologic mesh in ventral/incisional hernia repair.

Reference	Study design	Patients (*n*)	Mesh for replacement	Intervention details	Follow-up time	Outcome
Birolini et al. (15)	Retrospective case series	41	HW PP	Single stage Single surgeon Onlay	74 months	27 uneventful 10 (24%) inf 1 mesh removal 3 recur 1 EC fistula
Albino et al. (5)	Retrospective cases series	27	PADM	Two stages 6 bridging	32 months	6 wound rupt 5 inf 5 (19%) recur (all bridged rep)
Rosen et al. (16)	Retrospective case series	128 in total 45 (35%) inf*	102 Strattice 16 Alloderm 5 Biodesign 4 Xenmatrix 4 BioA	Single stage 87 rr mesh 40 ip mesh 70% comp sep 6% bridging	22 months	61 (48%) inf 28 major 33 minor 40 (31%) recur
Guerra (17)	Retrospective case series	13	PADM®	Single stage 2 bridged	22 months	1 inf 1 seroma 2 recur (both bridged repairs)
Cavallaro et al. (18)	Case report	2	Bovine pericardium graft	Single stage rr	5 years	0 inf 0 recur
Peppas et al. (19)	Case report	1 EC fistula Two meshes PTFE and PP	Porcine tissue Collamend®	Two stages	6 months	0 inf 0 recur
Coccolini et al. (20)	Case report	2	Collamend® Surgisis	Single stage	36 months	0 inf 0 recur

HW = heavy weight, PP = polypropylene, PTFE = polytetrafluoreten, rr = retro rectus, ip = intra peritoneal, PADM = porcine acellular dermal matrix, mo = months, inf = infection, recur = recurrence, rupt = rupture, EC = enterocutanous, rep = repair.

**Mesh infections cannot be identified for individual meshes.*

The treatment options were removal of the infected mesh alone, replacement of the infected with a new synthetic mesh, and replacement of an infected synthetic with a biological mesh.

RESULTS

Removal of the Infected Mesh Alone

In the following two studies, a total of 47 patients with mesh infection were treated by means of partial or complete mesh removal. Neither a synthetic nor a biological mesh was implanted to replace the explanted mesh.

In a retrospective case series by Akyol et al., 15 mesh removals were performed after inguinal hernia repair because of chronic mesh infection in 14 males and 1 female with a median age of 52 years (range 35–75 years) (13). At the time of presentation, 13 patients had chronic sinus at explanation, while 2 had abscesses. The interval from hernia repair to mesh removal was 4–204 months. The infected meshes were completely removed. None of the patients had the transversalis fascia reinforced, due to thickening by fibrosis from the former mesh. Follow-up was performed median 62 months (range 16–115 months). Infection resolved successfully in all patients. One patient reported paresthesia and another developed a recurrent hernia.

In a retrospective case series by Tolino et al., 32 mesh removals were performed due to chronic infection, 22 after incisional and 10 after inguinal hernia repair (8). The interval from repair to mesh removal ranged from 4 to 60 months. A total of 51 operations in the 32 patients were needed for definitive treatment, including partial or total mesh removal. The average follow-up was 40 months (range 30–97). Five hernia recurrences and one intestinal fistula were observed after incisional mesh removal. One recurrence and one fistula developed after inguinal hernia mesh removal.

Replacement of the Infected with a New Synthetic Mesh

In a single surgeon case series by Birolini et al., a 16-year retrospective review based on a prospective protocol was carried out in 41 patients having had ventral hernias surgery with their meshes removed (15). A total of 27 patients had a supportive infection and 14 had an exposed mesh. Bowel resection or an associated contaminated procedure was performed in 15 patients. An onlay polypropylene mesh was used for replacement in all patients. In the short-term follow-up, all, except one mesh, could be preserved. Three recurrences were seen after a mean follow-up of 74 months, out of which one was associated with an intestinal fistula. A total of 95% of the patients were considered cured from their chronic mesh infection. It was concluded that onlay polypropylene mesh yielded favorable outcomes, for high-risk ventral hernia patients, having an infected synthetic mesh removed in a single-stage repair setting.

Replacement of the Infected with a Biological Mesh

In the following six studies (three case series and three case reports), a total of 92 patients with mesh infection were treated by mesh removal followed by implant of a biological mesh in ventral hernia patients.

In a retrospective case series, Albino et al. reported on 27 patients with an infected synthetic mesh treated with a multistaged approach (5). The initial surgical procedure consisted of abdominal exploration with debridement and mesh removal followed by VAC® therapy. In the second stage, all patients underwent component separation and hernia repair reinforced by porcine acellular dermal matrix (PADM). Primary fascial closure was achieved in 21 (78%) of patients (19 meshes placed underlay and 2 onlay). Bridging was performed in six (22%) patients. The average follow-up was 32 months (range 8–52 months). Six (22%) patients were found to have wound dehiscence and five (19%) of these had had clinical evidence of a surgical site infection. Wound healing was achieved in all patients in average after 8 weeks (2–60 weeks). Five (19%) patients developed a recurrent hernia. Both bridging and a postoperative infection were found to increase the risk of a hernia recurrence ($p = 0.03$ and 0.001, respectively).

In a single institution, Rosen et al. reported on 128 patients who had a single-stage reconstruction using a biological mesh in a contaminated field, of whom 45 (35%) were operated on for a simultaneous removal of a contaminated mesh (16). The mesh removal patients were not reported on separately. A total of 27% of operations were considered "dirty" according to the CDC classification and would probably include most of the mesh infected patients. A total of 66% had a retromuscular and 31% an intraperitoneal mesh repair. Component separation was performed in 70% of patients and fascial closure was achieved in 94%. Overall wound morbidity was seen in 61 patients (48%), of whom 28 were re-operated and 33 managed by local treatment of the infection. All wounds resolved within 60 days. At a mean follow-up of 22 months, 31% recurrences were seen. It can be concluded that using a biological mesh in these situations is safe, but the long-term durability seems to be less favorable, even when fascial closure has been achieved.

In a retrospective case review by Guerra, 13 patients had an infected synthetic mesh removed after former incisional hernia surgery (17). Mesh replacement was performed with a porcine-derived acellular dermal matrix. The mean age was 60 years. Comorbidity was high. Facial closure was achieved in 11 and bridging in 2 patients. One wound infection, one seroma, and two hernia recurrences (both bridged patients) were observed at a median follow-up of 22 months. It was concluded that outcomes were favorable in high-risk patients with infected synthetic mesh if bridging was avoided.

Two patients were presented in a case report by Cavallaro et al. where one preperitoneal Prolene® mesh and one retromuscular polypropylene mesh were extracted and replaced with a retromuscular bovine pericardium graft. No complication and no recurrences were reported after 5 and 4 years, respectively. Closure of the gap was not reported on (18).

In a case report, Peppas et al. described drainage of an infected ePTFE together with a macro porous onlay polypropylene mesh for 1 month. The meshes were extracted and replaced by porcine onlay mesh (19). No complications were reported up to 6 months.

Two patients were reported by Coccolini et al. having a surgical site infection after a double-layered PP-e PTFE retromuscular

mesh repair (20). The first patient had a surgical site infection that discovered with substantial abdominal wall tissue loss 2 weeks after the operation for a recurrence. After 2 years of conservative treatment, the patient underwent mesh removal and retromuscular reconstruction using an acellular porcine dermal collagen cross-linked implant (CollaMend™). The second patient had an infection resulting in a sinus. The mesh was removed and replaced by a porcine mucosal non-cross-linked implant (Surgisis™). At 37 respective 35 months after the operation, the patients demonstrated no evidence of recurrence. The description of the technique used in these two patients implicates a bridging procedure (20).

DISCUSSION

Mesh procedures are standard practice for surgical repair of both inguinal, ventral and incisional hernias (1–3). As the number of hernias treated worldwide continues to grow, also the number of hernia meshes implanted each year rise inexorably. Mesh infection rate in inguinal hernia surgery is below 1% and is not regarded as a clinical problem. However, surgeons often have to deal with mesh infections after ventral and incisional hernia surgery, which is estimated to be between 1 and 8% (6). The primary treatment modality is conservative. This is successful in eliminating mesh infection in over 50% of cases without mesh removal (7, 10). The most common bacterial agent is *Staphylococcus aureus*. With increasing proportion of methicillin resistance (MRSA), the treatment options in long-standing wound infections might be problematic to handle (11). There are no recommendations on how long a conservative regime is acceptable. Polypropylene and polyester meshes can be saved in a higher proportion that a laminar mesh-like ePTFE. Extensive ePTFE mesh infections are best managed by mesh explantation (11). Pros and cons must though be weighed against each other according to the scenario presented. If conservative treatment fails, the mesh must be explanted (8, 15).

In mesh infection, biological meshes are increasingly used for replacement as synthetic meshes by some are regarded as contraindicated (5). The publications included in the present review demonstrated that there were three approaches that could be taken depending on the individual patient situation. The first option was to remove the infected mesh without a new implant. This is the most common option after inguinal hernia surgery, since the transversalis fascia is thickened by fibroses after the mesh removal (13). Using this approach, no inguinal hernia recurrence was seen on mean follow-up of 62 months in a case series (13). This does, however, not apply for incisional and ventral hernias. Tolino et al. reported on a recurrence rate of 23% after removal of an infected mesh following incisional hernia operation without reimplantation of a new mesh (8).

The second option was to replace the infected polypropylene mesh with a new polypropylene mesh (15). The short-term results showed a relative uneventful postoperative course after mesh replacement in 27 patients. Six (22%) patients developed a minor wound infection and were treated with dressings and antibiotics, five (19%) patients had wound infections requiring debridement and one required complete mesh removal. On follow-up, there were three hernia recurrences, one with an enterocutaneous fistula. Ninety-five percent of the patients undergoing mesh replacement were considered cured from chronic mesh infection after a mean follow-up of 74 months (15).

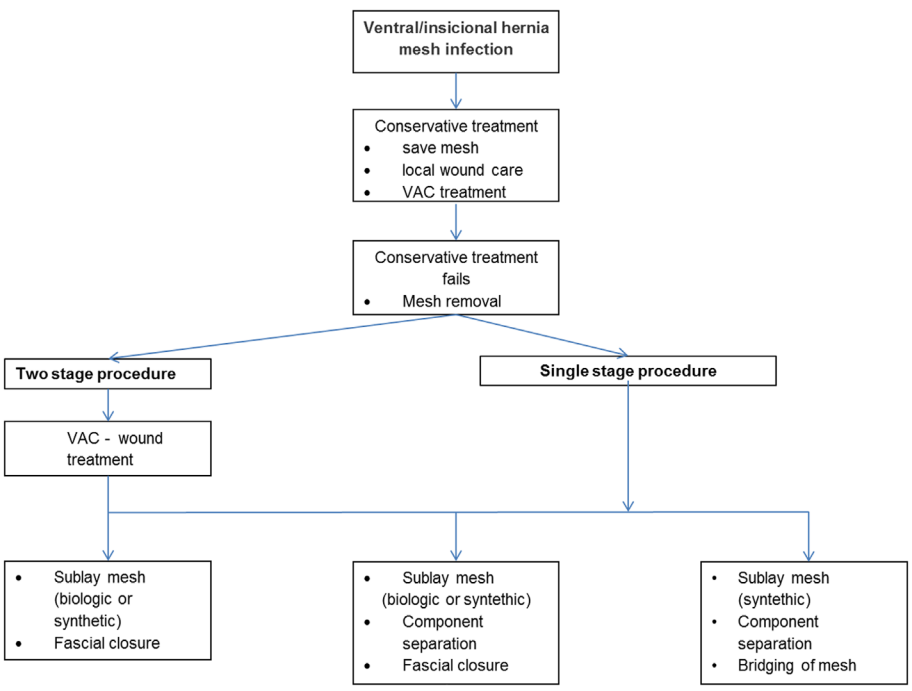

FIGURE 1 | Algorithm for treatment of ventral/incisional hernia mesh infection.

The third option was to replace the explanted synthetic mesh with a biological mesh (5, 16–20). Long-term results were successful only if bridging was omitted (5, 16, 17). An unacceptably high recurrence rate was observed following bridging with biological meshes (5, 16, 17). When bridging was avoided, good results were obtained for replacement of an infected synthetic mesh with a biological (5, 16, 17). An algorithm for treatment of ventral/incisional hernia mesh infection is presented in **Figure 1**.

It can be concluded that a mesh can be saved in more than half of patients suffering from an infection after implantation of a synthetic mesh for an incisional hernia. If mesh explanation is necessitated a replacement seems safe either using a synthetic or a biological mesh if fascia could be closed. Bridging seems to result in a high failure rate using a biological mesh. Further studies are needed to create a better evidence-based platform for specific therapeutic decision-making.

AUTHOR CONTRIBUTIONS

AM: literature search, selection of the literature, review of the literature, and writing of the manuscript. F Ka: literature search, selection of the literature, review of the literature, and revision of the manuscript. F Kö: literature search, selection of the literature, review of the literature, and revision of the manuscript.

REFERENCES

1. Scott NW, McCormack K, Graham P, Go PM, Ross SJ, Grant AM. Open mesh versus non-mesh for repair of femoral and inguinal hernia. *Cochrane Database Syst Rev* (2002) **4**:CD002197. doi:10.1002/14651858.CD002197
2. McCormack K, Scott NW, Go PM, Ross S, Grant AM; EU Hernia Trialists Colloboration. Laparoscopic techniques versus open techniques for inguinal hernia repair. *Cochrane Database Syst Rev* (2003) **1**:CD001785. doi:10.1002/14651858.CD001785
3. Luijendijk RW, Hop WC, van den Tol MP, de Lange DC, Braaksma MM, Jzermans JN, et al. A comparison of suture repair with mesh repair for incisional hernia. *N Engl J Med* (2000) **343**(6):392–8. doi:10.1056/NEJM200008103430603
4. Rutkow IM. Demographic and socioeconomic aspects of hernia repair in the United States in 2003. *Surg Clin North Am* (2003) **83**(5):1045–51. doi:10.1016/S0039-6109(03)00132-4
5. Albino FP, Patel KM, Nahabedian Y, Attinger CE, Bhanot P. Immediate, multistaged approach to infected synthetic mesh: outcomes after abdominal wall reconstruction with porcine acellular dermal matrix. *Ann Plast Surg* (2015) **75**(6):629–33. doi:10.1097/SAP.0000000000000186
6. Falagas ME, Kasiakou SK. Mesh-related infections after hernia repair surgery. *Clin Microbiol Infect* (2005) **11**:3–8. doi:10.1111/j.1469-0691.2004.01014.x
7. Stremitzer S, Bachleitner-Hofmann T, Gradl B, Gruenbeck M, Bachleitner-Hofmann B, Mittelboeck M, et al. Mesh graft infection following abdominal hernia repair: risk factor evaluation and strategies of mesh graft preservation. A retrospective analysis of 476 operations. *World J Surg* (2010) **34**(7):1702–9. doi:10.1007/s00268-010-0543-z
8. Tolino MJ, Tripoloni DE, Ratto R, Garcia MI. Infections associated with prosthetic repairs of abdominal wall hernias: pathology, management and results. *Hernia* (2009) **13**:631–7. doi:10.1007/s10029-009-0541-y
9. Liang MK, Nguyen MT, Berger RL, Hicks SC, Kao LS. Abdominal reoperation and mesh explantation following open ventral hernia repair with mesh. *Am J Surg* (2014) **208**(4):670–6. doi:10.1016/j.amjsurg.2013.10.024
10. Sauerland S, Walgenbach M, Habermalz B, Seiler CM, Miserez M. Laparoscopic versus open surgical techniques for ventral or incisional hernia repair. *Cochrane Database Syst Rev* (2011) **16**(3):CD007781. doi:10.1002/14651858.CD007781.pub2
11. Collage RD, Rosengart MR. Abdominal wall infections with in situ mesh. *Surg Infect (Larchmt)* (2010) **11**(3):311–8. doi:10.1089/sur.2010.029
12. Meagher H, Clarke Moloney M, Grace PA. Conservative management of mesh-site infection in hernia repair surgery: a case series. *Hernia* (2015) **19**(2):231–7. doi:10.1007/s10029-013-1069-8
13. Akyol C, Kocaay F, Orozakunov E, Genc V, Bayram IK, Cakmak A, et al. Outcome of the patients with chronic mesh infection following open inguinal hernia repair. *J Korean Surg Soc* (2013) **84**:287–91. doi:10.4174/jkss.2013.84.5.287
14. Darehzereshki A, Goldfarb M, Zehetner J, Moazzez A, Lipham JC, Mason RJ, et al. Biologic versus nonbiologic mesh in ventral hernia repair: a systematic review and meta-analysis. *World J Surg* (2014) **38**(1):40–50. doi:10.1007/s00268-013-2232-1
15. Birolini C, de Miranda JS, Utiyama EM, Rasslan S. A retrospective review and observations over a 16-year clinical experience on the surgical treatment of chronic mesh infection. What about replacing a synthetic mesh on the infected surgical field? *Hernia* (2015) **19**:239–46. doi:10.1007/s10029-014-1225-9
16. Rosen JM, Krpata DM, Ermlich B, Blatnik JA. A 5-year clinical experience with single-staged repairs of infected and contaminated abdominal wall defects utilizing biologic mesh. *Ann Surg* (2013) **257**:991–6. doi:10.1097/SLA.0b013e3182849871
17. Guerra O. Noncrosslinked procine-derived acellular dermal matrix for single-stage complex abdominal wall herniorrhaphy after removal of infected synthetic mesh: a retrospective review. *Am Surg* (2014) **80**(50):489–95.
18. Cavallaro A, Lo Menzo E, Di Vita M, Zanghi A, Cavallaro V, Veroux PF, et al. Use of biological meshes for abdominal wall reconstruction in highly contaminated fields. *World J Gastroenterol* (2010) **16**(15):1928–33. doi:10.3748/wjg.v16.i15.1928
19. Peppas G, Makris MC, Falagas ME. Biological mesh for abdominal wall hernia synthetic mesh multidrug-resistant *Pseudomonas aeruginosa* infection: report of case. *Surg Today* (2011) **41**:717–20. doi:10.1007/s00595-010-4326-9
20. Coccolini F, Catena F, Ansaloni L, Neri F, Gazzotti F, Lazzareschi D, et al. An innovative abdominal wall repair technique for infected prosthesis: the Eskimo technique. *Ulus Travma Acil Cerrahi Derg* (2011) **17**(4):354–8. doi:10.5505/tjtes.2011.56767

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

APPENDIX

BioMesh Study Group

Ferdinand Köckerling (Chairman), Stavros Antoniou, René Fortelny, Frank A. Granderath, Markus Heiss, Franz Mayer, Marc Miserez, Agneta Montgomery, Salvador Morales-Conde, Filip Muysoms, Alexander Petter-Puchner, Rudolph Pointner, Neil Smart, Marciej Smietanski, and Bernd Stechemesser.

Aim

The BioMesh Study Group has set itself the task of identifying how best to use biological meshes for the various indications. The first step toward achieving that goal is to compile systematic reviews of the different indications on the basis of the existing literature. The available literature sources will be evaluated in accordance with the Oxford Centre for Evidence-Based Medicine-Levels of Evidence (March 2009). Next, based on the review findings, corresponding Statements and Recommendations are to be formulated in a Consensus Conference for the use of biological meshes for the different indications. The findings of the Consensus Conference are then to be summarized for a joint publication. This present publication is a part of the project undertaken by the BioMesh Study Group.

frontiers in Surgery

REVIEW
published: 16 February 2016
doi: 10.3389/fsurg.2016.00009

Biologic Mesh Reconstruction of the Pelvic Floor after Extralevator Abdominoperineal Excision: A Systematic Review

*Nasra N. Alam[1], Sunil K. Narang[1], Ferdinand Köckerling[2], Ian R. Daniels[1] and Neil J. Smart[1]**

[1] Exeter Surgical Health Services Research Unit (HeSRU), Royal Devon and Exeter Hospital, Exeter, Devon, UK, [2] Department of Surgery, Center for Minimally Invasive Surgery, Academic Teaching Hospital of Charité Medical School, Vivantes Hospital, Berlin, Germany

Introduction: The aim of this review is to provide an overview of the evidence for the use of biologic mesh in the reconstruction of the pelvic floor after extralevator abdominoperineal excision of the rectum (ELAPE).

Methods: A systematic search of PubMed was conducted using the search terms: "ELAPE," "extralevator abdominoperineal excision of rectum," or "extralevator abdominoperineal resection." The search yielded 17 studies.

Results: Biologic mesh was used in perineal reconstruction in 463 cases. There were 41 perineal hernias reported but rates were not consistently reported in all studies. The most common complications were perineal wound infection (n = 93), perineal sinus and fistulae (n = 26), and perineal haematoma or seroma (n = 11). There were very few comparative studies, with only one randomized control trial (RCT) identified that compared patients undergoing ELAPE with perineal reconstruction using a biological mesh, with patients undergoing a conventional abdominoperineal excision of the rectum with no mesh. There was no significant difference in perineal hernia rates or perineal wound infections between the groups. Other comparative studies comparing the use of biologic mesh with techniques, such as the use of myocutaneous flaps, were of low quality.

Conclusion: Biologic mesh-assisted perineal reconstruction is a promising technique to improve wound healing and has comparable complications rates to other techniques. However, there is not enough evidence to support its use in all patients who have undergone ELAPE. Results from high-quality prospective RCTs and national/international collaborative audits are required.

Keywords: ELAPE, extralevator abdominoperineal excision of rectum, extralevator abdominoperineal resection, pelvic floor reconstruction, biological mesh

OPEN ACCESS

Edited by:
Evangelos P. Misiakos, University of Athens School of Medicine, Greece

Reviewed by:
Scott R. Kelley, Mayo Clinic, USA
Juan Manuel Suárez-Grau, General Hospital of Riotinto, Spain

****Correspondence:***
Neil J. Smart
drneilsmart@hotmail.com

Specialty section:
This article was submitted to Visceral Surgery, a section of the journal Frontiers in Surgery

Received: *27 July 2015*
Accepted: *28 January 2016*
Published: *16 February 2016*

Citation:
Alam NN, Narang SK, Köckerling F, Daniels IR and Smart NJ (2016) Biologic Mesh Reconstruction of the Pelvic Floor after Extralevator Abdominoperineal Excision: A Systematic Review. Front. Surg. 3:9. doi: 10.3389/fsurg.2016.00009

INTRODUCTION

Abdominoperineal excision of the rectum (APER) is used as a treatment modality in patients with rectal cancer where an anterior resection (AR) and an anastomosis cannot be performed (1). Extralevator abdominoperineal excision (ELAPE) involves the en bloc excision of the levator muscles and the rectum, in order to reduce the risk of tumor involvement in the circumferential resection margins (CRMs) and reduce the risk of tumor perforation intraoperatively. This method has been demonstrated as leading to a wider surgical margin and therefore fewer positive CRMs (2–5). Initially, the terminology used was "*cylindrical APER*" but with refinement and the use of MRI to highlight the area of risk of a positive CRM, the term ELAPE is more appropriate (4). The nomenclature surrounding the technique has been the source of much debate and confusion, with some authors noting that ELAPE is no different from the original description in English by Miles (6). Furthermore, what exactly constitutes "standard" surgery that allows differentiation of ELAPE has come under scrutiny (7).

Volumetric analysis has confirmed that ELAPE does remove more tissue (3), and the wider excision can, however, increase morbidity and wound complications and will require some form of perineal reconstruction (4). Perineal wound problems are reported in up to 57% of patients undergoing APER (8), although the precise rates following ELAPE are not yet known. Given that ELAPE produces a larger defect in the pelvic floor, leaving only the ischiorectal fat and skin to close the perineal wound; it is presumed that the perineal complication rate is higher. Furthermore, the changes in the proportion of patients having neoadjuvant (chemo)radiotherapy over the time course of ELAPE implementation are incompletely reported in individual studies and in national registries. If the wound fails to heal *via* primary intention, secondary wound healing can result in prolonged hospital stay that requires intensive wound care.

Various alternative techniques have been described to reconstruct the pelvic floor following ELAPE with the aim to reduce perineal wound complications and hernias. The optimal method of perineal reconstruction remains a matter of debate. Myocutaneous flaps, such as those derived from gluteus maximus (2, 4, 9), rectus abdominis, and latissimus dorsi muscles (4, 10), have been used but are associated with donor-site morbidity, flap necrosis, prolonged operative time, additional resources, and increased cost. Biologic mesh has recently been introduced as an alternative form of reconstruction in order to improve perineal wound healing and reduce perineal hernia rates (11). The mesh is usually placed as an inlay or bridge across the defect in the pelvic floor in close relation to the bony structures and sutured in 1-cm intervals to the origin of the levator muscles laterally (12). [**Figure 1** (13)] The mechanism by which the use of a bridging prosthesis reduces perineal wound problems is not clear. It has been suggested that biological mesh allows native cellular ingrowth and promotes tissue remodeling, which in turn reduces perineal wound problems (14, 15). Alternatively, the biologic mesh may act as a physical barrier, supporting the pelvic contents (omentum, small bowel, and uterus) and minimizing the pressure on the skin and ischiorectal fat as they heal.

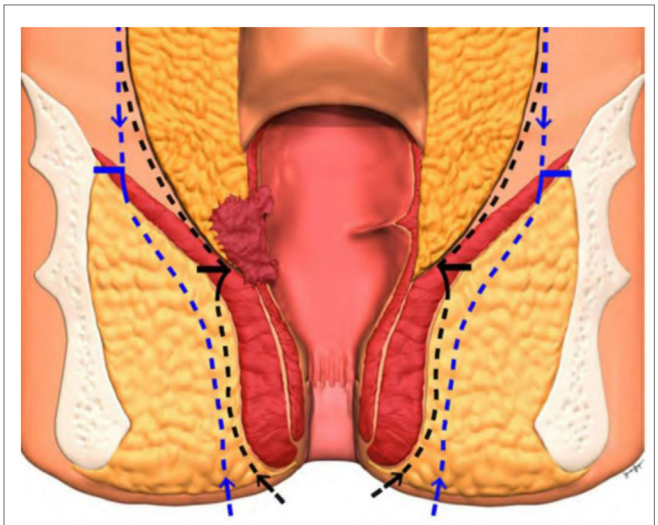

FIGURE 1 | ELAPE technique (13). Black line indicates dissection line of standard APE and blue line ELAPE. Horizontal line indicates meeting point of abdominal and perineal dissection.

Alternative methods for removing the pressure of small bowel that prolapses into the pelvis, directly on the perineum include the following:

(1) Omental pedicle flaps (16–18),
(2) Mobilization of the cecum (9),
(3) Retroversion of the uterus in female (19).

All of the above techniques are designed to close off the dead space in the pelvis, resulting from the removal of the rectum and to keep the small bowel out of the pelvis. Of these methods, the most widely established is the omental pedicle. However, these techniques largely related to an era of open surgery, and they have mostly been abandoned with the move to laparoscopic and other minimally invasive techniques and are not representative of contemporary practice. Omental pedicles are associated with perineal wound complication rates of 14–18% and decreased wound dehiscence in comparison to primary closure (16, 18) whereas others show no advantage to this technique (20). Mobilization of the cecum is uncommon and evidence is limited to case reports (9). Retroversion of the uterus involves retroverting the uterus and securing it to the bony pelvis at a level where it obliterates the pelvis, with the use of non-absorbable suture material (19). This can be achieved *via* the abdominal or perineal wound, although it has been associated with dyspareunia and positional menstruation (19).

The aim of this review is to provide an overview of the evidence for the use of biologic mesh in the reconstruction of the pelvic floor after extralevator abdominoperineal excision.

METHODS

A systematic search of PubMed was conducted using the search terms: "ELAPE," "extralevator abdominoperineal excision of rectum," or "extralevator abdominoperineal resection" in order to

identify studies evaluating the use of biologic mesh for reconstruction of the pelvic floor. Titles, abstracts, and full texts were analyzed for studies reporting on the use of biologic mesh for reconstruction of the pelvic floor. Inclusion criteria were studies that used biologic mesh for perineal reconstruction. Studies were excluded if only synthetic mesh was used or if there was no mention of a mesh. Furthermore, studies on patients under the age of 18 were excluded as well as non-English language studies, technical tips, conference abstracts, or duplicates series from the same research group. Overall, the search yielded 17 studies for analysis after the exclusion of review articles. The study characteristics are presented (**Table 1**).

RESULTS

There were 15 case series, one randomized control trial (RCT), and one case report identified. A biologic mesh was used in perineal reconstruction in 463 cases. The different types of biologic mesh used were cross-linked porcine dermal collagen (Permacol™) in 206 cases, 44 using porcine intestinal submucosa (Surgisis©), 136 using human acellular dermal matrix, and 9 using a combination of Permacol™ and Surgisis©. Two studies did not specify the type of biologic mesh used.

Perineal Hernia

There were 41 perineal hernias reported, but rates were not consistently reported in all studies. In those studies that did report perineal hernia rates, it was difficult to delineate whether hernias occurred in patients that had perineal reconstruction using a biological or synthetic mesh or a myocutaneous flap.

Perineal Wound Infection/Healing Problems

Perineal wound infection was reported explicitly in 93 cases, whereas the overall rate of perineal problems was much higher. Perineal sinus and fistulae were reported in 26 cases, with a further 11 cases of perineal hematoma or seroma. Some studies have described "perineal wound complications" but not specified whether they were related to infection, dehiscence, hernia, or pain (**Table 1**).

The most common complications were perineal wound infection and perineal sinus. However, there are no standardized measures for reporting perineal outcomes of any type following ELAPE. Definitions of wound infection, wound healing problems, perineal herniation, pain measurement, and functional status assessment are inconsistent between studies, thus limiting comparisons.

There are very few studies comparing the use of biologic mesh for perineal reconstruction for ELAPE. Two case series compared biologic mesh with myocutaneous flaps and one series compared laparoscopic ELAPE with laparoscopic and open APER. However, they are all of low-level evidence (level 4). Only one RCT was identified that compared patients undergoing ELAPE with perineal reconstruction using a biological mesh, with patients undergoing a conventional APER with no mesh. There was no significant difference in perineal hernia rates or perineal wound infections between the two groups.

DISCUSSION/SUMMARY

The use of ELAPE over conventional APER is becoming more widespread despite the reservations of some (13), and the optimal method of perineal wound closure remains a topic of discussion. The reported results of primary closure of the perineal defect are poor (34) and most surgeons performing ELAPE opt for an adjunct (35). The literature analyzed suggests that perineal closure using a biologic mesh produces wound infection and complication rates that are comparable to other methods of reconstruction, such as myocutaneous flaps. Myocutaneous flap reconstruction using a vertical rectus abdominis (VRAM), gracilis, or the gluteus maximus, however, has short-term disadvantages, such as longer operative times and the need for plastic surgical expertise, resulting in higher operative costs, flap necrosis, wound complications at the donor site, and longer bed rest (15). Longer term incisional hernias at the VRAM donor site and reduced abdominal wall strength have been reported (36). Biologic mesh reconstruction avoids all of these potential complications.

Synthetic non-absorbable mesh is associated with high infection rate in contaminated fields and consequently is considered by many to be contra-indicated for use in perineal reconstruction following ELAPE (37). The role of newer, absorbable synthetic meshes is, as yet, unclear. Biologic meshes are composed of an acellular collagen matrix that is believed to allow tissue regeneration, neovascularization, repopulation with fibroblasts, and therefore provides a scaffold for tissue incorporation (15, 23). This is thought to reduce the rate of infection. However, the overall volume and quality of evidence available regarding biologic mesh use for perineal reconstruction following ELAPE is poor, with observational retrospective studies predominating. There have been some attempts at comparative studies, but these too have been of low quality with a high risk of bias and confounding factors. Head-to-head randomized trials or high-quality prospective cohort studies comparing biological with synthetic mesh, types of biologic mesh, and biologic mesh with (myo)fasciocutaneous flaps are also lacking, partly because there is no consensus among surgeons as to the optimal biologic mesh or optimal tissue flap. Trials directly comparing any technical adjunct to primary closure alone as a control arm may be difficult to perform in light of the lack of equipoise among surgeons and possibly even unethical given the reported poor results of primary closure. Furthermore, there does not appear to be a consensus in the studies regarding perineal outcome reporting. There are a variety of different end points recorded across the studies, such as perineal defect size, blood loss, and operating time. There needs to be a focus on standardized definitions and reporting of perineal healing rates, perineal hernia, and functional outcomes following ELAPE (38).

Jensen et al. also examined the long-term follow-up for patients undergoing pelvic floor reconstruction with a biologic mesh following ELAPE (25). As well as low perineal hernia rates, there was no major restriction in movement or sitting. Chronic pain had resolved in all patients at a median of 8 months, and there was no major limitation to walking. However, other studies evaluating quality-of-life scores using validated tools (11) demonstrated a favorable comparison to the reference population of patients with colorectal cancer who had undergone a standard

TABLE 1 | Reconstruction of the pelvic floor after ELAPE.

Reference	Study design	No. of pts	Age	Sex (M:F)	Patient characteristics	Material used	Intervention	Follow-up (months)	Complications	LoE
Christensen et al. (21)	Case series	57	FLAP: 67.8 (32.7–86.2) MESH: 69.7 (48.7–84.5)	11:22 10:14	52 primary rectal cancer 5 local recurrence 48 patients (84%) received neoadjuvant CRT	Gluteal flaps: 33 Permacol: 24	ELAPE for low rectal cancer	Median follow-up: gluteal flap: 3.2 years (1.7– 4.3) Biologic mesh: 1.7 (0.4 –2.2) years	Gluteal flap vs. biologic Perineal hernia: 7 vs. 0, $P < 0.01$ Infectious complications: 2 (17%) vs. 4 (6%), $P < 0.26$ 1 patient per group with a persistent perineal sinus	4
Dalton et al. (22)	Case series	31	Mean 66.8 ± SD 11.4 years	8:23	Neoadjuvant CRT: 14	VRAM flap: 1 Permacol: 30	Open ELAPE	Median: 20 (0–45)	Breakdown of perineal wound: 6 Skin paddle necrosis of a VRAM flap: 1 Perineal wound hematoma: 1 Minor wound discharge: 9	4
Han et al. (23)	Case series	12	68 (49–80)	7:5	Ultra low rectal cancer. Neoadjuvant CRT: 3	HADM	Cylindrical APR-open	Median: 8 (2–16)	Asymptomatic seroma: 1 Perineal wound infection: 1	4
Han et al. (14)	Open label RCT	67	63 median (44–81)	20:15	Neoadjuvant therapy: 10	HADM	ELAPE: 35	Median: 29 (12–48)	Bowel perforation: 2 Perineal wound infection: 4 Perineal seroma: 4 Peristomal hernia: 16 Abdominal wound infection: 2 Perineal herniation: 5	2
			68 (32–84)	21:11	Neoadjuvant therapy: 9	None	APER: 32	Median: 22 (14–46)	Bowel perforation: 5 Perineal wound infection: 6 Peristomal hernia: 13 Abdominal wound infection: 3 Perineal herniation: 4	
Han et al. (24)	Multicenter prospective cohort study (case series)	109 (102)	61 years (27–78)	60:42		HADM	Biological mesh: 83 (81.4%) Primary closure: 19 (18.6%)	44 median (18–68)	Biological mesh Perineal wound complications: 15 Infection: 5 Seroma: 5 Hernia: 4 Abdominal wound infection: 3 Primary closure Perineal wound complications: 9 Infection: 3 Seroma: 1 Hernia: 2 Wound dehiscence: 3 Chronic sinus: 1 Abdominal wound infection: 2	4

(Continued)

TABLE 1 | **Continued**

Reference	Study design	No. of pts	Age	Sex (M:F)	Patient characteristics	Material used	Intervention	Follow-up (months)	Complications	LoE
Jensen et al. (25)	Case series	53 – 31 agreed to long-term f/u	69 (33–83) median	33:20	Neoadjuvant CRT: 23	Permacol	6 planned open 47 laparoscopic of which 7 converted to open	Median: 36 (1–67)	Perineal hernia: 3 Fistuale: 11 Perineal abscess: 4 Superficial wound infections: 4 Removal of mesh: 1 Implantation of new mesh: 1	4
Kipling et al. (26)	Case series	28	70 (52–81 years) median	20:8	Neoadjuvant therapy None: 9 (32%) Short course: 2 (7%) Long course: 17 (61%)	Permacol	Lap ELAPE, 5 conversions	Median 38 (23–66)	Bowel perforation: 1 Persistent perineal sinus at 6 months: 1 Delayed healing of the perineal wound: 1	4
Peacock et al. (15)	Case series (comparative)	15	68 median (48–74)	4:1	Long-course CT/RT: 4 Long-course RT: 1	VRAM: 5	Cylindrical APER	Median: 29 (23–35)	Perineal wound infection (wound dehiscence): 1 Flap necrosis: 1 Wound hematoma: 1	4
			57 median (47–68)	9:1	Long-course CT/RT: 6 Long-course RT: 2 (not suitable for CT): 2	Surgisis: 10		13 (3–27)	Perineal sinus: 1 Superficial perineal wound infection: 2 Abscess/collection: 3	
Peacock et al. (27)	Case series	34	Median 62 years (40–77)	27:7	Long-course CRT: 26 Long-course RT (not suitable for CT): 2 Not required/declined: 6	Surgisis:	Cylindrical APER	Median: 21 (1–54)	Perineal sinus: 5 Superficial perineal wound infection: 3 Abscess/collection: 3 Parastomal hernia: 1	4
Vaughan-Shaw et al. (28)	Case series (case–control)	16	71 (49–88)	7:9	Short-course RT: 7 Long-course CRT: 9	9 Permacol/ Surgisis (omentoplasty: 7)	Laparoscopic ELAPE: 14 (1 conversion) Open: 2 Lap APER: 10 Open APER: 10		Return to theater (<30 days): 2 Perineal wound complications: 2	4
		10	72 (52–87)	5:5	Short-course RT: 7 Long-course CRT: 2				Perineal wound complications: 5 Perineal hernia: 2 Infection: 1	
		10	72.5 (46–89)	8:2	Short-course RT: 2 Long-course CRT: 5				Return to theater (<30 days): 1 In-hospital mortality: 1 Perineal wound complications: 2	
Wille-Jørgensen et al. (29)	Case series	11	63 median (51–77)	7:4	Neoadjuvant CRT: 6	Permacol	Laparoscopic APER: 9 (2 conversions) Open APER: 2	Median: 12 (3–18)	Mesh removal 2nd to infection: 1 Rectal perforation: 1 Long-lasting perineal pain: 6 Fistula: 1	4
Chi et al. (30)	Case series	6	Mean: 69	4:2	Neoadjuvant CRT 4	HADM		Mean: 5 (2–19)	Surgical site infection: 2	4

(Continued)

TABLE 1 | **Continued**

Reference	Study design	No. of pts	Age	Sex (M:F)	Patient characteristics	Material used	Intervention	Follow-up (months)	Complications	LoE
Palmer et al. (31)	Case series	193	66 median (28–87)	81:112	Neoadjuvant CRT: 91 RT alone: 92 Locally advanced tumor on MRI (T4)-126 (65%)	Perineal closure Gluteal flap: 99 (51) Biological mesh: 66 (34) Closure directly: 28 (15)	Pelvic exenteration: 25, extended resection with parts of other organs: 56 ELAPE alone: 112	Median 31 (0–156)	Intra-operative perforation: 19 30-day postoperative mortality: 6	4
West et al. (4)	Retrospective case series (multicenter)	176	66 (58–73) Median	116:54 6-unknown	Neoadjuvant RT Yes: 135 No: 35 Unknown: 11 Neoadjuvant CT Given: 84 Not given: 81 Unknown: 11	Gluteus maximus: 60 Rectus abdominis: 12 Latissimus dorsi: 1 Permacol: 11	ELAPE: 176 Open surgery: 122 Laparoscopic surgery: 19 Unknown: 35	*NS*	Wound complications Yes: 57 Infection/breakdown/sinus: 41 Perineal hernia: 5 Other: 11	4
		124	68 (57–75) median	87:37	Neoadjuvant RT Yes: 90 No: 24 Unknown: 10 Neoadjuvant CT Given: 48 Not given: 66 Unknown: 10		APER: 124 Open surgery: 56 Laparoscopic surgery: 4 Unknown: 64	*NS*	Wound complications Yes: 11 Infection/breakdown/sinus: 7 Perineal hernia: 1 Other: 3 Unknown: 26	
Harries et al. (32)	Prospective case series	48	Median: 63 (40–86)	36:12	Neoadjuvant treatment: 43	Permacol	ELAPE Lap: 28 Conversion: 7 Open: 23	Median: 27 (1–85)	Specimen perforation: 3 (6.4%) Unhealed at 6 months: 4 (8.3%) Perineal sinus: 7 Abdominal wound dehiscence: 1 Ureteric injury: 1 Radiological drainage of pelvic collections: 2 Perineal wound infections: 9	4
Kavanagh et al. (33)	Case report	1	72	0:1	Long-course CRT	Permacol	Lap ELAPE	12	NS	4
Sayers et al. (34)	Case series	54	Median: 69.5 (31–90)	40:14	Neoadjuvant CRT: 52	Primary closure: 46 Bio: 2 FLAP: 6 (VRAM: 5 Gracilis: 1)	Lap ELAPE: 20 Open: 34	Median: 38 (9–61)	Perineal complications: 24 Perineal hernia: 14 Perineal hematoma: 1 Infected myocutaneous flap: 1 Total dehiscence of the perineum: 1	4

APER, abdominoperineal excision of the rectum; CRT, chemoradiotherapy; CT, chemotherapy; ELAPE, extralevator abdominoperineal excision; HADM, human acellular dermal matrix; LoE, level of evidence; RCT, randomized controlled trial; RT, radiotherapy; VRAM, vertical rectus abdominis muscle.

APE, whereas patients who had undergone flap reconstruction had a lower quality of life score (11).

Of note, a number of studies from Beijing have been included for analysis. The three studies include patients managed over an approximately 3-year period, and there is overlap of the studies within the time period, therefore suggesting some replication. One study is classified as a case series (23), the second a RCT (14), and the third another case series (24). It is unclear as to whether these three studies are from the same patient group or three different cohorts.

CONCLUSION

Overall, the use of a biologic mesh to close perineal defects has comparable complications rates to myocutaenous flaps but may offer advantages, such as shorter operating time and early mobilization, which results in a more cost-effective repair (15). Biologic mesh-assisted perineal reconstruction is a promising technique to improve wound healing, but there is not enough evidence to support its use in all patients who have undergone ELAPE. The results from high-quality prospective RCTs or national/international collaborative audits using statistical process control as a methodology of assessment of improvement are required.

AUTHOR CONTRIBUTIONS

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

REFERENCES

1. Perry WB, Connaughton JC. Abdominoperineal resection: how is it done and what are the results? *Clin Colon Rectal Surg* (2007) **20**(3):213–20. doi:10.1055/s-2007-984865
2. Holm T, Ljung A, Häggmark T, Jurell G, Lagergren J. Extended abdominoperineal resection with gluteus maximus flap reconstruction of the pelvic floor for rectal cancer. *Br J Surg* (2007) **94**(2):232–8. doi:10.1002/bjs.5489
3. West NP, Finan PJ, Anderin C, Lindholm J, Holm T, Quirke P. Evidence of the oncologic superiority of cylindrical abdominoperineal excision for low rectal cancer. *J Clin Oncol* (2008) **26**(21):3517–22. doi:10.1200/JCO.2007.14.5961
4. West NP, Anderin C, Smith KJ, Holm T, Quirke P. European Extralevator Abdominoperineal Excision Study Group. Multicentre experience with extralevator abdominoperineal excision for low rectal cancer. *Br J Surg* (2010) **97**(4):588–99. doi:10.1002/bjs.6916
5. Shihab OC, Heald RJ, Holm T, How PD, Brown G, Quirke P, et al. A pictorial description of extralevator abdominoperineal excision for low rectal cancer. *Colorectal Dis* (2012) **14**(10):e655–60. doi:10.1111/j.1463-1318.2012.03181.x
6. Miles WE. A method of performing abdomino-perineal excision for carcinoma of the rectum and of the terminal portion of the pelvic colon (1908). *CA Cancer J Clin* (1971) **21**(6):361–4. doi:10.3322/canjclin.21.6.361
7. Nicholls J. No more 'standard' abdominoperineal excision. *Colorectal Dis* (2013) **15**(11):1329–30. doi:10.1111/codi.12458
8. de Bruin AF, Gosselink MP, Wijffels NA, Coene PP, van der Harst E. Local gentamicin reduces perineal wound infection after radiotherapy and abdominoperineal resection. *Tech Coloproctol* (2008) **12**(4):303–7. doi:10.1007/s10151-008-0440-8
9. Habib K. Prevention of recurrent small bowel obstruction resulting from pelvic adhesions in patients who have previously undergone abdominoperineal excision of the rectum. *Tech Coloproctol* (2014) **18**(12):1179–80. doi:10.1007/s10151-014-1227-8
10. McMenamin DM, Clements D, Edwards TJ, Fitton AR, Douie WJ. Rectus abdominis myocutaneous flaps for perineal reconstruction: modifications to the technique based on a large single-centre experience. *Ann R Coll Surg Engl* (2011) **93**(5):375–81. doi:10.1308/003588411X572268
11. Foster JD, Pathak S, Smart NJ, Branagan G, Longman RJ, Thomas MG, et al. Reconstruction of the perineum following extralevator abdominoperineal excision for carcinoma of the lower rectum: a systematic review. *Colorectal Dis* (2012) **14**(9):1052–9. doi:10.1111/j.1463-1318.2012.03169.x
12. Svane M, Bulut O. Perineal hernia after laparoscopic abdominoperineal resection – reconstruction of the pelvic floor with a biological mesh (Permacol™). *Int J Colorectal Dis* (2012) **27**(4):543–4. doi:10.1007/s00384-011-1253-1
13. Prytz M, Angenete E, Ekelund J, Haglind E. Extralevator abdominoperineal excision (ELAPE) for rectal cancer – short-term results from the Swedish colorectal cancer registry. Selective use of ELAPE warranted. *Int J Colorectal Dis* (2014) **29**(8):981–7. doi:10.1007/s00384-014-1932-9
14. Han JG, Wang ZJ, Wei GH, Gao ZG, Yang Y, Zhao BC. Randomized clinical trial of conventional versus cylindrical abdominoperineal resection for locally advanced lower rectal cancer. *Am J Surg* (2012) **204**(3):274–82. doi:10.1016/j.amjsurg.2012.05.001
15. Peacock O, Pandya H, Sharp T, Hurst NG, Speake WJ, Tierney GM, et al. Biological mesh reconstruction of perineal wounds following enhanced abdominoperineal excision of rectum (APER). *Int J Colorectal Dis* (2012) **27**(4):475–82. doi:10.1007/s00384-011-1325-2
16. Hay JM, Fingerhut A, Paquet JC, Flamant Y. Management of the pelvic space with or without omentoplasty after abdominoperineal resection for carcinoma of the rectum: a prospective multicenter study. The French Association for Surgical Research. *Eur J Surg* (1997) **163**(3):199–206.
17. Moreaux J, Horiot A, Barrat F, Mabille J. Obliteration of the pelvic space with pedicled omentum after excision of the rectum for cancer. *Am J Surg* (1984) **148**(5):640–4. doi:10.1016/0002-9610(84)90342-8
18. Killeen S, Devaney A, Mannion M, Martin ST, Winter DC. Omental pedicle flaps following proctectomy: a systematic review. *Colorectal Dis* (2013) **15**(11):e634–45. doi:10.1111/codi.12394
19. Habib K. Uterus and extralevator abdominoperineal excision: a technique. *Dis Colon Rectum* (2013) **56**(9):1102–4. doi:10.1097/DCR.0b013e31829a2edc
20. O'Leary DP. Use of the greater omentum in colorectal surgery. *Dis Colon Rectum* (1999) **42**(4):533–9. doi:10.1007/BF02234183
21. Christensen HK, Nerstrøm P, Tei T, Laurberg S. Perineal repair after extralevator abdominoperineal excision for low rectal cancer. *Dis Colon Rectum* (2011) **54**(6):711–7. doi:10.1007/DCR.0b013e3182163c89
22. Dalton RS, Smart NJ, Edwards TJ, Chandler I, Daniels IR. Short-term outcomes of the prone perineal approach for extra-levator abdomino-perineal excision (elAPE). *Surgeon* (2012) **10**(6):342–6. doi:10.1016/j.surge.2011.10.001
23. Han JG, Wang ZJ, Gao ZG, Xu HM, Yang ZH, Jin ML. Pelvic floor reconstruction using human acellular dermal matrix after cylindrical abdominoperineal resection. *Dis Colon Rectum* (2010) **53**(2):219–23. doi:10.1007/DCR.0b013e3181b715b5
24. Han JG, Wang ZJ, Qian Q, Dai Y, Zhang ZQ, Yang JS, et al. A prospective multicenter clinical study of extralevator abdominoperineal resection for locally advanced low rectal cancer. *Dis Colon Rectum* (2014) **57**(12):1333–40. doi:10.1097/DCR.0000000000000235
25. Jensen KK, Rashid L, Pilsgaard B, Møller P, Wille-Jørgensen P. Pelvic floor reconstruction with a biological mesh after extralevator abdominoperineal excision leads to few perineal hernias and acceptable wound complication rates with minor movement limitations: single-centre experience including clinical examination and interview. *Colorectal Dis* (2014) **16**(3):192–7. doi:10.1111/codi.12492
26. Kipling SL, Young K, Foster JD, Smart NJ, Hunter AE, Cooper E, et al. Laparoscopic extralevator abdominoperineal excision of the rectum: short-term outcomes of a prospective case series. *Tech Coloproctol* (2014) **18**(5):445–51. doi:10.1007/s10151-013-1071-2
27. Peacock O, Simpson JA, Tou SI, Hurst NG, Speake WJ, Tierney GM, et al. Outcomes after biological mesh reconstruction of the pelvic floor following extra-levator abdominoperineal excision of rectum (APER). *Tech Coloproctol* (2014) **18**(6):571–7. doi:10.1007/s10151-013-1107-7
28. Vaughan-Shaw PG, Cheung T, Knight JS, Nichols PH, Pilkington SA, Mirnezami AH. A prospective case-control study of extralevator

abdominoperineal excision (ELAPE) of the rectum versus conventional laparoscopic and open abdominoperineal excision: comparative analysis of short-term outcomes and quality of life. *Tech Coloproctol* (2012) **16**(5):355–62. doi:10.1007/s10151-012-0851-4

29. Wille-Jørgensen P, Pilsgaard B, Møller P. Reconstruction of the pelvic floor with a biological mesh after abdominoperineal excision for rectal cancer. *Int J Colorectal Dis* (2009) **24**(3):323–5. doi:10.1007/s00384-008-0607-9
30. Chi P, Chen ZF, Lin HM, Lu XR, Huang Y. Laparoscopic extralevator abdominoperineal resection for rectal carcinoma with transabdominal levator transection. *Ann Surg Oncol* (2013) **20**(5):1560–6. doi:10.1245/s10434-012-2675-x
31. Palmer G, Anderin C, Martling A, Holm T. Local control and survival after extralevator abdominoperineal excision for locally advanced or low rectal cancer. *Colorectal Dis* (2014) **16**(7):527–32. doi:10.1111/codi.12610
32. Harries RL, Luhmann A, Harris DA, Shami JA, Appleton BN. Prone extralevator abdominoperineal excision of the rectum with porcine collagen perineal reconstruction (Permacol™): high primary perineal wound healing rates. *Int J Colorectal Dis* (2014) **29**(9):1125–30. doi:10.1007/s00384-014-1963-2
33. Kavanagh DO, Imran H, Almoudaris A, Ziprin P, Faiz O. Dynamic magnetic resonance imaging demonstrates the integrity of perineal reconstruction following cylindrical abdominoperineal excision with reconstruction of the pelvic floor using porcine collagen. *Case Rep Med* (2012) **2012**:752357. doi:10.1155/2012/752357
34. Sayers AE, Patel RK, Hunter IA. Perineal hernia formation following extralevator abdominoperineal excision. *Colorectal Dis* (2015) **17**(4):351–5. doi:10.1111/codi.12843
35. Dabbas N, Adams K, Chave H, Branagan G. Current practice in abdominoperineal resection: an email survey of the membership of the Association of Coloproctology. *Ann R Coll Surg Engl* (2012) **94**(3):173–6. doi:10.1308/003588412X13171221589973
36. Daigeler A, Simidjiiska-Belyaeva M, Drücke D, Goertz O, Hirsch T, Soimaru C, et al. The versatility of the pedicled vertical rectus abdominis myocutaneous flap in oncologic patients. *Langenbecks Arch Surg* (2011) **396**(8):1271–9. doi:10.1007/s00423-011-0823-6
37. Choi JJ, Palaniappa NC, Dallas KB, Rudich TB, Colon MJ, Divino CM. Use of mesh during ventral hernia repair in clean-contaminated and contaminated cases: outcomes of 33,832 cases. *Ann Surg* (2012) **255**(1):176–80. doi:10.1097/SLA.0b013e31822518e6
38. Haapamäki MM, Pihlgren V, Lundberg O, Sandzén B, Rutegård J. Physical performance and quality of life after extended abdominoperineal excision of rectum and reconstruction of the pelvic floor with gluteus maximus flap. *Dis Colon Rectum* (2011) **54**(1):101–6. doi:10.1007/DCR.0b013e3181fce26e

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

frontiers in Surgery

REVIEW
published: 24 November 2015
doi: 10.3389/fsurg.2015.00060

Anal Sphincter Augmentation Using Biological Material

*Nasra N. Alam[1], Sunil K. Narang[1], Ferdinand Köckerling[2], Ian R. Daniels[1] and Neil J. Smart[1]**

[1] Exeter Surgical Health Services Research Unit (HeSRU), Royal Devon and Exeter Hospital, Exeter, UK, [2] Department of Surgery, Center for Minimally Invasive Surgery, Academic Teaching Hospital of Charité Medical School, Vivantes Hospital, Berlin, Germany

Introduction: The aim of this review is to provide an overview of the use of biological materials in the augmentation of the anal sphincter either as part of an overlapping sphincter repair (OSR) or anal bulking procedure.

Methods: A systematic search of PubMed was conducted using the search terms "*anal bulking agents,*" "*anal sphincter repair,*" or "*overlapping sphincter repair*." Five studies using biological material as part of an overlapping sphincter repair (OSR) or as an anal bulking agent were identified.

Results: 122 patients underwent anal bulking with a biological material. Anorectal physiology was conducted in 27 patients and demonstrated deterioration in maximum resting pressure, and no significant change in maximum squeeze increment. Quality of life scores (QoLs) demonstrated improvements at 6 weeks and 6 months, but this had deteriorated at 12 months of follow up. Biological material was used in 23 patients to carry out an anal encirclement procedure. Improvements in QoLs were observed in patients undergoing OSR as well as anal encirclement using biological material. Incontinence episodes decreased to an average of one per week from 8 to 10 preoperatively.

Conclusion: Sphincter encirclement with biological material has demonstrated improvements in continence and QoLs in the short term compared to traditional repair alone. Long-term studies are necessary to determine if this effect is sustained. As an anal bulking agent the benefits are short-term.

Keywords: fecal incontinence, anal sphincter repair, overlapping sphincter repair, anal encirclement, anal bulking, biological material

OPEN ACCESS

Edited by:
Hesham Abdeldayem, National Liver Institute, Egypt

Reviewed by:
Essam Salah Hammad, National Liver Institute and Menoufia University, Egypt
Ahmed Farag El-Kased, Menoufia University, Egypt

****Correspondence:***
Neil J. Smart
drneilsmart@hotmail.com

Specialty section:
This article was submitted to Visceral Surgery, a section of the journal Frontiers in Surgery

Received: *27 July 2015*
Accepted: *02 November 2015*
Published: *24 November 2015*

Citation:
Alam NN, Narang SK, Köckerling F, Daniels IR and Smart NJ (2015) Anal Sphincter Augmentation Using Biological Material. Front. Surg. 2:60. doi: 10.3389/fsurg.2015.00060

INTRODUCTION

Fecal incontinence (FI) affects between 1 and 10% of adults in varying degrees. Current epidemiological studies have shown that up to 1% of adults have regular episodes of FI that adversely impacts on their quality of life (1). Treatment modalities vary from conservative, with the use of anti-diarrheal medications such as loperamide and codeine, to non-operative interventions such biofeedback strategies, to surgical management. Surgical options are usually indicated when continence is affected secondary to an anatomic disruption, such as a sphincter weakness or defect (2). Patients who have a history of colorectal surgery (dilatation), obstetric sphincter injury, or pelvic irradiation are also prone to fecal seepage and soiling (3).

TABLE 1 | Biologic materials augmenting the anal sphincter for the treatment of fecal incontinence.

Reference	Study design	No. of patients	Age	Sex (M:F)	Patient characteristics	Material used	Follow-up (months)	Outcome	Complications	LofE
ANAL BULKING										
Kumar et al. (16)	Case series	17	NS	5:12	Idiopathic fecal incontinence secondary to weakness of the internal anal sphincter:9 incontinent following hemorrhoidectomy: 3. Following an internal sphincterotomy. obstetric injury: 2. Following surgical treatment for fistula in ano: 1	Glutaraldehyde cross-linked (GAX) collagen	8 (4–12)	Mean resting pressures: preop: mean 30 cm H_2O, Postop: 45 cm H_2O Squeeze pressures: were not significantly different before Preop: 125 cm H_2O, Postop: 130 cm H_2O	None	4
Maeda et al. (17)	RCT (pilot)	10	68 (45–79) median	1:9	Passive fecal incontinence due to internal anal sphincter (IAS) dysfunction	Bulkamid™: 5 Permacol™: 5	19 (14–22) 1 lost to f/u	Median St Mark's incontinence score: baseline: 16 (11–24), 6 weeks: 14 (3–18), 6 months:15 (8–22) Maximum resting pressure (cm H_2O): baseline:28 (15–58), 6 weeks: 27 (19–56), 6 months: 22 (10–38) ($P < 0.05$, baseline vs. 6 months) Median maximum squeeze increment: baseline: 36 (16–109), 6 weeks: 44 (13–102), 6 months: 38 (15–186) ($P < 0.32$, baseline vs. 6 months) FIQL: (preop vs. postop), Lifestyle score: median 3.10–3.50 ($P < 0.05$), Coping: 2.36–2.75 ($P < 0.05$). Depression: 2.42–3.70 ($P < 0.005$). Embarrassment: 1.67–1.84 ($P < 0.05$). SF-36: preop: median 29, Postop: 100	None Improved at 6/52 but deteriorated at 6/12, No difference between Bulkamid™ and Permacol™	2
Maslekar et al. (15)	Case Series	100	61 (36–82) mean	30:70	Fecal incontinence: Idiopathic 70% Traumatic 15% Neuropathic 10% Mixed 5%	Permacol®	Min 36, 10 lost to f/U	Preop: median squeeze pressures 54.7 (21.1–112.2) Median resting pressures 40.4 (18.1–89.9) CCFIS Preop: median 14 (9–18), 6 weeks: 6 (5–14), 36 months: 8 (6–12) 38% repeat injection after first injection at a median of 12 months (4–16 months). 15% required an additional injection at a median of 18 months (14–20 months) from first injection.	None	4

(Continued)

TABLE 1 | Continued

Reference	Study design	No. of patients	Age	Sex (M:F)	Patient characteristics	Material used	Follow-up (months)	Outcome	Complications	LofE
SPHINCTER REPAIR										
Zutshi et al. (18)	Case Control (age matched)	10 Permacol® + 10 OSR	Group 1: 61.6 (46.7–76.3). Group 2: 64.7 (43.7–72.6)	0:10	Fecal incontinence (moderate to severe) with sphincter defect	Group 1: OSR with Permacol® Group 2: traditional OSR	Group 1: 12.6 (8.8–22.7) Group 2: 17 (9.6–34.4)	Group 1: FISI preop: 33.5 (21–46) Postop:14 (0–43) $P = 0.02$ CCFIS preop: 15 (11–18) Postop:10 (0–17) $P = 0.005$ FIQL improved in coping/behavior, $P = 0.02$, and embarrassment, $P = 0.01$ Patient satisfaction with procedure: group 1 = 80% vs. Group 2 = 40%	None	4
Zutshi et al. (19)	Case series	13	68.6 (59–79)	NS	Fecal incontinence with anal sphincter defect	Anal encirclement with sphincter repair Surgisis™	16.3 (6–24) mean	Mean anal resting pressure Preop: 33.23 (20–60.75) mmHg Mean squeeze pressure: 70.09 (46.75–99) mmHg Preop: FISI Preop: 39.22 (±16.1). Postop: 9.66 (±1.9) Wexner Preop:18.33 (±5.04). Postop: 7.5 (±4.94) Decrease of incontinence episodes from 8 to 10/week to 1/week	None	4

FISI, Fecal Incontinence Severity Index; CCFIS, Cleveland Clinic Fecal Incontinence Score; FIQL, Fecal Incontinence Quality of Life scale; NS, not specified.

The most common surgical procedure performed for the direct repair of an anatomic sphincter defect for FI is an overlapping sphincter repair (OSR) (4). Repairing the ends of the sphincter in an "overlapping" fashion has been shown to have slightly better results in comparison to a direct end-to-end repair (4). OSR is ideal for an isolated single defect (often obstetric trauma related) and bulking is reported ideal for a reduced hemorrhoidal cushion: anal canal ratio (5, 6). An anal encirclement, usually referred to as a Thiersch procedure, is the insertion of a prosthesis around the anal sphincter, thus narrowing the anal opening and is performed in patients with rectal prolapse who have high operative risk and/or extreme old age (7). Originally carried out using a silver wire, but due to ulcers and other complications, newer sutures are used including nylon, Dacron, Silastic, Teflon, and silicon rubber materials have been described.

Passive FI results in fecal leakage and is more likely to be due to internal sphincter damage (8). This can occur during childbirth or as a complication from anal surgery, particularly following a lateral sphincterotomy or hemorrhoidectomy (9–11).

Injecting bulking agents into the anal sphincter complex is a relatively new modality for patients with passive FI or mild–moderate incontinence (2). It is proposed that the bulking agents act to augment the anal cushions, thus providing an improved seal and therefore increasing the anal zone pressure (12). Furthermore, bulking agents are believed to improve anal canal symmetry and again, improve anal canal sealing (12). Neuromodulation techniques have recently become the reference standard for FI, but concerns persist regarding long-term effectiveness, costs, and complications arising from implanted devices. Sacral nerve stimulation has been used increasingly for FI in patients with external anal sphincter defects, but it is invasive and expensive (13).

The aim of this review is to provide an overview of the biological materials that have been used to augment an overlapping sphincter repair and as a bulking agent (14).

METHODS

A systematic search of PubMed was conducted using the search terms "*anal bulking agents," "anal sphincter repair" or "overlapping sphincter repair*." Titles, abstracts, and finally full texts were analyzed for studies reporting on the use of biological mesh. Inclusion criteria were studies that utilized biological material for either sphincter repair or as a bulking agent. Studies were excluded if only synthetic material was used. Furthermore, studies on patients under the age of 18 were excluded as well as non-English language studies, technical tips or duplicates series from the same research group. Overall, the search yielded five studies for analysis after the exclusion of review articles. The study characteristics are presented (**Table 1**).

RESULTS

Anal Bulking

There were three studies (a case series of 100 patients, a case series with 17 patients and an RCT pilot study with 10 patients)

(15–17) where patients underwent anal bulking. Of these, 122 patients received a biological material as a bulking agent. Overall, 105 patients received additionally cross-linked porcine dermal collagen paste (Permacol™) and a further 17 received Glutaraldehyde cross-linked (GAX) collagen, a highly purified bovine dermal collagen. Anorectal physiology was carried out in only 27 patients and demonstrated deterioration in maximum resting pressure, and no significant change in maximum squeeze increment.

St Mark's incontinence score was used in the RCT of 10 patients and demonstrated an improvement at 6 weeks, but deteriorated at 6-month follow up (17). The SF-36 quality of life scale showed a significant improvement in the role of a physical score from 29 to 100 after the injections. Similarly the Cleveland Clinic Florida Incontinence Score (CCFIS) was used in the second study on 100 patients and demonstrated an improvement in scores at 6 weeks and 6 months, but this had deteriorated at 12-month follow up (15). Another study carried out anorectal physiology in 17 patients but did not use any scoring system (16). There were no complications reported in any of the studies.

Sphincter Repair

One study with 10 patients used an additionally cross-linked porcine dermal collagen (Permacol™) to augment an OSR (18). A traditional OSR dissection was carried out and the Permacol™ implant sutured to the under surface of the two muscle arms. Another study with 13 patients used porcine intestinal submucosa (Surgisis©) to carry out an anal encirclement procedure (19). A tunnel was created around the anal canal through which the Surgisis©graft was passed through and tightened. Validated incontinence scores such as the Fecal Incontinence Severity Index (FISI), Wexner, CCFIS and Fecal Incontinence Quality of Life (FIQL) have been used to assess outcome. Improvements in FISI, CCFIS and two sub scales of FIQL (coping/behavior and embarrassment) were observed in the group of patients undergoing OSR (18). Furthermore, the FISI, Wexner score and all components of FIQL score (lifestyle, coping/behavior, depression and embarrassment) showed an improvement following anal encirclement using biological material (19). Incontinence episodes decreased to an average of one per week from 8 to 10 preoperatively and there were no complications reported.

DISCUSSION/SUMMARY

There are many different methods to improve symptoms of FI and despite limited evidence; they have been adopted to varying degrees. Agents such as autologous fat were first injected into the anal canal to create bulk and resistance in 1995 (20). Since then, other agents have been injected into the anal canal including polytetrafluoroethylene, carbon-coated zirconium oxide beads (Durasphere) and dextranomer microspheres in non-animal stabilized hyaluronic acid gel (NASHA) hydrogel cross-linked with polyacrylamide to name but a few (21) biologic materials are relatively new in comparison and their use is becoming more widespread. However, as the literature search above demonstrates, the evidence advocating their use is limited. There is only one pilot study for a controlled trial that randomized five patients to receive a biological injectable agent and five to receive a synthetic injectable agent (17) and the remainder are small case series of low level evidence. Short-term outcomes are promising and show some improvement in incontinence scores, but only half the studies used patient reported outcomes in the form of the FIQL scale. With regards to anal bulking with biologic material; there is an initial improvement but this improvement does not appear to be sustained at 12-month follow up. It was postulated that the operative technique may play an important role as biological agents injected sub mucosally, proximal to the dentate line, had better outcomes than agents injected via the trans-sphincteric route (22). Long-term follow up data is required in the form of prospective controlled trials. Outcomes are poor in comparison to NASHA DX, which has high quality RCT evidence to support its use. Anal bulking may offer some improvement to a select subgroup of patients, but NASHA DX should be the agent of choice. The use of biologics, especially given the cost, cannot be justified.

Anal encirclement with a prosthetic sling of silicone, which aims to reinforce the repair and the damaged external anal sphincter muscle has been demonstrated to have similar outcomes to alternative surgical procedures, although a high risk of breakage and fecal impaction (23, 24). Only one study was identified using biological material for anal encirclement and did not report any complications. In the small group analyzed, patients benefited from augmentation of the external anal sphincter, but long-term follow up is required to determine if this benefit is sustained (19).

Finally, OSR using biological tissue does not appear add morbidity. Sphincter augmentation has been in significant improvement in continence and quality of life scores (QoLs) compared with the preoperative scores in the short term over traditional repair (18). Long-term studies are necessary to determine if this effect is sustained.

AUTHOR NOTE

The data in this paper has, in part, been presented as a poster at the following meeting: Digestive Disorders Federation, ExCel London, June 2015.

REFERENCES

1. National Institute for Health and Clinical Excellence. *Faecal Incontinence: The Management of Faecal Incontinence in Adults*. National Institute for Health and Clinical Excellence (2007). Available from: https://www.nice.org.uk/guidance/cg49
2. Maeda Y, Laurberg S, Norton C. Perianal injectable bulking agents as treatment for faecal incontinence in adults. *Cochrane Database Syst Rev* (2010) **12**(5):CD007959. doi:10.1002/14651858.CD007959.pub2
3. Kamm MA. Faecal incontinence. *BMJ* (2003) **327**(7427):1299–300. doi:10.1136/bmj.327.7427.1299
4. Tjandra JJ, Han WR, Goh J, Carey M, Dwyer P. Direct repair vs. overlapping sphincter repair: a randomized, controlled trial. *Dis Colon Rectum* (2003) **46**(7):937–42. doi:10.1007/s10350-004-6689-8
5. Thekkinkattil DK, Dunham RJ, O'Herlihy S, Finan PJ, Sagar PM, Burke DA. Measurement of anal cushions in continent women. *Colorectal Dis* (2011) **13**(9):1040–3. doi10.1111/j.1463-1318.2010.02316.x

6. Thekkinkattil DK, Dunham RJ, O'Herlihy S, Finan PJ, Sagar PM, Burke DA. Measurement of anal cushions in idiopathic faecal incontinence. *Br J Surg* (2009) **96**(6):680–4. doi:10.1002/bjs.6597
7. Thiersch C. Carl Thiersch 1822–1895. Concerning prolapse of the rectum with special emphasis on the operation by Thiersch. *Dis Colon Rectum* (1988) **31**:154–5.
8. Kenefick NJ, Vaizey CJ, Malouf AJ, Norton CS, Marshall M, Kamm MA. Injectable silicone biomaterial for faecal incontinence due to internal anal sphincter dysfunction. *Gut* (2002) **51**(2):225–8. doi:10.1136/gut.51.2.225
9. Sultan AH, Kamm MA, Hudson CN, Thomas JM, Bartram CI. Anal-sphincter disruption during vaginal delivery. *N Engl J Med* (1993) **329**(26):1905–11. doi:10.1056/NEJM199312233292601
10. Chaliha C, Sultan AH, Bland JM, Monga AK, Stanton SL. Anal function: effect of pregnancy and delivery. *Am J Obstet Gynecol* (2001) **185**(2):427–32. doi:10.1067/mob.2001.115997
11. Sultan AH, Kamm MA, Nicholls RJ, Bartram CI. Prospective study of the extent of internal anal sphincter division during lateral sphincterotomy. *Dis Colon Rectum* (1994) **37**(10):1031–3. doi:10.1007/BF02049319
12. Ahmad M, McCallum IJ, Mercer-Jones M. Management of faecal incontinence in adults. *BMJ* (2010) **340**:c2964. doi:10.1136/bmj.c2964
13. Hull T, Giese C, Wexner SD, Mellgren A, Devroede G, Madoff RD, et al. Long-term durability of sacral nerve stimulation therapy for chronic fecal incontinence. *Dis Colon Rectum* (2013) **56**(2):234–45. doi:10.1097/DCR.0b013e318276b24c
14. Hussain ZI, Lim M, Stojkovic SG. Systematic review of perianal implants in the treatment of faecal incontinence. *Br J Surg* (2011) **98**(11):1526–36. doi:10.1002/bjs.7645
15. Maslekar S, Smith K, Harji D, Griffiths B, Sagar PM. Injectable collagen for the treatment of fecal incontinence: long-term results. *Dis Colon Rectum* (2013) **56**(3):354–9. doi:10.1097/DCR.0b013e3182805276
16. Kumar D, Benson MJ, Bland JE. Glutaraldehyde cross-linked collagen in the treatment of faecal incontinence. *Br J Surg* (1998) **85**(7):978–9. doi:10.1046/j.1365-2168.1998.00751.x
17. Maeda Y, Vaizey CJ, Kamm MA. Pilot study of two new injectable bulking agents for the treatment of faecal incontinence. *Colorectal Dis* (2008) **10**(3):268–72. doi:10.1111/j.1463-1318.2007.01318.x
18. Zutshi M, Ferreira P, Hull T, Gurland B. Biological implants in sphincter augmentation offer a good short-term outcome after a sphincter repair. *Colorectal Dis* (2012) **14**(7):866–71. doi:10.1111/j.1463-1318.2011.02808.x
19. Zutshi M, Hull T, Gurland B. Anal encirclement with sphincter repair (AESR procedure) using a biological graft for anal sphincter damage involving the entire circumference. *Colorectal Dis* (2012) **14**(5):592–5. doi:10.1111/j.1463-1318.2011.02675.x
20. Shafik A. Perianal injection of autologous fat for treatment of sphincteric incontinence. *Dis Colon Rectum* (1995) **38**(6):583–7. doi:10.1007/BF02054115
21. Watson NF, Koshy A, Sagar PM. Anal bulking agents for faecal incontinence. *Colorectal Dis* (2012) **14**(Suppl 3):29–33. doi:10.1111/codi.12047
22. Smart N, Mercer-Jones M. Response to Y. Maeda, C. J. Vaizey & M. A. Kamm. Pilot study of two new injectable bulking agents for the treatment of faecal incontinence. *Colorectal Dis* (2008) **10**(6):628. doi:10.1111/j.1463-1318.2008.01475.x
23. Devesa JM, Hervás PL, Vicente R, Rey A, Die J, Moreno I, et al. Anal encirclement with a simple prosthetic sling for faecal incontinence. *Tech Coloproctol* (2011) **15**(1):17–22. doi:10.1007/s10151-010-0673-1
24. Sainio AP, Halme LE, Husa AI. Anal encirclement with polypropylene mesh for rectal prolapse and incontinence. *Dis Colon Rectum* (1991) **34**(10):905–8. doi:10.1007/BF02049706

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

APPENDIX

BioMESH STUDY GROUP

Ferdinand Köckerling (Chairman), Stavros Antoniou, René Fortelny, Frank A. Granderath, Markus Heiss, Franz Mayer, Marc Miserez, Agneta Montgomery, Salvador Morales-Conde, Filip Muysoms, Alexander Petter-Puchner, Rudolph Pointner, Neil Smart, Marciej Smietanski, and Bernd Stechemesser.

AIM

The BioMesh Study Group has set itself the task of identifying how best to use biological meshes for the various indications. The first step toward achieving that goal is to compile systematic reviews of the different indications on the basis of the existing literature. The available literature sources will be evaluated in accordance with the Oxford Centre for Evidence-based Medicine-Levels of Evidence (March 2009). Next, based on the review findings, corresponding Statements and Recommendations are to be formulated in a Consensus Conference for the use of biological meshes for the different indications. The findings of the Consensus Conference are then to be summarized for a joint publication. This present publication is part of the project undertaken by the BioMesh Study Group.

frontiers in Surgery

REVIEW
published: 22 October 2015
doi: 10.3389/fsurg.2015.00053

Prevention of a parastomal hernia by biological mesh reinforcement

René H. Fortelny[1], Anna Hofmann[1], Christopher May[1], Ferdinand Köckerling[2] and BioMesh Study Group[†]*

[1] Department of General, Visceral and Oncological Surgery, Wilhelminenspital, Vienna, Austria, [2] Department of Surgery and Center for Minimally Invasive Surgery, Vivantes Hospital, Berlin, Germany

Introduction: In the field of hernia prevention, the prophylactic mesh-reinforcement of stoma-sites is one of the most controversially discussed issues. The incidence of parastomal hernias in the literature reported to be up to 48.1% after end colostomy and up to 30.8% after loop of colostomy, but still remains uncertain due to diagnostic variety of clinical or radiological methods, heterogeneous patient groups and variable follow-up intervals. Anyway, the published data regarding the use of synthetic or bio-prostethic meshes in the prevention of parastomal hernia at the primary operation are very scarce.

Methods: A literature search of the Medline database in terms of biological prophylactic mesh implantation in stoma creation identified six systematic reviews, two randomized controlled trials (RCT), two case-controlled studies, and one technical report.

Results: In a systematic review focusing on the prevention of parastomal hernia including only RCTs encompassing one RCT using bio-prosthetic mesh the incidence of herniation was 12.5% compared to 53% in the control group ($p < 0.0001$). In one RCT and two case-control studies, respectively, there was a significant smaller incidence of parastomal herniation as well as a similar complication rate compared to the control group. Only in one RCT, no significant difference regarding the incidence of parastomal hernia was reported with comparable complication rates.

Conclusion: Thus, so far two RCT and two case-control studies are published with prophylactic bio-prosthetic reinforcement in stoma sites. The majority revealed significant better results in terms of parastomal herniation and without any mesh-related complications in comparison to the non mesh group. Further, multicenter RCT are required to achieve a sufficient level of recommendation.

Keywords: parastomal hernia, parastomal hernia repair, parastomal hernia prevention, biologic mesh, bio mesh, bio-prostethic mesh

OPEN ACCESS

Edited by:
Vincenzo Neri, University of Foggia, Italy

Reviewed by:
Michael Ardelt, University Hospital Jena, Germany
Walter Brunner, Kantonsspital St. Gallen, Switzerland

****Correspondence:***
René H. Fortelny
rene.fortelny@wienkav.at

[†]Members of the BioMesh Study Group are listed in the Appendix.

Specialty section:
This article was submitted to Visceral Surgery, a section of the journal Frontiers in Surgery

Received: *29 July 2015*
Accepted: *30 September 2015*
Published: *22 October 2015*

Citation:
Fortelny RH, Hofmann A, May C, Köckerling F and Biomesh Study Group (2015) Prevention of a parastomal hernia by biological mesh reinforcement. Front. Surg. 2:53. doi: 10.3389/fsurg.2015.00053

INTRODUCTION

The BioMesh Study Group has set itself the task of identifying the best way to use biological meshes for various indications. The first step toward achieving that goal is to compile systematic reviews of the different indications on the basis of the existing literature. The available literature sources will be evaluated in accordance with the Oxford Centre for Evidence-based Medicine-Levels of Evidence (March 2009). Next, based on the review findings, corresponding Statements and Recommendations are to be formulated in a Consensus Conference for the use of biological meshes for the different

indications. The findings of the Consensus Conference are then to be summarized for a joint publication. This present publication is part of the project undertaken by the BioMesh Study Group.

In the field of hernia prevention, the prophylactic mesh-reinforcement of stoma-sites is one of the most controversially discussed issues. The exact incidence of parastomal hernias remains uncertain due to diagnostic variety of clinical or radiological methods like ultrasound and computed tomography, heterogeneous patient groups, and variable follow-up intervals (1). Based on a meta-analysis by Carne et al. (2), the incidence for parastomal hernia ranges from 1.8 to 28.3% for end ileostomies and 0–6.2% for loop ileostomies. In case of end colostomy, the hernia rates are reported as 4.0–48.1% and in case of loop colostomy, the hernia rates are 0–30.8% after 10-year follow up. In a life time analysis of stomal complications such as bulge, abdominal discomfort, abdominal pain, constipation, incarceration, ileus, and parastomal herniation following colostomy can be occur in a time frame of up to 20 years postoperatively (3). It seems that one of the most successful prevention of stoma site hernias is the use of a prophylactic mesh. The risk of colostomy herniation seems to be doubled in comparison to an ileostomy. The relation of a larger diameter of the trephine to the abdominal wall defect in case of colostomy creation might be the main reason. There are different surgical options for parastomal hernia repair. In the current review of Aquina et al. (4) the cumulative recurrence rates in the literature for open surgery are reported to be 67.6% after suture repair, 18.2%, after mesh only repair and 9.6% after retromuscular mesh repair. For laparoscopic surgery recurrence rates were 30% after mesh repair by keyhole technique, 8.1% by Sugarbaker technique and 2.1% after sandwich technique respectively. In another review concerning the use of biologic grafts for parastomal hernia repair by Slater et al. (5), four retrospective studies (combined enrollment of 57 patients) obtained a cumulative recurrence rate 15.7% [95% confidence interval (CI) 7.8–25.9] and wound-related complications in 26.2% (95% CI 14.7–39.5). No mortality or graft infections were reported.

But anyhow following questions still remain: first, the selection of mesh type and location at the primary operation for the prevention of hernia development and second is there any indication for the use of bio mesh in a clean contaminated field.

METHODS

A literature search of the Medline database using the PubMed search engine, using the keywords (parastomal hernia OR parastomal hernia repair OR parastomal hernia prevention AND biologic mesh AND biomesh AND bio mesh) returned 236 hits up to June 2015. Titles and abstracts were scrutinized on the use of prophylactic biologic mesh reinforcement of the stoma site at the primary operation. The full text of 25 articles was assessed and 11 relevant papers were identified including six systematic reviews (4, 6–10), two randomized controlled studies (RCT) (11, 12), two case-controlled studies (13, 14), and one technical report (14). A summary of study characteristics and outcomes is presented in **Table 1**. Qualitative assessment of all included studies was performed using the Oxford Centre for Evidence-Based Medicine 2009 levels of evidence.

TABLE 1 | Studies of prevention of parastomal hernia.

Author	Study design	Patient (*n*) (mesh vs. control)	Mean age/BMI (mesh vs. control)	Stoma type	Mesh type	Mesh size/mesh position	Fixation	Follow up in month (mesh vs. control)	Herniation (mesh vs. control)	Infection (mesh vs. control)	LoE
Williams et al. (14)	Pilot CS	33 (22 vs. 11)	49 vs. 59 33 vs. 29	Ileostomy, colostomy	Permacol	7 cm diameter onlay	sutures	18 (10–24) vs. 9 (4–25)	3 vs. 8	0	2b
Fleshman et al. (12)	Multicenter RCT	113 (55 vs. 58)	60.25 vs. 59.1 26.6 vs. 24.7	Ileostomy, colostomy	Strattice	4.8 cm × 4.8 cm sublay	No	24	6 vs. 7	3 vs. 2	1b
Figel et al. (13)	Retrospective CS	16 (no controls)	63.1 11 patients > 30	End stoma	Surgisis EXL	13 cm × 22 cm sugarbaker (75%) and keyhole (25%)	NR	38 (24–53)	0	NR	3b
Hammond et al. (11)	RCT	20 (10 vs. 10)	42.6 vs. 50 26.3 vs. 26.3	Defunctioning loop stoma	Permacol	10 cm × 10 cm pre-peritoneal	sutures	12	0 vs. 3	0	1b

n, number; CS, Case-controlled study; RCT, Randomized Controlled Trial; LoE, Level of Evidence; Permacol, porcine-derived, cross-linked acellular dermal matrix; Strattice, porcine-derived, non-cross-linked acellular dermal matrix; Surgisis EXL, porcine-derived, non-cross-linked submucosa matrix; NR, no report.

RESULTS

The reviews of Aquina et al., Hotouras et al., Shabbir et al., Sajid et al., Wijeyekoon et al., and Tam et al. (4, 6–10) all focused on parastomal hernia prevention by the placement of a mesh (synthetic and biological) at the primary operation. Aquina et al. (4) reported a cumulative incidence of parastomal hernia rate of 10.7% including the RCT of Hammond et al. (11) using a biologic mesh (Permacol). In the systematic review of Shabbir et al. (7), three RCT [Hammond et al., Jänis et al., and Serra-Aracil et al. (11, 15, 16)] were enclosed. The analysis of the three RCT comprising a total of 128 patients (64 with mesh, 64 without mesh) revealed a hernia incidence of 12.5% compared to 53% in the control group [risk ratio, 95%, CI, 0.25 (0.13, 0.48), $p < 0.0001$] in a follow up period of 7–83 months. Two of the studies (11, 16) used clinical and radiological examinations. Concerning mesh-related morbidity, no difference was detected. The systematic review of Sajid et al., Wijeyekoon et al., and Tam et al. (7–9) all including the same RCT (11, 15, 16) obtained identical results.

In 2008, the first RCT focusing on the use of biological mesh for parastomal hernia prevention was published by Hammond et al. (11). Twenty patients undergoing a defunctioning stoma operation were randomized to an interventional group with reinforcement by porcine-derived, acellular dermal sheet, cross-linked acellular dermal sheet (Permacol, Tissue science laboratories, Aldershot, Hants, UK) or a conventional group without mesh. The trephine of the abdominal wall including the rectus sheath was defined by 2 cm × 2 cm. The biological mesh measuring 10 cm × 10 cm was supplied with a center keyhole of 2 cm and positioned between posterior layer of the rectus sheath and the peritoneal membrane – described as pre-peritoneal position and fixated by interrupted 3/0 prolene sutures to the rectus sheath by an inner and outer suturing at four positions.

The patient controls were performed at the time of stoma reversal or in cases of non-stoma reversal, at 12 months. At a median follow up of 6.5 months, three patients suffered from a parastomal hernia in the control group and no patient in the treatment group. Stoma site ultrasound assessment was performed in 7 of 10 patients in the treatment group and 9 of 10 in the control group. There were no detected differences concerning the infection signs or other complications. The shortcomings of this randomized controlled phase 1 study are the low number of patients enrolled, the short follow-up period and an unexpected very high percentage of stoma site hernias in the control group in comparison to the published literature (2).

The second study selected in this review published in 2012 is a retrospective case-control study by Figel et al. (13). A biologic mesh derived from porcine submucosa (Surgisis EXL, Cook Surgical, Bloomington, IN, USA) and non-cross-linked with a size of 13 cm × 22 cm was placed at the time of creation of an intestinal end stoma in a Sugarbaker position (12 patients) and in keyhole-technique (four patients). Sixteen patients were enrolled. No mesh related complications and no parastomal hernias were detected in a median follow-up of 38 months. This study confirmed the safety, efficacy, and cost-effectiveness, respectively, of prophylactic bio-prosthetic mesh reinforcement at the time-point of permanent stoma creation.

In the year 2014, another prospective, multicenter, randomized, controlled, double-blinded study of non-cross-linked porcine acellular dermal matrix (PADM; Strattice, LifeCell Corporation, Branchburg, NJ) in patients undergoing elective surgery for permanent end stoma (71 colostomies, 42 ileostomies) was published by Fleshman et al. (12). Fifty-five patients were treated with the use of PADM in a size of 6 cm × 6 cm or 8 cm × 8 cm (median size after trimming 4.8 cm × 4.8 cm) with a cruciate incision of 2 cm for the bowel passage (incision was enlarged in 78.2%) in a retro-muscular sublay position using no fixation. The control group consisted of 58 patients without mesh reinforcement. Intraoperative complications, blood loss, and quality of life-scores were without significant differences in either group. The postoperative investigations were performed by a blinded assessor and an abdominal CT (11 patients) was followed in case of suspected herniation at the stoma site. The incidence of parastomal hernias in a follow up of 24 months was 12.2% in the PADM-group and 13.2% in the controls without significant difference. The ostomy circumference in the PADM group was significant larger (6.4 ± 3.9 vs. 4.8 ± 2.9 cm; $p = 0.002$) compared to the control group, which may be a predisposition for the development of a parastomal hernia and represents a potential bias of the study. In a letter to the editor, Hontouras (17) discussed the important role and risk of oversized stoma aperture for the development of a hernia. Based on the study of Pilgrim et al. (18), a stoma aperture >35 mm is an independent risk factor for hernia development – increasing by 10% for every millimeter increase in size. In summary, the RCT of Fleshmann et al. confirms the safety of prophylactic biological reinforcement. However, based on the results of parastomal hernia incidence in comparison to the control group, no recommendation for the use of bio-prosthesis can be given.

Recently published in 2015, Williams et al. (14) reported a case-controlled pilot study based on a stapled mesh stoma reinforcement technique (SMART), which was already introduced in 2011 (19). A special designed circular stapler gun (Compact™, Frankemann International Limited) was used in combination with a porcine-derived cross-linked acellular dermal sheet (Permacol™, Covidien plc, 20 Lower Hatch St, Dublin 2, Ireland), which is configured in a circular design with a diameter of 7 cm. After excising, a cylinder of abdominal wall and subcutaneous fat a cruciate incision of the rectus sheath is performed. The knife diameter used (17, 21, or 24 mm) is dependent on the diameter of the bowel used to be traverse the stoma trephine. The shaft of the anvil is delivered through the posterior rectus sheath and mated with the trocar of the circular stapling device after preloading with the mesh. The circular stapling device is closed, fired, and removed, encompassing a disc of mesh, posterior rectus sheath and peritoneum and leaving a precise reinforced stapled trephine. Finally, the outer mesh circumference is sutured to the anterior rectus sheath. Twentytwo patients were included and received stoma formation with SMART-technique and another 11 were assigned to the control group without reinforcement of the stoma site (18 open: 4 laparoscopic; 11 ileostomies: 11 colostomies). All SMART stomas were fashioned using a circular stapler with a 24-mm knife diameter. Patients with either complications from a pre-existing

stoma ($n = 15$) – large parastomal hernia unsuitable for local repair ($n = 6$) or recurrent herniation as a result of previous repair ($n = 9$) or underlying conditions ($n = 7$) – such as obesity, asthma, corticosteroid use, collagen disorder or combination of these respectively underwent a resiting SMART-procedure at the index operation.

There were no intraoperative or early stoma complications. Recurrent parastomal herniation was diagnosed in four patients (19%) of the SMART group, which was significantly lower ($p = 0.003$) in comparison to 8 patients (73%) in the control group. Designed as a pilot study, there are some basic limitations, such as missing randomization, heterogeneity of patients and short follow up. But this new technique could be promising in high risk patients and the results of an ongoing randomized trial (ISRCTN 94943190) in this technique should be give us more detailed information and conclusions.

Another ongoing multicenter RCT from France (Centre Hospitalier Universitaire, Amiens) comparing prophylactic biological mesh vs. no mesh in colorectal surgery with colostomy ("Prospective, Multicenter, Randomized, Parallel Group Clinical Study Evaluating the Efficacy of a Biological Mesh (Strattice™) for the Prevention of Parastomal Hernia After Colorectal Surgery With Colostomy," NCT02121743), should be completed by April 2016.

DISCUSSION/SUMMARY

The current literature supports the significant risk reduction of parastomal hernia development by mesh reinforcement of the permanent stoma at the primary operation. Based on the published literature, the prophylactic mesh application is not associated with a significant increase of mesh-specific complications and comorbidities such as seroma, infection and migration. Concerning the choice of mesh, synthetic or biologic prosthesis, there are only four level 1 b studies – two with the use of synthetic meshes in retro-muscular position (15, 16) as well as two with biologic mesh reinforcement in sublay position (11, 12). The best option of mesh placement – onlay, sublay, or intraperitoneal – keyhole, sugarbaker, sandwich, or by a 3D funnel mesh type (20) – remains unclear and has to be compared in further RCT. In summary, so far now only two RCT (11, 12) and two case-control studies with prophylactic biomesh reinforcement in stoma sites are published. Both studies have to be looked at very critically due to limitations [too small numbers of patients and short follow up (11)] and a heterogeneity of patients regarding the different trephine sizes to the abdominal wall (12). However, in both RCT as well in the two case-control studies (13, 14), no bio-mesh related complication was observed. The discussion addressing the topic of crosslinking vs. non-crosslinking in terms of susceptibility to infection and failure of remodeling (bulging) in this special indication remains unclear, since we do not have any late term results and both studies used different bio-prosthesis (Permacol™, Surgisis™).

Nevertheless, we have to consider that only 50% of patients will develop a parastomal hernia by using non-mesh techniques and there is a risk of overtreatment if all patients receive a prophylactic mesh. So, it is mandatory to investigate which patients are at a significant risk of developing a parastomal hernia. In conclusion, it seems to be beneficial to place a mesh at the primary operation when performing a permanent stoma based on the available literature, which describes no increase of complications, easy performance, and cost-effectiveness (13).

In summary, based on the data available, the prophylactic placement of mesh at the index operation associated with stoma creation needs scientific attention in the near future.

The remaining questions concerning the choice of mesh material, mesh design, and most favorable anatomical location for the mesh have to be answered by additional well-designed prospective multicenter studies.

REFERENCES

1. Carne PW, Frye JN, Robertson GM, Frizelle FA. Parastomal hernia following minimally invasive stoma formation. *ANZ J Surg* (2003) **73**:843–5. doi:10.1046/j.1445-2197.2003.02779.x
2. Carne PW, Robertson GM, Frizelle FA. Parastomal hernia. *Br J Surg* (2003) **90**:784–93. doi:10.1002/bjs.4220
3. Londono-Schimmer EE, Leong AP, Phillips RK. Life table analysis of stomal complications following colostomy. *Dis Colon Rectum* (1994) **37**:916–20. doi:10.1007/BF02052598
4. Aquina CT, Iannuzzi JC, Probst CP, Kelly KN, Noyes K, Fleming FJ, et al. Parastomal hernia: a growing problem with new solutions. *Dig Surg* (2014) **31**(4–5):366–76. doi:10.1159/000369279
5. Slater NJ, Hansson BM, Buyne OR, Hendriks T, Bleichrodt RP. Repair of parastomal hernias with biologic grafts: a systematic review. *J Gastrointest Surg* (2011) **15**(7):1252–8. doi:10.1007/s11605-011-1435-8
6. Hotouras A, Murphy J, Thaha M, Chan CL. The persistent challenge of parastomal herniation: a review of the literature and future developments. *Colorectal Dis* (2013) **15**(5):e202–14. doi:10.1111/codi.12156
7. Shabbir J, Chaudhary BN, Dawson R. A systematic review on the use of prophylactic mesh during primary stoma formation to prevent parastomal hernia formation. *Colorectal Dis* (2012) **14**:931–6. doi:10.1111/j.1463-1318.2011.02835.x
8. Sajid MS, Kalra L, Hutson K, Sains P. Parastomal hernia as a consequence of colorectal cancer resections can prophylactically be controlled by mesh insertion at the time of primary surgery: a literature based systematic review of published trials. *Minerva Chir* (2012) **67**(4):289–96.
9. Wijeyekoon SP, Gurusamy K, El-Gendy K, Chan CL. Prevention of parastomal herniation with biologic-composite prosthetic mesh – a systematic review and meta-analysis of randomized controlled trials. *J Am Coll Surg* (2010) **211**(5):637–45. doi:10.1016/j.jamcollsurg.2010.06.111
10. Tam KW, Wei PL, Kuo LJ, Wu CH. Systematic review of the use of a mesh to prevent parastomal hernia. *World J Surg* (2010) **34**(11):2723–9. doi:10.1007/s00268-010-0739-2
11. Hammond TM, Huang A, Prosser K, Frye JN, Williams NS. Parastomal hernia prevention using a novel collagen implant: a randomised controlled phase 1 study. *Hernia* (2008) **12**(5):475–81. doi:10.1007/s10029-008-0383-z
12. Fleshman JW, Beck DE, Hyman N, Wexner SD, Bauer J, George V, et al. A prospective, multicenter, randomized, controlled study of non-cross-linked porcine acellular dermal matrix fascial sublay for parastomal reinforcement in patients undergoing surgery for permanent abdominal wall ostomies. *Dis Colon Rectum* (2014) **57**(5):623–31. doi:10.1097/DCR.0000000000000106
13. Figel NA, Rostas JW, Ellis CN. Outcomes using a bioprosthetic mesh at the time of permanent stoma creation in preventing a parastomal hernia: a value analysis. *Am J Surg* (2012) **203**(3):323–6. doi:10.1016/j.amjsurg.2011.10.006
14. Williams NS, Hotouras A, Bhan C, Murphy J, Chan CL. A case-controlled pilot study assessing the safety and efficacy of the Stapled Mesh stomA Reinforcement Technique (SMART) in reducing the incidence of parastomal herniation. *Hernia* (2015). doi:10.1007/s10029-015-1346-9

15. Jänes A, Cengiz Y, Israelsson LA. Preventing parastomal hernia with a prosthetic mesh: a 5-year follow-up of a randomized study. *World J Surg* (2009) **33**(1):118–21. doi:10.1007/s00268-008-9785-4
16. Serra-Aracil X, Bombardo-Junca J, Moreno-Matias J, Darnell A, Mora-Lopez L, Alcantara-Moral M, et al. Randomized, controlled, prospective trial of the use of a mesh to prevent parastomal hernia. *Ann Surg* (2009) **249**(4):583–7. doi:10.1097/SLA.0b013e31819ec809
17. Hotouras A, Bhan C, Murphy J, Chan CL, Williams NS. Parastomal hernia prevention – is it all about mesh reinforcement? *Dis Colon Rectum* (2014) **57**(12):e443–4. doi:10.1097/DCR.0000000000000255
18. Pilgrim CH, McIntyre R, Bailey M. Prospective audit of parastomal hernia: prevalence and associated comorbidities. *Dis Colon Rectum* (2010) **53**:71–6. doi:10.1007/DCR.0b013e3181bdee8c
19. Williams NS, Nair R, Bhan C. Stapled mesh stoma reinforcement technique (SMART). A procedure to prevent parastomal herniation. *Ann R Coll Surg Engl* (2011) **93**:169. doi:10.1308/003588411X12851639107313d
20. Köhler G, Hofmann A, Lechner M, Mayer F, Wundsam H, Emmanuel K, et al. Prevention of parastomal hernias with 3D funnel meshes in intraperitoneal onlay position by placement during initial stoma formation. *Hernia* (2015). doi:10.1007/s10029-015-1380-7

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

APPENDIX

BioMesh Study Group:
Ferdinand Köckerling (Chairman), Stavros Antoniou, René H. Fortelny, Frank A. Granderath, Markus Heiss, Franz Mayer, Marc Miserez, Agneta Montgomery, Salvador Morales-Conde, Filip Muysoms, Alexander Petter-Puchner, Rudolph Pointner, Neil Smart, Marciej Smietanski, Bernd Stechemesser.

frontiers in Surgery

REVIEW
published: 05 September 2016
doi: 10.3389/fsurg.2016.00049

Repair of Perineal Hernia Following Abdominoperineal Excision with Biological Mesh: A Systematic Review

*Sunil K. Narang[1], Nasra N. Alam[1], Ferdinand Köckerling[2], Ian R. Daniels[1] and Neil J. Smart[1]**

[1] Exeter Surgical Health Services Research Unit (HeSRU), Royal Devon and Exeter Hospital, Exeter, Devon, UK, [2] Department of Surgery, Center for Minimally Invasive Surgery, Vivantes Hospital, Academic Teaching Hospital of Charité Medical School, Berlin, Germany

Introduction: Perineal hernia (PerH) following abdominoperineal excision (APE) procedure is a recognized complication. PerH was considered an infrequent complication of APE procedure; however, PerH rates of up to 45% have been reported in recent publications following a laparoscopic APE procedure. Various methods of repair of PerH with the use of synthetic meshes or myocutaneous flap have been described, although there is no general agreement on an optimal strategy. The use of biological meshes for different operations is growing in popularity, and these have been promoted as being superior and safer when compared to synthetic meshes. Although the use of biologics is becoming popular claims of better outcomes are largely unsupported by evidence. The aim of this systematic review is to evaluate the currently available evidence supporting the use of biologic or biosynthetic meshes for the repair of PerH that develop following an APE.

Methods: A systematic review of all English language literature relevant to repair of PerH following APE with biologic or biosynthetic mesh published between January 1, 2000 and July 31, 2016 was carried out using MEDLINE, EMBASE, and the Cochrane Library of Systematic Reviews for relevant literature. Searches were performed using a combination of Medical Subject Headings (MeSH) terms and text words "PerH," "APE," "morbidity," "biologics," "biosynthetic," and "hernia." Studies in which the use of biological meshes was not reported were excluded from the review. Various outcome measures, including operative technique, complication rates, recurrence rates, type of mesh, management of recurrences, and risk factors, were extracted. Oxford Centre for Evidence-based Medicine – Levels of Evidence (March 2009) was used to assess the quality of evidence.

Results: The systematic review of the literature identified three case reports, four case series, and one pooled analysis that were included in the final review. Overall, these studies were of poor quality providing level 4 evidence. Various different approaches and techniques of repair of PerH were described; however, it was difficult to extract information with regard to the primary and secondary outcome measures.

OPEN ACCESS

Edited by:
Hakan Kulacoglu, Recep Tayyip Erdoğan University, Turkey

Reviewed by:
Gabriel Sandblom, Karolinska Institutet, Sweden
Ulf Gunnarsson, Umeå University, Sweden
Juan Manuel Suárez-Grau, Riotinto Hospital and Clinic QUIRON Sagrado Corazon, Spain

****Correspondence:***
Neil J. Smart
dmeilsmart@hotmail.com

Specialty section:
This article was submitted to Visceral Surgery, a section of the journal Frontiers in Surgery

Received: *04 July 2016*
Accepted: *22 August 2016*
Published: *05 September 2016*

Citation:
Narang SK, Alam NN, Köckerling F, Daniels IR and Smart NJ (2016) Repair of Perineal Hernia Following Abdominoperineal Excision with Biological Mesh: A Systematic Review. Front. Surg. 3:49. doi: 10.3389/fsurg.2016.00049

Conclusion: There is no general agreement to the optimal operative strategy to repair PerH following an APE. There is insufficient evidence to recommend any specific operative approach or repair technique for PerH following an APE.

Keywords: perineal hernia, abdominoperineal excision, biologic mesh, biosynthetic mesh

INTRODUCTION

The finding of a perineal hernia (PerH) following an abdominoperineal excision (APE) is a recognized complication; however, it is unclear as to how frequently this occurs. Until a few years ago, they were considered to be an infrequent complication following an APE and prevalence rates of 0.6–7% were reported (1–6). However, the surgical management of rectal cancer has evolved over the recent years with the acceptance of the principle of total mesorectal excision (TME) and the recognition of the importance of a clear surgical resection and avoidance of tumor perforation during an APE (7). This procedure has evolved into the extra levator abdominoperineal excision (eLAPE) with the potential surgical resection margin information being identified through MRI staging (7, 8). This has resulted in a reduction in circumferential resection margin involvement and intra-operative perforation of the tumor (9). However, an eLAPE creates a wider defect in the pelvic floor leaving only the ischioanal fat and skin for closure of the defect as the entire pelvic floor muscle complex has been excised surrounding the distal rectum. Perineal herniation in this group of patients is increasingly recognized and a recent publication has reported an overall PerH rate of 26% and this can be as high as 45% in those having a laparoscopic eLAPE procedure (10).

A PerH repair may be necessary as the hernia is not only painful but can also result in urinary dysfunction or bowel obstruction causing impairment of daily activities of living. Various methods or repair have been described in the literature, including primary tissue repair, synthetic mesh, biological mesh, and myocutaneous flaps. This repair can be facilitated by either using an abdominal and/or perineal approach although none of the described repairs are well established.

The use of synthetic meshes is associated with problems, such as mesh infection, chronic inflammation, and foreign body reaction. If bowel is in direct contact with the synthetic mesh used for a PerH repair, then there is a risk of adhesions and erosion into the bowel wall by the mesh. Biologic and biosynthetic meshes were developed to overcome such problems. The role of biologic mesh for primary reconstruction of the pelvic floor after eLAPE has been the subject of a systematic review, and this was considered a promising technique for improving wound healing and complication rates comparable to other techniques (11). Biologic meshes have been used recently as an alternative for repairing PerH following an eLAPE. The biologic mesh acts not only as a structural support for the hernia repair but also as a scaffold allowing the ingrowth of native fibroblasts, which in turn lay down the fibrous tissue and promote tissue remodeling (12). The aim of this systematic review is to evaluate the currently available evidence supporting the use of biologic or biosynthetic meshes for the repair of PerH.

METHODS

Search Strategy

A systematic review of all English language literature relevant to the repair of a PerH following an APE with biologic or biosynthetic mesh published between January 1, 2000 and July 31, 2016 was carried out using MEDLINE (PubMed and Ovid), EMBASE (Ovid), and the Cochrane Library of Systematic Reviews/ Controlled Trials for relevant literature. Searches were performed using a combination of Medical Subject Headings (MeSH) terms and text words "*perineal hernia*," "abdominoperineal excision," "*morbidity*," "*biologics*," "*biosynthetic*," and "*hernia.*" All randomized/non-randomized, controlled/non-controlled clinical trials, prospective observational studies, clinical registry data, retrospective case series, and case reports that reported on repair of PerH following APE were included for analysis. Conference abstracts, letters, technical notes, and commentaries were excluded. In addition, bibliographies from the papers requested were manually checked to identify additional relevant papers.

Study Selection

Titles and abstracts of the identified studies were screened by the main reviewer Sunil K. Narang and independently checked by Nasra N. Alam. Studies that were irrelevant were rejected. The full texts of identified papers were independently assessed by two reviewers (Sunil K. Narang and Nasra N. Alam) to determine whether they met the predetermined inclusion/exclusion criteria. Disagreements were resolved by discussion or adjudication by the senior author (Neil J. Smart).

Inclusion Criteria

All studies should have been published in print or electronic format between 1 January, 2000 and July 31, 2016. Only adult patients undergoing PerH repair following APE were included in the review. An APE may have been performed as an open procedure, laparoscopic, hand-assisted or robot-assisted. PerH repair may have been done using open, laparoscopic, or combined approach. The diagnosis of PerH may have been established based on clinical examination or cross-sectional imaging.

Exclusion Criteria

Studies on the pediatric population or using synthetic mesh or myocutaneous flaps were excluded from this review. Diagnosis of PerH established on the basis of patient-reported symptoms of PerH or telephone or postal follow-up were excluded from the review.

Outcomes

The primary outcome measure of the systematic review was to assess the recurrence of PerH following repair with biologic

or biosynthetic meshes. Other factors, such as time interval to development of PerH and diagnostic definition of PerH (clinical, cross-sectional imaging, patient-reported or telephone interview), were also noted.

The secondary outcome measures recorded were:

1. Complications following repair.
2. Management of recurrences.
3. Patient-reported outcome measures or quality of life scores.

Definitions

Clinically, a PerH is defined as a palpable bulge in the perineum associated with protrusion of intra-abdominal or pelvic viscera through the defect in the pelvic floor fascia and musculature. Radiographic definition of PerH unclear as the landmarks for defining the pelvic floor are not universally agreed.

Quality Assessment

Oxford Centre for Evidence-based Medicine – Levels of Evidence (March 2009) was used to assess the quality of evidence (13).

Data Extraction (Selection and Coding)

Data on the study type, number of patients treated, length of follow-up, cross-sectional imaging, and symptoms from PerH were extracted from the included studies by the reviewers. These data were extracted separately by reviewers (Sunil K. Narang and Nasra N. Alam) to guard against reviewer bias. Any discrepancies were resolved by adjudication by the senior author Neil J. Smart. All data and results of statistical tests were extracted from the papers and entered into an electronic data sheet (Microsoft Excel). For particular outcomes that were to be evaluated, if the data were not specifically reported, they were regarded as not reported or missing and no assumptions were made regarding the missing data.

Statistical Analysis

There was a significant heterogeneity in the included studies in the study design, intervention design, study cohorts, and outcome measures. A weighted analysis of variables for risk factors for PerH development was not possible because of the lack of both uniformity and the quantity of the data reported. For this reason, a meta-analysis of the data could not be performed; therefore, primary and secondary outcome measure parameters are expressed as a range.

RESULTS

A total of 190 potential articles were identified from the initial literature search. After removal of duplicate articles 176 articles remained (**Figure 1**). Using the inclusion criteria described above, 146 articles were eliminated on title and abstract review. Full text articles were obtained for 30 articles out of which 22 articles were rejected, as they did not meet the inclusion criteria. Eight articles were included for final analysis. Out of the eight articles that were included, three were case reports, four were case series, and one article was a pooled analysis. The quality assessment of the included studies is presented in **Tables 1–3**. The level of evidence based on the Oxford Centre for Evidence-based Medicine (March 2009) was 4 at best. The pooled analysis included all publications from 1944 to 2010 and has probably included data from Skipworth et al. (14) and de Campos et al. (15). There was a significant variation among studies in their description of diagnostic method, selection criteria, operative technique, type of mesh used, and duration of follow-up, recurrence rates, complications, and management of recurrences. None of the studies in the review used the Clavien Dindo grading of post-operative complications (16).

In the three case reports, there were no recurrences following repair of PerH on follow-up ranging from 12 to 18 months (11, 13, 14). Of the four case series, the duration of follow-up and final outcome was not reported in one publication (4, 8, 12). In the remaining three case series, different types of cross and non-cross-linked biologic meshes were used and some patients underwent myocutaneous flap repair and/or omentoplasy in addition to the mesh repair.

The operative technique to repair a PerH varied significantly ranging from perineal repair, open abdominal repair, or combined approach with or without the use of laparoscope. The type of biological mesh used was not reported in three studies. Others described the use of additionally cross-linked acellular porcine collagen (Permacol™), non-cross-linked porcine collagen (Strattice™), Human-derived Acellular Dermal graft (DermaMatrix), Dura mater patch, and Bovine pericardium. Complications following repair were not reported in any of the case reports although the pooled analysis reported a perineal wound breakdown rate of 12% with the use of all different types of synthetic and biologic meshes. Management of recurrence of PerH was reported by Musters et al. and four recurrent PerH were repaired using prolene mesh (19). None of the studies used patient-reported outcome measures to assess the impact of surgery on the quality of life of the patients.

DISCUSSION

A PerH is an incisional hernia through the pelvic floor, which results in protrusion of abdominal or pelvic viscera. There is no universally accepted clinical or radiological definition of a PerH. They are typically diagnosed based on symptoms, such as an expansile cough impulse in the perineum, which is not only uncomfortable but can also cause bowel or bladder symptoms. In the majority of cases, this hernia remains asymptomatic and may be incidentally detected on cross-sectional imaging performed for oncologic follow-up. It is vital that there should be a universally agreed clinical and radiological definition of PerH in order to make meaningful comparison between studies.

Most publications reporting PerH repair following APE are either individual case reports or small retrospective case series with relatively short follow-up. This review includes mostly small case series over a long period of time reporting different techniques performed by different surgeons. These papers are focused on the description of successful technique and are, therefore, prone to publication bias. It appears that myocutaneous flap techniques have a role in repair of PerH when the operative field has been severely damaged by irradiation and can provide

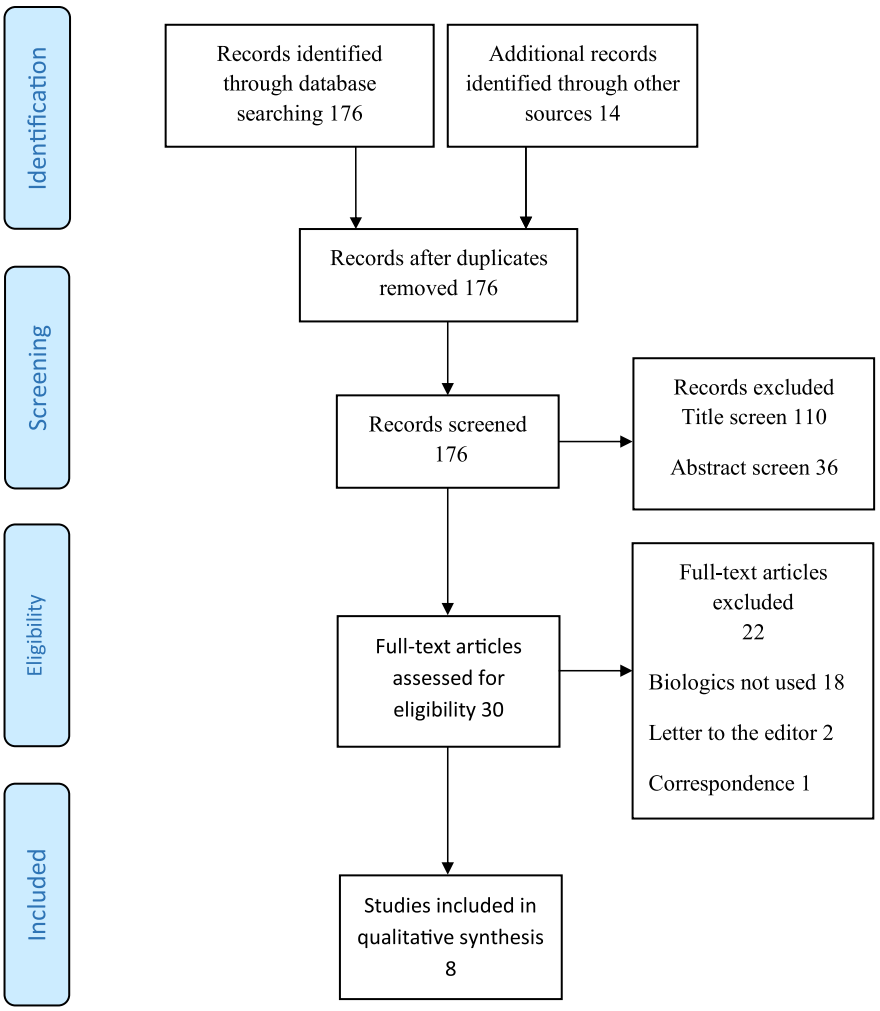

FIGURE 1 | PRISMA flow diagram outlining study selection.

TABLE 1 | Case reports.

Reference	*n*	Study period	M:F	Age (years)	Treatment of primary disease	Approach to perineal hernia repair	Mesh type	Follow-up	Outcome	Complications
Ong and Miller (17)	1	12 months after APR		72	Neoadjuvant CRT	Transperineal using Mitek suture anchors	Acellular porcine dermal mesh (Permacol)	6 months	No recurrence	Nil
Kathju et al. (18)	1	2011	M	56	Neoadjuvant CRT, APR	Abdominoperineal Mesh anchored anteriorly to pubic bone using Mitek suture anchors	Human-derived acellular dermal graft (Derma Matrix)	1 year	No complications or recurrence	NR
Skipworth et al. (14)	1	2006	M	46	Pre op CRT	Perineal approach Trendelenburg lithotomy positon	Porcine collagen matrix	18 months	No recurrence	NR

a well-vascularized tissue for repair (19, 22). None of the studies compared the use of biologics with either prosthetic mesh or myocutaneous flaps and, therefore, findings of individual studies are difficult to interpret.

Some of the risk factors that may predispose an individual to the development of PerH include female gender, previous hysterectomy, coccygectomy, pre-operative pelvic irradiation, post-operative wound infection, a long small bowel mesentery, high BMI, smoking, and non-closure of the pelvic peritoneum (1, 6, 21, 23, 24). Patients with rectal cancer may have been treated with neoadjuvant chemoradiotherapy. The role of these risk factors has not been evaluated in these studies.

TABLE 2 | Case series.

Reference	*n*	Study period	M:F	Age	Treatment of primary disease	Approach to perineal hernia repair	Mesh type	Follow-up	Outcome	Complications
Musters et al. (19)	15	50 months	9:6	62 ± 11 years mean	Conventional APR (*n*, %) 5 (33) Extralevator APR (*n*, %) 5 (33) Ischio-anal APR (*n*, %) 4 (27) Intersphincteric APR (*n*, %) 1 (7)	Transperineal 14 Laparoscopic Omental plasty + Transperinal 1	Permacol™ 3 Strattice™ 12 Myocutaneous flap + Biological mesh 3	17 months median (IQR 12–24)	Clinical recurrence 7 (47%)	Wound infection 3 patients
Sayers et al. (10)	14/54	54 months	40:14	69.5 years median (31–90)	eLAPE 20 Neo-CRT 52 Biological mesh 2 Myocutaneous flap 6 (5 rectus and 1 gracilis) Simple suture in 46	Not reported	Biologic mesh 5/8 Myocutaneous flap 3/8	57.5 months, median (29–61)	Biologic mesh, 1/5 had recurrence Myocutaneous flap, 1/3 had recurrence	NR
Abbas and Garner (20)	7	Over 66 months	4:3	64 years median (44–77)	0.5 after lap APER 1 had gluteal rotation flap All had RT 1 had adjuvant CT	Lap repair 5 Lap converted to open 1 Perineal approach 1 (sublay)	Synthetic composite 4 Biological 2 Direct suture repair 1	25 months (16–64)	No recurrences	NR
de Campos et al. (15)	7	1995–2004	NR	NR	35 patients in one center had pre op CT. 4/35 developed PERH 3 patients from another center		Dura mater patch via laparotomy 1 Bovine pericardium 1 via perineal approach Bovine pericardium via abdominal approach 1 Conservative 1	NR	NR	NR

TABLE 3 | Pooled analysis evidence.

Reference	*n*	Study period	M:F	Age	Treatment of primary disease	Approach to perineal hernia repair	Mesh type	Follow-up	Outcome	Complications
Mjoli et al. (21)	43	1944–2010	23:20	63 years mean (10 SD, range 45–89)	RT 18 Open APE24 (55.8%) Open APE + coccyx 4 (9.3%) Laparoscopic APE 9 (20.9%) Laparoscopic APE + posterior vaginal wall 3 (7.0%) Staged Laney procedure 1 (2.3%) Staged Laney procedure + coccyx 1 (2.3%) Open APE + perineal colostomy 1 (2.3%)	Perineal 22 Open abdominal in 11 Open abdominoperineal 3 Laparoscopic 5 Laparoscopic-perineal 2	**Perineal** Non-absorbable 3 Composite 1 Biological 4 Non-specific 1 **Open abdominal** Absorbable mesh 1 Non-absorbable 3 Biologic 3 **Open Abd-Perineal** Non-absorbable 3 **Laparoscopic** Composite 5 **Laparoscopic-perineal** Non-absorbable 1 Composite 1	NR	Primary recurrence 13 Second recurrence 3 Recurrence rate: 5/25 synthetic or biological mesh 6/12 primary closure; 2/6 remaining techniques Recurrences repaired: synthetic or biologic mesh 6 Primary closure 5 Gluteal/Gracilis flap 4	Perineal wound breakdown 12%

The decision to repair PerH is based on the symptoms, fitness of the patient and oncological stage. Repair may be performed via abdominal, perineal, or combined approach. Laparoscopy has been used in patients with reasonable access. There is no evidence to support the use of any particular approach. The pooled analysis by Mjoli et al. reported 22 perineal repairs, 11 open abdominal operations, 3 combined abdominoperineal approach, 5 laparoscopic repairs, and 2 laparoscopic-perineal procedures (21).

Within the last decade, the eLAPE procedure has become increasing popular and has led to reduction in the circumferential margin positivity rate. However, due to the wider resection of the pelvic floor, the risk of herniation may be higher. The pelvic floor may or may not have been reconstructed using flaps/meshes, etc. There is evidence that laparoscopy results in fewer adhesion in the abdomen and this may contribute to increasing PerH rates as the small and large bowel are free to descend into the pelvis (25, 26). It is likely that the incidence and prevalence of PerH will increase unless there is a much better technique of primary reconstruction of the pelvic floor at the time of APE.

The advent of synthetic absorbable meshes has generated considerable interest within the surgical community. These materials promote fibroblast activity and generate a foreign body reaction. Following complete absorption within 30–90 days, the synthetic material is replaced by collagen rich connective tissue. In this review, only one patient was identified to have undergone repair with an absorbable mesh and this hernia recurred within 16 months (21). The use of biologic mesh for repairing PerH appears attractive as the acellular collagen matrix is believed to allow migration of fibroblasts, neovascularization, and incorporation within the native tissues. This is thought to reduce the risk of wound infection. A recently published case series of 15 patients undergoing PerH repair with porcine acellular dermal mesh reported recurrence rates of 47% after a median follow-up of 17 months (IQR 12–24) (19). However, the low volume, quality of available data, and lack of any comparative studies make it difficult to evaluate the use of biologic meshes as a technique.

CONCLUSION

There is no general agreement to the optimal operative strategy to repair PerH following an APE. There is insufficient evidence to recommend any specific operative approach or repair technique for PerH following APE.

AUTHOR NOTES

Previous presentations: The data in this paper have been presented at the Consensus Conference on the clinical use of biologic and biosynthetic meshes in abdominal surgery on Wednesday, January 27, 2016 at Hotel Ellington, Nürnberger Straße 50-55, D-10789 Berlin.

AUTHOR CONTRIBUTIONS

SN, FK, ID, and NS designed the search; SN and NA performed the search; FK, ID, and NS contributed analytic tools; SN and NA analyzed the data. SN wrote the first draft paper. All authors contributed to revision of the manuscript.

REFERENCES

1. Aboian E, Winter DC, Metcalf DR, Wolff BG. Perineal hernia after proctectomy: prevalence, risks, and management. *Dis Colon Rectum* (2006) 49(10):1564–8. doi:10.1007/s10350-006-0669-0
2. Beck M. Perineal hernia: the ventral decubitus perineal approach. *J Visc Surg* (2011) 148(1):39–41. doi:10.1016/j.jviscsurg.2010.12.006
3. Dulucq J-L, Wintringer P, Mahajna A. Laparoscopic repair of postoperative perineal hernia. *Surg Endosc* (2006) 20(3):414–8. doi:10.1007/s00464-005-0193-7
4. Rayhanabad J, Sassani P, Abbas MA. Laparoscopic repair of perineal hernia. *JSLS* (2009) 13(2):237–41.
5. Śmietański M, Szczepkowski M, Alexandre JA, Berger D, Bury K, Conze J, et al. European Hernia Society classification of parastomal hernias. *Hernia* (2014) 18(1):1–6. doi:10.1007/s10029-013-1162-z
6. So JB, Palmer MT, Shellito PC. Postoperative perineal hernia. *Dis Colon Rectum* (1997) 40(8):954–7. doi:10.1007/BF02051204
7. Shihab OC, Brown G, Daniels IR, Heald RJ, Quirke P, Moran BJ. Patients with low rectal cancer treated by abdominoperineal excision have worse tumors and higher involved margin rates compared with patients treated by anterior resection. *Dis Colon Rectum* (2010) 53(1):53–6. doi:10.1007/DCR.0b013e3181c70465
8. Shihab OC, Taylor F, Salerno G, Heald RJ, Quirke P, Moran BJ, et al. MRI predictive factors for long-term outcomes of low rectal tumours. *Ann Surg Oncol* (2011) 18(12):3278–84. doi:10.1245/s10434-011-1776-2
9. West NP, Anderin C, Smith KJE, Holm T, Quirke P; European Extralevator Abdominoperineal Excision Study Group. Multicentre experience with extralevator abdominoperineal excision for low rectal cancer. *Br J Surg* (2010) 97(4):588–99. doi:10.1002/bjs.6916
10. Sayers AE, Patel RK, Hunter IA. Perineal hernia formation following extralevator abdominoperineal excision. *Color Dis* (2015) 17(4):351–5. doi:10.1111/codi.12843
11. Alam NN, Narang SK, Köckerling F, Daniels IR, Smart NJ. Biologic mesh reconstruction of the pelvic floor after extralevator abdominoperineal excision: a systematic review. *Front Surg* (2016) 3:9. doi:10.3389/fsurg.2016.00009
12. Peacock O, Pandya H, Sharp T, Hurst NG, Speake WJ, Tierney GM, et al. Biological mesh reconstruction of perineal wounds following enhanced abdominoperineal excision of rectum (APER). *Int J Colorectal Dis* (2012) 27(4):475–82. doi:10.1007/s00384-011-1325-2
13. *OCEBM Levels of Evidence – CEBM [Internet]*. (2015). Available from: http://www.cebm.net/ocebm-levels-of-evidence/
14. Skipworth RJE, Smith GHM, Anderson DN. Secondary perineal hernia following open abdominoperineal excision of the rectum: report of a case and review of the literature. *Hernia* (2007) 11(6):541–5. doi:10.1007/s10029-007-0234-3
15. de Campos FGCM, Habr-Gama A, Araújo SE, Sousa AH, Nahas CR, Lupinacci RM, et al. Incidence and management of perineal hernia after laparoscopic proctectomy. *Surg Laparosc Endosc Percutan Tech* (2005) 15(6):366–70. doi:10.1097/01.sle.0000191592.93326.63
16. Dindo D, Demartines N, Clavien P-A. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* (2004) 240(2):205–13. doi:10.1097/01.sla.0000133083.54934.ae
17. Ong SL, Miller AS. A transperineal approach to perineal hernia repair using suture anchors and acellular porcine dermal mesh. *Tech Coloproctol* (2013) 17(5):605–7. doi:10.1007/s10151-011-0774-5
18. Kathju S, Lasko LA, Medich DS. Perineal hernia repair with acellular dermal graft and suture anchor fixation. *Hernia* (2011) 15(3):357–60. doi:10.1007/s10029-010-0664-1
19. Musters GD, Lapid O, Stoker J, Musters BF, Bemelman WA, Tanis PJ. Is there a place for a biological mesh in perineal hernia repair? *Hernia* (2016). Available from: http://link.springer.com/10.1007/s10029-016-1504-8
20. Abbas Y, Garner J. Laparoscopic and perineal approaches to perineal hernia repair. *Tech Coloproctol* (2014) 18(4):361–364. doi:10.1007/s10151-013-1060-5
21. Mjoli M, Sloothaak DAM, Buskens CJ, Bemelman WA, Tanis PJ. Perineal hernia repair after abdominoperineal resection: a pooled analysis. *Colorectal Dis* (2012) 14(7):e400–6. doi:10.1111/j.1463-1318.2012.02970.x
22. Hansen MT, Bell JL, Chun JT. Perineal hernia repair using gracilis myocutaneous flap. *South Med J* (1997) 90(1):75–7. doi:10.1097/00007611-199701000-00018
23. Kelly AR. Surgical repair of post-operative perineal hernia. *Aust N Z J Surg* (1960) 29:243–5. doi:10.1111/j.1445-2197.1960.tb03845.x
24. Perl JI. Repair of postoperative perineal hernia. Report of a case. *J Int Coll Surg* (1960) 34:86–92.
25. Svane M, Bulut O. Perineal hernia after laparoscopic abdominoperineal resection – reconstruction of the pelvic floor with a biological mesh (Permacol™). *Int J Colorectal Dis* (2012) 27(4):543–4. doi:10.1007/s00384-011-1253-1
26. Beck DE, Fazio VW, Jagelman DG, Lavery IC, McGonagle BA. Postoperative perineal hernia. *Dis Colon Rectum* (1987) 30(1):21–4. doi:10.1007/BF02556914

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

APPENDIX

BioMesh Study Group

Ferdinand Köckerling (Chairman), Stavros Antoniou, René Fortelny, Frank A. Granderath, Markus Heiss, Franz Mayer, Marc Miserez, Agneta Montgomery, Salvador Morales-Conde, Filip Muysoms, Alexander Petter-Puchner, Rudolph Pointner, Neil Smart, Marciej Smietanski, Bernd Stechemesser.

Aim

The BioMesh Study Group has set itself the task of identifying how best to use biological meshes for the various indications. The first step toward achieving that goal is to compile systematic reviews of the different indications on the basis of the existing literature. The available literature sources will be evaluated in accordance with the Oxford Centre for Evidence-based Medicine-Levels of Evidence (March 2009). Next, based on the review findings, corresponding Statements and Recommendations are to be formulated in a Consensus Conference for the use of biological meshes for the different indications. The findings of this study were presented at the Consensus Conference in Berlin in January 2016 as a part of the project undertaken by the BioMesh Study Group. The findings of the Consensus Conference are currently being summarized for a joint publication.

frontiers in Surgery

REVIEW
published: 19 October 2015
doi: 10.3389/fsurg.2015.00054

Rectopexy for rectal prolapse

*Nasra N. Alam[1], Sunil K. Narang[1], Ferdinand Köckerling[2], Ian R. Daniels[1] and Neil J. Smart[1]**

[1] Exeter Surgical Health Services Research Unit (HeSRU), Royal Devon and Exeter Hospital, Exeter, UK, [2] Department of Surgery, Center for Minimally Invasive Surgery, Academic Teaching Hospital of Charité Medical School, Vivantes Hospital, Berlin, Germany

Introduction: Ventral mesh rectopexy (VMR) is a recognized treatment for posterior compartment pelvic organ prolapse (POP). The aim of this review is to provide a synopsis of the evidence for biological mesh use in VMR, the most widely recognized surgical technique for posterior compartment POP.

Methods: A systematic search of PubMed was conducted using the search terms "VMR," "ventral mesh rectopexy," or "mesh rectopexy." Six studies were identified.

Results: About 268/324 patients underwent ventral rectopexy using biological mesh with a further 6 patients having a combination of synthetic and biological mesh. Recurrence was reported in 20 patients; however, 6 were from studies where data on biological mesh could not be extracted. There are no RCTs in VMR surgery and no studies have directly compared types of biological mesh. Cross-linked porcine dermal collagen is the most commonly used mesh and has not been associated with mesh erosion, infection, or fistulation in this review. The level of evidence available on the use of biological mesh in VMR is of low quality (level 4).

Conclusion: Ventral mesh rectopexy has become prevalent for posterior compartment POP. The evidence base for its implementation is not strong and the quality of evidence to inform choice of mesh is poor.

Keywords: ventral mesh rectopexy, mesh rectopexy, pelvic organ prolapse, biological mesh, vMR

OPEN ACCESS

Edited by:
Hesham Abdeldayem, National Liver Institute, Egypt

Reviewed by:
Essam Salah Hammad, Menoufia University, Egypt
Ahmed Farag El-Kased, Menoufia University, Egypt

****Correspondence:***
Neil J. Smart
n.smart@nhs.net

Specialty section:
This article was submitted to Visceral Surgery, a section of the journal Frontiers in Surgery

Received: *27 July 2015*
Accepted: *30 September 2015*
Published: *19 October 2015*

Citation:
Alam NN, Narang SK, Köckerling F, Daniels IR and Smart NJ (2015) Rectopexy for rectal prolapse. Front. Surg. 2:54. doi: 10.3389/fsurg.2015.00054

INTRODUCTION

Ventral mesh rectopexy (VMR) is a recognized treatment for posterior compartment pelvic organ prolapse (POP). It is believed to address functional bowel symptoms by providing suspensory support to the prolapsing organ (in this case the rectum ± the vaginal vault) and avoiding the autonomic denervation that results in *de novo* symptomatology. Consequently, it improves obstructive defaecatory symptoms as well as symptoms of incontinence (1–4) without initiating significant new onset constipation (1, 5). VMR comprises dissection of the rectovaginal septum from above to the level of the pelvic floor. This is followed by fixation of a synthetic or biological prosthesis to the anterior wall of the rectum and proximally to the sacral promontory (**Figures 1** and **2**). The vaginal vault may also be fixed to the mesh to provide support and help obliterate the deep rectovaginal pouch. VMR has rapidly established itself in Europe as the procedure of choice for posterior compartment POP in spite of a limited evidence base.

A variety of synthetic meshes have been used for a wide range of POP surgery but there have been reports of high rates of pelvis sepsis, as well as concerns regarding mesh erosion, dyspareunia, fistulation. and stricturing (6–8). The Food and Drug Administration (FDA) issued a warning in 2011 that, *"serious complications associated with surgical mesh for transvaginal repair of POP are not rare"* (9). It is not clear to what extent this warning is relevant to POP surgery carried out via

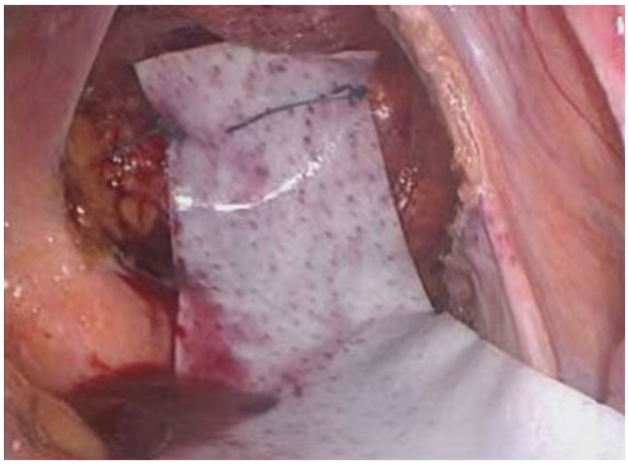

FIGURE 1 | Placement of mesh anterior to rectum and suturing to the anterior wall of the rectum ± suture to vaginal vault.

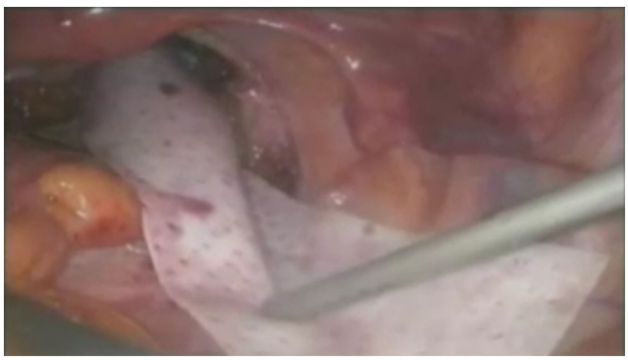

FIGURE 2 | Tacking of mesh to sacral promontory. Photographs by kind permission of Mr. Mark Mercer-Jones, Consultant Colorectal Surgeon, Gateshead, UK.

abdominal approaches. Nevertheless, since it has been postulated that biological mesh may cause fewer complications in comparison to synthetic mesh in certain high-risk circumstances (10–12). This has led to an increase in the popularity of biological mesh use for POP surgery. The aim of this review is to provide a synopsis of the evidence for biological mesh use in VMR, the most widely recognized surgical technique for posterior compartment POP.

METHODS

A systematic search of PubMed was conducted using the search terms "VMR," "ventral mesh rectopexy," or "mesh rectopexy." Titles, abstracts, and finally full texts were analyzed for studies reporting on the use of biological mesh in rectopexy. Inclusion criteria were studies that described a ventral rectopexy using a biological mesh in either an open or laparoscopic technique. Studies were excluded if only synthetic mesh was used or if there was no mention of a mesh. Furthermore, studies on patients under the age of 18 were excluded as well as non-English language studies, technical tips, or duplicates series from the same research group. Overall, the search yielded six studies for analysis after the exclusion of review articles. The study characteristics are presented (**Table 1**).

RESULTS

In the 6 case series, there was a total of 324 patients. Of these, 268 patients underwent ventral rectopexy using biological mesh with a further 6 patients having a combination of synthetic mesh and biological mesh. Overall, 155 patients underwent VMR using additionally cross-linked porcine dermal collagen (Permacol™ or Pelvicol™) and 89 using porcine intestinal submucosa (Surgisis©). Recurrence was reported in 20 patients; however, 6 of these were from studies where data on biological mesh could not be extracted. One study did not report recurrence. Complications are outlined (**Table 1**).

There are no randomized controlled trials in VMR surgery generally and no studies have directly compared types of biological mesh, e.g., cross-linked vs. non-cross-linked. Cross-linked porcine dermal collagen is the most commonly used mesh and has not been associated with mesh erosion, infection, or fistulation in this current review. The level of evidence available on the use of biological mesh in VMR is of low quality (level 4) (13).

DISCUSSION/SUMMARY

Ventral mesh rectopexy has become established as the current procedure of choice for posterior compartment POP without a high quality evidence base in support of its adoption and therefore this has consequently been called into question (14). In light of the limited evidence base for VMR generally, it is perhaps of no surprise that the level of evidence for any specific mesh type, either synthetic or biological, is level 4. The expert consensus assumes that VMR is the optimal treatment paradigm in many circumstances (15). This may well turn out to be the case, but as yet the evidence basis is lacking and recommendations regarding any specific type of mesh are at best grade C (16).

All the included studies are retrospective, often with short follow-up, have small numbers of patients and are usually derived from single institutions. The applicability of the findings to a wider population is uncertain. There is one comparative case series with 29 patients undergoing laparoscopic VMR using a biological mesh and 29 patients matched for age and surgical indication, undergoing laparoscopic VMR using a synthetic mesh (17). However, it did not meet the inclusion criteria for the review as it was a subset analysis of data that has already been presented and discussed and was therefore excluded. Furthermore, the other key limitation for most of the included studies is the variability of outcome reporting and the lack of standardization of outcome measures. Some studies report functional outcome scores for both constipation and incontinence, e.g., Wexner/FISI, but these scoring systems are not necessarily appropriate for obstructed defaecation syndrome (ODS) or prolapse (18, 19). Disease-specific scoring systems such as pelvic organ prolapse quantification system (POP-Q) or the ODS score (20), and quality of life scores (e.g., SF-36 EQ-5D) may be more appropriate but, these have not been used in any of the studies included in this review. Anorectal physiology results are reported in some studies but correlation to anatomy,

TABLE 1 | Study characteristics.

Author (year)	Study design	No. of pts	Age	Sex (M:F)	Patient characteristics	Material used	Intervention	Follow-up (months)	Recurrence	Complications	LoE	Notes
Enríquez-Navascués et al. (23)	Case Series	57	Mean: 66 (19–81)	2:55	Total rectal prolapse: 11	Acellular porcine dermis biological mesh (Pelvicol®): 4 polypropylene macroporous synthetic mesh (Ginemesh®, Ethicon): 4 Combination: 3	Laparoscopic rectopexy	25 (4–48) Median	1 (Biologic)	1 reoperation	4	
					Rectoenteroceles with or without descending perineal syndrome: 4	Pelvicol®: 1 Combination: 3	Laparoscopic rectopexy			-		
					Genitourinary pelvic organ prolapse: 42	Pelvicol®: 36 Ginemesh®: 6	Pfannenstiel: 31 Laparoscopic: 11		9 (Biologic)	4 reoperation		
Wahed et al. (24)	Case series	65	62 (31–89) Median	3:62	Full thickness rectal prolapse: 27 rectocele with obstructive defecation symptoms: 23 vaginal vault prolapse: 14 Fecal Incontinence: 1	Permacol™	Lap ventral rectopexy	12 (1–29) Median	2	Diarrhea: 2 UTI: 1 MI: 1 Sacral osteomyelitis: 1 Intersphincteric abscess: 1 Port site pain: 2 Strangulated port site hernia: 1	4	
Sileri et al. (25)	Case Series	34	59 (5–78) median	0:34	Grade III or IV rectal prolapse	Permacol™	Lap ventral rectopexy	12 months (6–28) mean	2	SBO: 1 UTI: 4 Subcutaneous emphysema: 2 Sacral pain: 1 Hematoma: 1	4	
Powar et al. (26)	Case series	120	62.5 years (25–93)	0:120	Rectocele and internal prolapse: 57 Full-thickness rectal prolapse: 53 Other (solitary rectal ulcer): 3	Surgisis Biodesign© : 89 Non-absorbable polypropylene mesh: 31	Lap ventral rectopexy	7.6 months median	3 (Bio mesh)	Biologic group: exacerbation of chronic pain: 3 Lumbar discitis: 1 Pelvic pain: 2 Post-operative hypotension: 1 Port site pain: 1 Vaginal discharge: 1 Nausea: 1 Urinary retention: 1 Atelectasis: 1	4	Cannot separate out pts who had Surgisis©
Evans et al. (27)	Case Series	36 (30 surgery)	44 (15–81) median	5:31	SRUS: obstructive defecation: 36 Clinical external rectal prolapse: 4 External prolapse: 10 Internal rectal prolapse Grade I: 2(6%), Grade III: 6 (17%), Grade IV: 14 (39%)	Polypropylene: 27 Permacol™: 3	Laparoscopic ventral mesh rectopexy: 29 STARR: 1	36 months (3–78) Median	3 (unknown whether related to Biological mesh)	Vaginal stitch sinus: 1 Wound infection: 1 Port site hernia: 1 Mortality: 1	4	Cannot separate out 3 pts who had Permacol™
Sileri et al. (28)	Case series	12	Mean age 63 years, range 23–78)	0:12		Permacol™	Lap ventral rectopexy	5 months	Not reported	Port site hematoma: 1 Subcutaneous emphysema: 1	4	

recurrence or symptomology is not clearly defined. For those studies where VMR was used to treat ODS, post-operative defaecography that supports long-term anatomical correction of prolapse has not been reported.

Complications in the included studies are inconsistently reported and standardized methods of reporting, such as Clavien–Dindo have not been used (21). Two studies did not meet the inclusion criteria because they only addressed complications pertaining to VMR. The first was a systematic review of reported complications, which failed to demonstrate any difference in complications between synthetic and biological mesh although the follow-up was short (22). The second study has reported 50 patients referred for complications following VMR and has documented operative strategies and techniques. Although complications from both biological and synthetic meshes are discussed, there is no denominator provided and therefore it is not possible to ascertain the relative frequency of complications with each type of mesh (6). It is interesting to note that the concerns raised by the FDA have not been reported in the literature pertaining to VMR to the same extent. Although most series have follow-ups of short duration, in the transvaginal approach mesh complications were mainly reported within 12 months (8). This suggests that the concerns relating to mesh placement via the transvaginal or other perineal approaches may not be extrapolated to transabdominal approaches.

CONCLUSION

Ventral mesh rectopexy has become prevalent for posterior compartment POP. The evidence base for its implementation is not strong and the quality of evidence to inform choice of mesh is poor.

REFERENCES

1. Boons P, Collinson R, Cunningham C, Lindsey I. Laparoscopic ventral rectopexy for external rectal prolapse improves constipation and avoids de novo constipation. *Colorectal Dis* (2010) **12**(6):526–32. doi:10.1111/j.1463-1318.2009.01859.x
2. Tou S, Brown SR, Malik AI, Nelson RL. Surgery for complete rectal prolapse in adults. *Cochrane Database Syst Rev* (2008) (4):CD001758. doi:10.1002/14651858.CD001758.pub2
3. D'Hoore A, Cadoni R, Penninckx F. Long-term outcome of laparoscopic ventral rectopexy for total rectal prolapse. *Br J Surg* (2004) **91**(11):1500–5. doi:10.1002/bjs.4779
4. Collinson R, Wijffels N, Cunningham C, Lindsey I. Laparoscopic ventral rectopexy for internal rectal prolapse: short-term functional results. *Colorectal Dis* (2010) **12**(2):97–104. doi:10.1111/j.1463-1318.2009.02049.x
5. Samaranayake CB, Luo C, Plank AW, Merrie AE, Plank LD, Bissett IP. Systematic review on ventral rectopexy for rectal prolapse and intussusception. *Colorectal Dis* (2010) **12**(6):504–12. doi:10.1111/j.1463-1318.2009.01934.x
6. Madiba TE, Baig MK, Wexner SD. Surgical management of rectal prolapse. *Arch Surg* (2005) **140**(1):63–73. doi:10.1001/archsurg.140.1.63
7. Badrek-Al Amoudi AH, Greenslade GL, Dixon AR. How to deal with complications after laparoscopic ventral mesh rectopexy: lessons learnt from a tertiary referral centre. *Colorectal Dis* (2013) **15**(6):707–12. doi:10.1111/codi.12164
8. Abed H, Rahn DD, Lowenstein L, Balk EM, Clemons JL, Rogers RG, et al. Incidence and management of graft erosion, wound granulation, and dyspareunia following vaginal prolapse repair with graft materials: a systematic review. *Int Urogynecol J* (2011) **22**(7):789–98. doi:10.1007/s00192-011-1384-5
9. Available from: http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm142636.htm
10. Smart NJ, Marshall M, Daniels IR. Biological meshes: a review of their use in abdominal wall hernia repairs. *Surgeon* (2012) **10**(3):159–71. doi:10.1016/j.surge.2012.02.006
11. Williams NS, Giordano P, Dvorkin LS, Huang A, Hetzer FH, Scott SM. External pelvic rectal suspension (the Express procedure) for full-thickness rectal prolapse: evolution of a new technique. *Dis Colon Rectum* (2005) **48**(2):307–16. doi:10.1007/s10350-004-0806-6
12. Smart NJ, Mercer-Jones MA. Functional outcome after transperineal rectocele repair with porcine dermal collagen implant. *Dis Colon Rectum* (2007) **50**(9):1422–7. doi:10.1007/s10350-007-0219-4
13. OCEBM Levels of Evidence Working Group. *The Oxford 2011 Levels of Evidence*. Oxford Centre for Evidence-Based Medicine (2015). Available from: http://www.cebm.net/index.aspx?o=5653
14. Lundby L, Laurberg S. Laparoscopic ventral mesh rectopexy for obstructive defaecation syndrome: time for a critical appraisal. *Colorectal Dis* (2015) **17**(2):102–3. doi:10.1111/codi.12830
15. Mercer-Jones MA, D'Hoore A, Dixon AR, Lehur P, Lindsey I, Mellgren A, et al. Consensus on ventral rectopexy: report of a panel of experts. *Colorectal Dis* (2014) **16**(2):82–8. doi:10.1111/codi.12415
16. Available from: http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/
17. Ogilvie JW Jr., Stevenson AR, Powar M. Case-matched series of a non-cross-linked biologic versus non-absorbable mesh in laparoscopic ventral rectopexy. *Int J Colorectal Dis* (2014) **29**(12):1477–83. doi:10.1007/s00384-014-2016-6
18. Rusavy Z, Jansova M, Kalis V. Anal incontinence severity assessment tools used worldwide. *Int J Gynaecol Obstet* (2014) **126**(2):146–50. doi:10.1016/j.ijgo.2014.02.025
19. Renzi A, Brillantino A, Di Sarno G, d'Aniello F. Five-item score for obstructed defecation syndrome: study of validation. *Surg Innov* (2013) **20**(2):119–25. doi:10.1177/1553350612446354
20. Altomare DF, Spazzafumo L, Rinaldi M, Dodi G, Ghiselli R, Piloni V. Set-up and statistical validation of a new scoring system for obstructed defaecation syndrome. *Colorectal Dis* (2008) **10**(1):84–8. doi:10.1111/j.1463-1318.2007.01262.x
21. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* (2004) **240**(2):205–13. doi:10.1097/01.sla.0000133083.54934.ae
22. Smart NJ, Pathak S, Boorman P, Daniels IR. Synthetic or biological mesh use in laparoscopic ventral mesh rectopexy: a systematic review. *Colorectal Dis* (2013) **15**(6):650–4. doi:10.1111/codi.12219
23. Enríquez-Navascués JM, Elósegui JL, Apeztegui FJ, Placer C, Borda N, Irazusta M, et al. Ventral rectal sacropexy (colpo-perineal) in the treatment of rectal and rectogenital prolapse. *Cir Esp* (2009) **86**(5):283–9. doi:10.1016/j.ciresp.2009.02.014
24. Wahed S, Ahmad M, Mohiuddin K, Katory M, Mercer-Jones M. Short-term results for laparoscopic ventral rectopexy using biological mesh for pelvic organ prolapse. *Colorectal Dis* (2012) **14**(10):1242–7. doi:10.1111/j.1463-1318.2011.02921.x
25. Sileri P, Franceschilli L, de Luca E, Lazzaro S, Angelucci GP, Fiaschetti V, et al. Laparoscopic ventral rectopexy for internal rectal prolapse using biological mesh: postoperative and short-term functional results. *J Gastrointest Surg* (2012) **16**(3):622–8. doi:10.1007/s11605-011-1793-2
26. Powar MP, Ogilvie JW Jr, Stevenson AR. Day-case laparoscopic ventral rectopexy: an achievable reality. *Colorectal Dis* (2013) **15**(6):700–6. doi:10.1111/codi.12110
27. Evans C, Ong E, Jones OM, Cunningham C, Lindsey I. Laparoscopic ventral rectopexy is effective for solitary rectal ulcer syndrome when associated with rectal prolapse. *Colorectal Dis* (2014) **16**(3):O112–6. doi:10.1111/codi.12502
28. Sileri P, Capuano I, Franceschilli L, Giorgi F, Gaspari AL. Modified laparoscopic ventral mesh rectopexy. *Tech Coloproctol* (2014) **18**(6):591–4. doi:10.1007/s10151-013-1094-8

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

frontiers in Surgery

REVIEW
published: 16 October 2015
doi: 10.3389/fsurg.2015.00055

Treatment of fistula-in-ano with fistula plug – a review under special consideration of the technique

Ferdinand Köckerling[1], Nasra N. Alam[2], Sunil K. Narang[2], Ian R. Daniels[2] and Neil J. Smart[2]*

[1] Department of Surgery and Center for Minimally Invasive Surgery, Academic Teaching Hospital of Charité Medical School, Vivantes Hospital, Berlin, Germany, [2] Exeter Surgical Health Services Research Unit (HeSRU), Royal and Exeter Hospital, Exeter, UK

Introduction: In a recent Cochrane review, the authors concluded that there is an urgent need for well-powered, well-conducted randomized controlled trials comparing various modes of treatment of fistula-in-ano. Ten randomized controlled trials were available for analyses: There were no significant differences in recurrence rates or incontinence rates in any of the studied comparisons. The following article reviews the studies available for treatment of fistula-in-ano with a fistula plug with special attention paid to the technique.

Material and Methods: PubMed, Medline, Embase, and the Cochrane medical database were searched up to July 2015. Sixty-four articles were relevant for this review.

Results: Healing rates of 50–60% can be expected for treatment of complex anal fistula with a fistula plug, with a plug-extrusion rate of 10–20%. Such results can be achieved not only with plugs made of porcine intestinal submucosa but also those made of other biological or synthetic bioabsorbable mesh materials. Important technical steps are firm suturing of the head of the plug in the primary opening and wide drainage of the secondary opening.

Discussion: Treatment of a complex fistula-in-ano with a fistula plug is an option with a success rate of 50–60% with low complication rate. Further improvements in technique and better studies are needed.

Keywords: complex anal fistula, fistula plug, biological mesh, fistula closure rate, incontinence

OPEN ACCESS

Edited by:
Sanoop Koshy Zachariah, MOSC Medical College, India

Reviewed by:
Jose M. Ramia, Regional Public Health System of Castilla La Mancha, Spain
Boris Eugeniev Sakakushev, University Hospital St George Plovdiv, Bulgaria
Tzu-An Chen, Taiwan Landseed Hospital, Taiwan

****Correspondence:***
Ferdinand Köckerling
ferdinand.koeckerling@vivantes.de

Specialty section:
This article was submitted to Visceral Surgery, a section of the journal Frontiers in Surgery

Received: *22 July 2015*
Accepted: *30 September 2015*
Published: *16 October 2015*

Citation:
Köckerling F, Alam NN, Narang SK, Daniels IR and Smart NJ (2015) Treatment of fistula-in-ano with fistula plug – a review under special consideration of the technique. Front. Surg. 2:55. doi: 10.3389/fsurg.2015.00055

INTRODUCTION

Fistula-in-ano is a difficult problem that physicians have struggled with since the time of Hippocrates (1). Despite the long-standing history of fistula-in-ano and the multiple approaches that are utilized, there is a paucity of high quality data to guide decision (1). In a recent Cochrane review, the authors concluded that there is an urgent need for well-powered, well-conducted randomized controlled trials comparing various modes of treatment of fistula-in-ano (2).Ten randomized controlled trials were available for analyses: there were no significant differences in recurrence rates or incontinence rates in any of the studied comparisons. The American Gastroenterological Association divides the fistula-in-ano into simple and complex (1). Simple fistulas are low – i.e., they involve a small or no portion of the sphincter complex. These fistulas include superficial, low intersphincteric, or low transsphincteric fistula. In addition, communication between the anal canal end skin is only via one tract and is not associated with inflammatory bowel disease, radiation or involve any other organ (1). Complex fistulas are anatomically higher: they involve a significant portion of the sphincter

musculature, may have multiple tracts, involve other organs (i.e., vagina) and may be associated with radiation or inflammatory bowel disease. Recurrent fistulas are usually included in this category as well (1).

Fistulotomy, although extremely effective in treating low anal fistulas, is not a feasible option when the fistula tract incorporates a significant amount of the internal and external anal sphincter, as is the case for many high transsphincteric fistulas (3). It is also frequently contraindicated for anterior transsphincteric fistulas in women, for most fistulas in patients with Crohn's disease, and for fistulas in patients who have diminished continence (3).

The alternative treatment option of a transanal mucosal advancement flap for patients with high transsphincteric fistulas has reported success rates ranging from 59 to 98%. However, these procedures are technically challenging and some authors report incontinence rates of up to 20% (3).

In Crohn's disease-related high perianal fistulas, the mucosa advancement flap was combined with platelet-rich plasma (4).

Fibrin glue has also been used as treatment option, but with modest or poor success rates of between 0 and 74% (3–8).

Cutting seton procedures result in low recurrence rates, but can cause incontinence in up to 12–25% of patients (3, 9).

Ligation of the intersphincteric tract (LIFT) is a further alternative technique and has been associated with fistula closure rates of between 57 and 94% (3, 9). In a recent systematic review of 26 studies, including only 1 randomized controlled trial and 24 case series, 7 technical variations were used. Primary healing rates ranged from 47 to 95% (10).

Johnson et al. (11) first described the anal fistula plug, a bioabsorbable xenograft made of lyophilized porcine intestinal submucosa.

The following article reviews the studies available on treatment of fistula-in-ano with a fistula plug and calculates the success rates, while paying special attention to the fistula closure rate and the techniques used. The literature reports a success rate ranging from 24 to 88% with the mean follow up of 8 months. A possible explanation for this discrepancy could be differences in patient selection and variation of the technique (5). In a Consensus Conference, it was stated that a frequent issue affecting the plug procedure is a failure in the plug placement technique (5, 12). Therefore, each publication was carefully reviewed to identify the surgical technique employed. This sets this systematic review apart from those published hitherto.

MATERIALS AND METHODS

PubMed, Medline, Embase, and the Cochrane medical databases were searched up to December 2014 using the key words: "Anal fistula" AND "Plug," "Fistula-in-ano" AND "Plug," "Anal fistula" AND "Fistula plug." In addition, the references of articles retrieved were searched for relevant articles not previously identified. Sixty-four articles were relevant for this review.

RESULTS

The first systematic review of the efficacy of a SIS-anal-fistula plug was published in 2010 (13). All randomized/non-randomized, controlled/non-controlled clinical trials, which studied SIS-anal-fistula plug or compared SIS-anal-fistula plug with other treatment methods for anal fistula and which reported clinical healing of the fistula as the outcome, were included. Studies on patients with rectovaginal fistula who were treated by SIS-anal-fistula plug and patients undergoing additional procedure (advancement flap or fibrin glue) along with SIS-anal-fistula plug were excluded from the review. One study reporting the usage of an acellular extracellular matrix was not included because the material used was different.

Twelve studies were analyzed in the systematic review (**Table 1**). These consisted of one RCT (11), seven prospective case series (14–20), and four retrospective case series (21–24). Since the majority of studies analyzed in the systematic review are prospective or retrospective case series, the level of evidence is only 4. **Table 2** gives details of the surgical technique used in the studies included in the review.

A total of 317 patients were analyzed in the review by Garg (13) with a follow-up of range 3.5–12 months (**Table 1**). The SIS-anal-fistula plug procedure had a success rate of $n = 180/317$ (59.9%) ranging from 24 to 92%. The number of complex fistulae reported in 8 out of 12 studies was 186 with a success rate of $n = 119/186$ (64.0%) ranging from 35–87%. In patients with recurrent fistula, the success rate was $n = 16/34$ (47.1%) ranging from 13 to 71%. The success rate in patients with Crohn's disease was $n = 26/41$ (63.4%) ranging from 29 to 86%. The success rate in patients with single tracts ($n = 123/184$; 66.8%, range 44–93%) seemed better than for patients with multiple tracts ($n = 21/43$; 48.8% range 20–71%). If the patients with plug extrusion were excluded from the analysis, the success rate was $n = 121/189$ (64.0%), ranging from 40 to 90%.The plug extrusion rate was $n = 43/232$ (18.5%), ranging from 4 to 41%.

In 2012, another systematic review was published (3). This systematic review included studies whose results for patients with and without Crohn's disease could be differentiated. Patients with rectovaginal, anovaginal, rectouretral, or ileal-pouch vaginal fistulas were excluded as were studies where the mean or median follow-up was <3 months.

The systematic review contained 20 studies, consisting of 18 articles and 2 abstracts (26, 27). Among the 20 studies included are two RCTs (28, 29), 10 prospective case series (15, 16, 20, 26, 30–35),

TABLE 1 | Results of systematic reviews about the efficacy of anal fistula plug in fistula-in-ano.

Author	Year	Conflict of interest	LoE	Patients	Follow-up	Success rate	Plug extrusion rate
Garg et al. (13)	2010	None	4	317	3.5–12 months	59.9% (range: 24–92%)	18.5% (range: 4–41%)
O'Riordan et al. (3)	2012	None	4	530	3–24, 5 months	54.3%	–
Leng and Jin (25)	2012	NR	2a	167	5.7–14 months	51.5% (range: 20.0–82.82%)	11.1 + 18.9%

TABLE 2 | Surgical techniques used in the studies included in the systematic review of Garg et al. (13).

Reference	Surgical technique
Johnson et al. (11)	Self made SIS-anal-fistula plug from a 2 cm × 3 cm SIS – sheet rolled into a conical configuration Plug was pulled tip-first into the internal opening Suture fixation of the plug at the primary and secondary opening Plug was trimmed at the mucosa and skin level No complete occlusion of the secondary opening to allow drainage
O'Connor et al. (14)	Tracts were irrigated with hydrogen peroxide SIS-anal-fistula plug Plug was pulled tip-first into the internal opening Excess plug material was trimmed flush with the mucosa and skin Suture fixation of the plug at the primary and secondary opening Case was taken not to occlude the secondary opening
Champagne et al (15)	Hydrogen-peroxide installation SIS-anal-fistula plug Plug was pulled tip-first into the internal opening Excess plug material was trimmed flush with the primary opening Mechanical stability of the plug relies on firmly suturing the head of the plug into the primary opening Fixation of the tip of the plug to the edge of the secondary opening No complete occlusion of the secondary opening to allow drainage
Ellis (21)	Hydrogen-peroxide installation SIS-anal-fistula plug No debridement of the fistula tract was performed Occasionally, the distal most portion of the fistula tract was opened to ensure adequate drainage
van Koperen (16)	Cleaning with hydrogen peroxide SIS-anal-fistula plug No surgical debridement Remaining portion of the plug was removed Plug fixation at the internal and external opening The external fistula opening was not completely closed, enabling further drainage from the fistula tract Tract was irrigated with polyhexamide solution
Schwandner et al. (17)	SIS-anal-fistula plug No currettage, mechanical debridement, or fistulectomy was performed Plug was pulled tip-first into the internal opening Plug fixation at the internal opening The excess plug was trimmed at the mucosa and the former internal opening was covered with mucosa Finally, the excess plug material of the external opening was trimmend at skin level, but no further fixation was made
Ky et al. (18)	SIS-anal-fistula plug Plug was pulled tail-first into the internal opening Excess plug material was trimmed flush at the internal opening with the mucosa Plug was sutured deep to the internal opening A small mucosal flap was raised as advancement flap over the top of the plug Excess material protruding the external opening was excised The secondary opening was left open to allow drainage
Lawes et al. (22)	Tract was washed out with hydrogen peroxide SIS-anal-fistula plug Plug was pulled tip-first into the internal opening Excess plug material was trimmed flush with the internal and external opening Suture fixation to the mucosa and internal sphincter
Christoforidis et al. (23)	SIS-anal-fistula plug Plug was pulled through the internal opening Plug was secured at the internal opening The excess plug was trimmed of and the rectal mucosa was closed over the plug The plug was trimmed flush with the skin It was then secured with a stitch on one side of the external opening (15 procedures) or left unsecured (49 procedures)
Thekkinkattil et al. (19)	Tract was irrigated with saline or hydrogen peroxide SIS-anal-fistula plug The fistula plug was inserted from the internal opening The rectal mucosa was closed over the plug at the internal opening along with a deep suture through the internal sphincter Special attention has been made so ensure that the external opening was not completely occluded
Garg (20)	SIS-anal-fistula plug Plug was pulled through the track from the internal opening Any excess plug was cut flush with the internal opening The internal opening was then closed over the plug including the submucosa and internal sphincter muscle The distal end of the plug was sutered to the side of the external opening taking, care not to occlude it and allow drainage

and 8 retrospective case series (22, 24, 27, 36–40). Only 5 out of 20 of the publications listed were also included in the review by Garg (13, 15, 16, 20, 22, 24). This systematic review, too, was supported only by level of evidence 4 in view of the predominant number of prospective and retrospective case series.

Table 3 lists the exact surgical technique employed in the studies that were included in the review by O'Riordan (3) and not already analyzed in the Garg (13) review in Ref. (15, 16, 22, 24). Details of the surgical technique are not given for studies for which only an abstract is available (26, 27).

The study sample sizes ranged from 4 to 60 patients with a pooled total of 530 patients for this review. Forty-two of these patients had Crohn's disease, whereas 488 patients did not have Crohn's disease. The shortest mean or median follow-up in the 20 studies was 3 months, and the longest follow-up was 24.5 months.

Closure of the fistula was successful in 288 of the 530 patients with fistula-in-ano (54.3%; 95% CI 0.50–0.59). The overall success rate for patients with Crohn's disease was 23 of 42 patients (54.8%), whereas for patients without Crohn's disease it was 265 of 488 patients (54.3%).

A total of 46 patients experienced plug extrusion (8.7%). Eight of the 20 included articles reported continence levels pre- and post-insertion of the SIS-anal-fistula plug (20, 23, 24, 29, 31, 34, 40). There were no reported cases of any significant change in continence after insertion of the SIS-anal-fistula plug in any of the patients in these studies ($n = 196$ patients).

Leng et al. (25) then published a meta-analysis comparing anal fistula plug vs. mucosa advancement flap in complex fistula-in-ano. The studies included were three RCTs (28, 29, 41), one prospective cohort study (33) and two retrospective case series (37, 38). Hence the level of evidence is 2a. Apart from the RCT by

TABLE 3 | Surgical techniques used in the studies included in the systematic review of O'Riordan et al. (3) minus abstracts and studies already analyzed in the review of Garg et al. (13).

Reference	Surgical technique
Christoforidis et al. (37)	Fistula irrigated with hydrogen peroxide SIS-anal-fistula plug Suture fixation of the internal opening The excess plug was trimmed of and the rectal mucosa was closed over the plug Plug was trimmed flush at skin level and was secured at the external opening in only 30%
Chung et al. (38) Chung et al. (40)	Hydrogen peroxide installation SIS-anal-fistula plug Excess plug material was trimmed flush with the mucosa at the internal opening and at the external fistula opening at skin level Sutures were used to secure The plug to the internal sphincter muscle and to cover the mucosal opening of the fistula The external end of the plug was secured to 1 side of the external fistula opening
Wang et al. (39)	Fistula tract irrigation with hydrogen peroxide Plug was pulled through internal opening of the fistula The plug was then trimmed The head of the play was secured to the internal opening by a suture incorporating mucosa, submucosa and internal sphincter Closurre of the internal opening of the fistula over the plug No fixation of the plug to the external opening
Ortiz et al. (28)	Injection of hydrogen peroxide SIS-anal-fistula plug Suture fixation of the plug to the internal sphincter Closure of the internal opening of the fistula over the plug Care was taken to ensure that the external orifice of the fistula was not completely occluded so that the track could drain The remaining Plug was cut of the level of the external opening
Schwandner and Fuerst (30) Schwandner et al. (31)	Fistula passage was rinsed with hydrogen peroxide and debrided with a soft-bristle brush The external fistula opening was debrided SIS-anal-fistula plug Insertion Into the fistula through internal opening Plug was fixed with several sutures to the sphincter muscle and the inner fistula opening closed The external fistula opening was kept open to allow drainage Plug was trimmed, but not fixed to the external opening
Zubaidi and Al-Obeed (32)	Curetage and irrigation with hydrogen peroxide Plug was inserted through the internal opening Excess fistula plug was trimmed from both ends Plug was buried into the primary opening using a figure-of-eight absorbable suture, which was inserted deep into the internal sphincter muscle At the secondary opening the tip of the plug was tacked to the edge, making sure to not completely occlude the secondary opening to allow drainage of exudates
Adamina et al. (33)	No irrigation SIS-anal-fistula plug Plug was inserted through the internal opening Plug sutured to the internal sphincter The tip of the plug was cut at skin level and not sutured to allow drainage
McGee et al. (34)	Irrigation with hydrogen peroxide SIS-anal-fistula plug Plug was pulled from the internal opening into the fistula Excess fistula plug was trimmed from both ends The fistula plug was fixed and buried within the internal sphincter at the internal opening Avoidance of occluding the external opening
El-Gazzaz et al. (36)	Irrigation with hydrogen peroxide SIS-anal-fistula plug Pull-through technique from the internal to the external opening Fixation to the internal sphincter muscle Plug material was trimmed Former internal opening was closed deeply with sutures Plug material at the external opening was trimmed at skin level No further fixation
Lupinacci et al. (35)	Tract washed out with hydrogen peroxide Plug was inserted via the primary internal orifice and pulled toward the external orifice Plug was cut flush with the anal mucosa Plug was anchored With sutures to the internal sphincter Plug was carefully covered with anal mucosa The external orifice was left open Plug was cut again and affixed to the skin
van Koperen et al. (29)	Clearing of the fistula tract with hydrogen peroxide Plug was pulled in the tract from the internal opening Plug was trimmed Plug was sutured in place with of least two sutures The external opening was left open to allow for drainage of the tract

A ba-bai-Ke-re et al. (41), the other studies had also been taken into account in the systematic review by O'Riordan et al. (3) and Garg et al. (13).

The six studies encompassed 408 patients with 167 cases of SIS-anal-fistula plug treatment and 241 with mucosa advancement flap. The difference in the overall success rates and incidence of fistula recurrence was not statistically significant between SIS-anal-fistula plug and mucosa advancement flap in complex fistula-in-ano treatment (risk difference = −0.12. 95% CI: −0.39–0.14; risk difference = 0.13; 95% CI: −0.18–0.43, respectively). However, for the SIS-anal-fistula plug, the risk of postoperative impaired continence was lower (risk difference = −0.08. 95% CI: −0.15–0.02) as was the incidence of other complications (risk difference = −0.06. 95% CI: −0.11 to 0.00). Patients treated with the SIS-anal-fistula plug had less persistent pain of a shorter duration and the healing time of the fistula and hospital stay were also reduced. Another comparative study identified similar results for treatment, in addition to cost savings for the plug-in technique because of the shorter hospital stay (42).

Other studies (43–51), which had not been included in the systematic reviews and the meta-analysis (**Table 4**) do not have any implications for the results of the systematic reviews.

It can thus be stated that treatment of complex anal fistula with SIS-anal-fistula plug is likely to be associated with a failure rate of about 50%. This result is not worse than that obtained for the mucosa advancement flap. However, the plug technique

TABLE 4 | Case series of SIS-anal-fistula plug treatment not included in the systematic reviews and meta-analyses.

Author	Year	Conflict of interest	Study design	LoE	Patients	Follow-up	Success rate	Surgical technique
Safar et al. (43)	2009	NR	Retrospective case series	4	35	Mean: 126 days	13.9%	Clearing with hydrogen peroxidate SIS-anal-fistula plug Plug was pulled through the internal opening in the fistula track The excess plug is cut and then secured to the internal opening The internal sphincter was incorporated into the stitch to have at least mucosa and submucosa covering the plug. The part protruding Through the external opening was trimmed back flush with the skin and an optimal tacking stick was placed
Owen et al. (44)	2010	NR	Retrospective case series	4	32	Median: 15 months	37%	Clearing with hydrogen peroxidate SIS-anal-fistula plug Plug was drown into the tract from the internal opening Internal aspect of the plug was trimmed to length and fixed with sutures The overlying mucosa of the anal canal was closed over the internal opening The tail of the plug was trimmed to length
Lenisa et al. (45)	2010	None	Prospective case series	4	60	Mean: 13 months	60%	Irrigation with hydrogen peroxide and gentle debridement with an endoluminal brush SIS-anal-fistula plug Pull-through technique from the internal opening The plug was than tightly secured to the internal sphincter muscle Excess material was trimmed flush to both openings The external opening was left open to drain
Kleif et a. (46)	2011	None	Retrospective case series	4	37	Median: 60.5 days	45.9%	Fistula tract was irrigated with hydrogen peroxide and brushed with a fistula brush SIS-anal-fistula plug Plug was drown through the fistula tract from the inside opening The plug was fixed to the internal sphincter. Remaining plug inside was excised and the inner Opening closed with a mucosal flap The plug in the external opening was left free of fixation, and sometimes the outer opening was even opened a bit
Chan et al. (47)	2012	None	Prospective case series	4	44	Mean: 10.5 months	50%	Track was flushed with hydrogen peroxide SIS-anal-fistula plug Pull-through from the internal opening Plurg secured at the internal opening by suture including the mucosa and submucosa The internal opening was covered by a limited mucosal flap Distal end of the plug was trimmed flush with the external end of the opening without fixation
Tan et al. (48)	2013	None	Prospective case Series	4	26	Median: 59 weeks	13.3%	Cleaning of the track with saline and hydrogen peroxide SIS-anal-fistula plug Pull-through from internal opening The plug was secured at the internal opening The plug was attached loosely to the skin at the external opening
Cintron et al. (49)	2013	Yes	Prospective case series	4	73	Mean: 15 months	Primary 38% Recurrence 40%	Fistula tract was either gently roughened with a cytette brush or debrided with curette Irrigation with hydrogen peroxide SIS-anal-fistula plug Pull-through-technique from the internal opening Plug was trimmed flush with the inner opening The plug was anchored to the mucosa/submucosa and internal sphincter The plug was completely covered with mucosa The end of the plug was then trimmed flush with the external opening

(Continued)

TABLE 4 | Continued

Author	Year	Conflict of interest	Study design	LoE	Patients	Follow-up	Success rate	Surgical technique
Blom et al. (50)	2014	NR	Retrospective case series	4	126	Median: 13 months	24%	Fistula track was flushed clean with saline or hydrogen peroxide and brushed clean of biofilm SIS-anal-fistula plug Plug was fixed to the internal sphincter Any redundant plug was trimmed of the skin level The external opening was excised to secure drainage
Adamina et al. (51)	2014	NR	Prospective case series	4	46	Median: 68.1 months	43.5%	Irrigation of track with saline or hydrogen peroxide SIS-anal-fistula plug Plug was inserted through the internal fistula opening Plug was sutured to the internal sphincter The tip of the plug was cut at the skin level and not sutured, left open for drainage

has the advantage of a lower postoperative complication rate and no negative impact on continence. More studies and technical modifications are needed to further improve the plug technique.

For example, Köckerling et al. (52) reported on a modified plug technique in which the extra-sphincteric portion of the complex anal fistula was removed by means of a limited fistulectomy and the remaining section of the fistula in the sphincter muscle was repaired using the fistula plug with fixing button. After a mean of 19.32 ± 6.9 months with a follow-up rate of 77% the success rate was 90%.

Another modification entails the use of plugs made of acellular dermal matrix instead of intestine submucosa (53–56). These are not preconfigured as a plug but are cut out from flat biological meshes. Details of the technique as well as the results are given in **Table 5**. The studies available show that success rates similar to those achieved with the SIS-anal-fistula plug can also be obtained with plugs made from acellular dermal matrix under similar technical conditions. In comparison to traditional surgical treatment, the fistula recurrence rate was significantly lower in the group treated with acellular dermal matrix (57).

In a pilot study, 10 patients with a median of 3 previous fistula operations were successfully operated on with an autologous cartilage plug from the nose or the ear. The treatment was initially successful in 90% of the patients, but two patients later developed a recurrence (58).

A relative new product for treatment of anal fistulas consists of a synthetic bioabsorbable anal fistula plug composed of a copolymer, from polyglycolic acid trimethylene carbonate, which is gradually absorbed by the body. This plug consists of a button or disc, with numerous tubes attached to it. Depending on the diameter of the fistula canal, several tubes are trimmed. The bioabsorption process is supposed to have been completed after 6–7 months (59). To date, there are only six prospective and retrospective cases series that report on treatment of anal fistulas with this synthetic bioabsorbable anal fistula plug (59–64). The results are illustrated in **Table 6**. The results obtained for the bioabsorbable fistula plug, too, are very variable, ranging from 15.8–72.7%. As in the case of the biological plug, that may be due to differences in the technical conduct of the operation (Tab. 6) or to differences in patient selection. Otherwise, the results obtained for the synthetic bioabsorbable anal fistula plug are comparable with those obtained for the plug made of biological material.

DISCUSSION

In summary, healing rates of 50–60% can be expected for treatment of complex anal fistula with a fistula plug, with a plug extrusion rate of 10–20%. That result is not worse than that achieved for the mucosa advancement flap, fibrin glue treatment or ligation of the intersphincteric tract.

The anal fistula plug poses a lower risk of postoperative impairment of sphincter muscle function and other postoperative complications than the transanal mucosal advancement flap. Such results can be achieved not only with plugs made of porcine intestinal submucosa, but also those made of other biological mesh materials, such as acellular dermal matrix, and synthetic bioabsorbable material.

TABLE 5 | Case series of complex anal fistula repair with acellular dermal matrix.

Author	Year	Conflict of interest	Study design	LoE	Patients	Follow-up	Plug material	Success rate	Surgical technique
Song et al. (53)	2008	NR	Prospective case series	4	30 with low anal fistula	30 days	Human acellular dermal matrix (ADM)	100%	Instillation of hydrogen peroxide The plug was cut out with three or four strips The ADM – plug was pulled trough from external to internal opening The ADM – material was inserted deep to the internal sphincter The excess was at skin level Care was taken to avoid complete closure of the outer opening to allow drainage. At the end of the procedure, the plug was completely buried within the fistula tract
Hammond et al. (54)	2010	Yes	RCT	2b	26 (two inter-sphincteric, seven mid transsphinteric, four low transsphinteric	Median: 29 months	Porcine acellular dermal matrix, cross-linked (Permacol)	54%	The collagen implant was cut into a strip that approximated the dimensions (width and length) of the fistula tract Drawn into position via the inner opening Excess material was trimmed at the internal and external opening Implant sutured into the tract at both openings The mucosa at the internal opening was closed over the tip of the implant
Han et al. (55)	2011	NR	Prospective case series	4	114	Median: 19.5 months	Human acellular dermal matrix	54.4%	Instillation of hydrogen peroxide Mechanical debridement with a blunt curette A conical biologic plug was fashioned from a 3 × 5 cm sheet of human ADM The plug was pulled tip-first into the internal opening The excess plug was trimmed flush with the primary opening The plug was sutured deep into the interal sphincter ADM material protruding from the secondary opening was trimmed at skin level No further fixation
Sarzo et al. (56)	2013	NR	Prospective case series	4	12	Mean: 9.3 months	Porcine acellular dermal matrix	75%	The design of the plug (wedge-shaped with sharp edges) neutralizes the forces of axial displacement and rotation Mechanical courettage of the fistular tract was performed The device was pulled into the fistula track from the internal opening A small mucosal periorificial flap was created The plug was then secured to the internal sphincter The internal opening was then closed with a mucosa plastic The plug was sutured to the external opening Finally the external opening was enlarged for drainage

TABLE 6 | Case series of complex anal fistula repair with synthetic bioabsorbable anal fistula plug.

Author	Year	Conflict of interest	Study design	LoE	Patients	Follow-up	Success rate	Surgical technique
de la Portilla et al. (60)	2011	NR	Prospective observational study	3	19	12 months	15.8%	The button or disc of the synthetic plug was secured in place at the internal opening with 2 or 3 sutures. The number of tubes was removed based on the estimated diameter. The remaining tubes were sutured together. Tubes were visible at the external opening
Ommer et al. (61)	2012a	yes	Prospective observational study	3	12	6 months	50%	Fixation of the button or disc of the synthetic plug to the sphincter at the internal opening. Coverage of the button by a mucosa flap. Excision of the external opening for better drainage
Ratto et al. (62)	2012	NR	Prospective observational study	3	11	5 months	72.7%	A small submucosal pocket was created around the internal opening. The submucosal pocket was closed including the disc of the plug in the suture. The excess tubes were trimmed of the base of the disc. The prutrading tubes were trimmed 2–3 mm beyond the surface of the perianal skin. The external opening was left open to drainage
Ommer et al. (63)	2012b	yes	Multicenter retrospective case series	4	40	6 months	50%	See Ommer et al. (61)
Heydari et al. (64)	2013	yes	Retrospective case series	4	49	12 months	69.3%	The button or disc was fixed to the mucosa by the use of absorbable sutures. One suture was run through the distal ends of the retained tubes to pull them together. Any tube segments that prutraded beyond the perineal skin were trimmed 1cm over skin level
Stamos et al. (59)	2015	yes	Prospective multicenter case series	3	93	12 months	49%	The button or disc was sutured to the anorectal wall by using at least 3 sutures. Button or disc was not covered by mucosa. The end of the retained tubes was trimmed flush with the skin. No sutures were placed in the external opening, which was left sufficiently open to allow drainage

It is possible that additional modifications to the technique, e.g., limited fistulectomy of the extrasphincter portion of the anal fistula, will further improve the outcome. Important technical steps in the successful performance of a complex anal fistula plug repair are a mechanical debridement of the fistula tract or partial removal of the extra sphincteric portion of the tract, pulling the plug tip-first in the internal opening, trimming excess plug material flush with the primary opening, suturing firmly the head of the plug into the primary opening, fixation of the tip of the plug to the edge of the secondary opening and no complete occlusion, but wide secondary opening to allow drainage.

There is a need for more high-quality prospective comparative studies which, in addition to the anal fistula diagnosis, give precise technical details of the operation technique, design and biological or synthetic material of the plugs employed as well as their fixation. Both RCTs and registries lend themselves to that effect.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at http://journal.frontiersin.org/article/10.3389/fsurg.2015.00055

REFERENCES

1. Bleier JIS, Moloo H. Current management of cryptoglandular fistula-in-ano. *World J Gastroenterol* (2011) **17**(28):3286–91. doi:10.3748/wjg.v17.i28.3286
2. Jacob TJ, Perakath B, Keighley MR. Surgical intervention for anorectal fistula. *Cochrane Database Syst Rev* (2010) **12**(5):CD006319. doi:10.1002/14651858.CD006319.pub2
3. O'Riordan JM, Datta I, Johnston C, Baxter NN. A systematic review of the anal fistula plug for patients with Crohn's and non-Crohn's related fistula-in-ano. *Dis Colon Rectum* (2012) **55**:351–8. doi:10.1097/DCR.0b013e318239dle4
4. Göttgens KWA, Smeets RR, Stassen LPS, Beets GL, Pierik M, Breukink SO. Treatment of Crohn's disease-related high perianal fistulas combining the mucosa. advancement flap with platelet-rich plasma: a pilot study. *Tech Coloproctol* (2015) **19**:455–9. doi:10.1007/s10151-015-1311-8
5. Limura E, Giordano P. Modern management of anal fistula. *World J Gastroenterol* (2015) **21**(1):12–20. doi:10.3748/wjg.v21.i1.12
6. Zmora O, Neufeld D, Ziv Y, Tulchinsky H, Scott D, Khaikin M, et al. Prospective, multicenter evaluation of highly concentrated fibrin glue in the treatment of complex cryptogenic perianal fistulas. *Dis Colon Rectum* (2005) **48**:2167–72. doi:10.1007/s10350-005-0199-1
7. Hammond TM, Grahn MF, Lunniss PJ. Fibrin glue in the management of anal fistulae. *Colorectal Dis* (2004) **6**:308–19. doi:10.1111/j.1463-1318.2004.00676.x
8. Swinscoe MT, Ventakasubramaniam AK, Jayne DG. Fibrin glue for fistula-in-ano: the evidence reviewed. *Tech Coloproctol* (2005) **9**(2):89–94. doi:10.1007/s10151-005-0204-7
9. Shawki S, Wexner SD. Idiopathic fistula-in-ano. *World J Gastroenterol* (2011) **17**(28):3277–85. doi:10.3748/wjg.v17.i28.3277
10. Sirany AME, Nygaard RM, Morken JJ. The ligation of the intersphincterеic fistula tract procedure for anal fistula: a mixed bag of results. *Dis Colon Rectum* (2015) **58**:604–12. doi:10.1097/DCR.0000000000000374
11. Johnson EK, Gaw JU, Armstrong DN. Efficacy of anal fistula plug vs fibrin glue in closure of anorectal fistulas. *Dis Colon Rectum* (2006) **49**:371–6. doi:10.1007/s10350-005-0288-1
12. The surgisis® AFP™ anal fistula plug: report of a consensus conference. *Colorectal Dis* (2007) **10**:17–20. doi:10.1111/j.1463-1318.2007.01423.x
13. Garg P, Song J, Bhatia A, Kalia H, Menon GR. The efficacy of anal fistula plug in fistula-in-ano: a systematic review. *Colorectal Dis* (2010) **12**:965–70. doi:10.1111/j.1463-1318.2009.01933.x
14. O'Connor L, Champagne BJ, Ferguson MA, Orangio GR, Schertzer ME, Armstrong DN. Efficacy of anal fistula plug in closure of Crohn's anorectal fistulas. *Dis Colon Rectum* (2006) **49**:1569–73. doi:10.1007/s10350-006-0695-y
15. Champagne BJ, O'Connor LM, Ferguson M, Orangio GR, Schertzer ME, Armstrong DN. Efficacy of anal fistula plug in closure of cryptoglandular

fistulas: long-term follow-up. *Dis Colon Rectum* (2006) **49**:1817–21. doi:10.1007/s10350-006-0755-3
16. van Koperen PJ, Hoore A, Wolthuis AM, Bemelman WA, Slores JFM. Anal fistula plug for closure of difficult anorectal fistula: a prospective study. *Dis Colon Rectum* (2007) **50**:2168–72. doi:10.1007/s10350-007-0298-2
17. Schwandner O, Stadler F, Dietle O, Wirsching RP, Fuerst A. Initial experience on efficacy in closure of cryptoglandular and Crohn's transsphincteric fistulas by the use of the anal fistula plug. *Int J Colorectal Dis* (2008) **23**:319–24. doi:10.1007/s00384-007-0398-4
18. Ky AJ, Sylla P, Steinhagen R, Steinhagen E, Khaitov S, Ly EK. Collagen fistula plug for the treatment of anal fistulas. *Dis Colon Rectum* (2008) **51**:838–43. doi:10.1007/s10350-007-9191-2
19. Thekkinkattil DK, Botterill I, Ambrose NS, Lundby L, Sagar PM, Buntzen S, et al. Efficacy of the anal fistula plug in complex anorectal fistulae. *Colorectal Dis* (2009) **11**:584–7. doi:10.1111/j.1463-1318.2008.01627.x
20. Garg P. To determine the efficacy of anal fistula plug in the treatment of high fistula-in-ano: an initial experience. *Colorectal Dis* (2009) **11**:588–91. doi:10.1111/j.1463-1318.2008.01632.x
21. Ellis CN. Bioprosthetic plugs for complex anal fistulas: an early experience. *J Surg Educ* (2007) **64**(1):36–40. doi:10.1016/j.cursur.2006.07.005
22. Lawes DA, Efron JE, Abbas M, Heppell J, Young-Fadok TM. Early experience with the bioabsorbale anal fistula plug. *World J Surg* (2008) **32**:1157–9. doi:10.1007/s00268-008-9504-1
23. Christoforidis D, Etzioni DA, Goldberg SM, Madoff RD, Mellgren A. Treatment of complex anal fistulas with the fistula plug. *Dis Colon Rectum* (2008) **51**:1482–7. doi:10.1007/s10350-008-9374-5
24. Echenique I, Mella JR, Rosado F, Echenique IA, Mella MT, Quevedo G. Puerto Rico experience with plugs in the treatment of anal fistulas. *Bol Asoc Med P R* (2008) **100**:8–12.
25. Leng QL, Jin HY. Anal fistula plug vs mucosa advancement flap in complex fistula-in-ano: a meta-analysis. *World J Gastrointest Surg* (2012) **4**(11):256–61. doi:10.4240/wjgs.v4.i11.256
26. Starck M, Bohe M, Zawadzki A. Success rate of closure of high transsphincteric fistulas using anal fistula plug. *Dis Colon Rectum* (2008) **51**:692.
27. Anyadike C, Attuwaybi B, Visco J, Butler B, Barrios G. The anal fistula plug in simple and complex fistula-in-ano: a western New York expience. *Dis Colon Rectum* (2010) **53**:575.
28. Ortiz H, Marzo J, Ciga MA, Oteiza F, Armendáriz P, Miguel de M. Randomized clinical trial of anal fistula plug versus endorectal advancement flap for the treatment of high cryptoglandular fistula in ano. *Br J Surg* (2009) **96**:608–12. doi:10.1002/bjs.6613
29. van Koperen PJ, Bemelman WA, Gerhards MF, Janssen LWM, Tets van WF, Dalsen van AD, et al. The anal fistula plug treatment compared with the mucosal advancement flap for cryptoglandular high transsphincteric perianal fistula: a double-blinded multicenter randomized trial. *Dis Colon Rectum* (2011) **54**:387–93. doi:10.1007/DCR0b013e318206043e
30. Schwandner O, Fuerst A. Preliminary results on efficacy in closure of transsphincteric and rectovaginal fistulas associated with Crohn's disease using new biomaterials. *Surg Innov* (2009) **16**(2):162–8. doi:10.1177/1553350609338041
31. Schwandner T, Roblick MH, Kierer W, Brom A, Padberg W, Hirschburger M. Surgical treatment of complex anal fistulas with the anal fistula plug: a prospective, multicenter study. *Dis Colon Rectum* (2009) **52**:1578–83. doi:10.1007/DCR0b013e3181a8fbb7
32. Zubaidi A, Al-Obeed O. Anal fistula plug in high fistula-in-ano: an early Saudi experience. *Dis Colon Rectum* (2009) **52**:1584–8. doi:10.1007/DCR.0b013e3181a90b65
33. Adamina M, Hoch JS, Burnstein MJ. To plug or not to plug: a cost-effectiveness analysis for complex anal fistula. *Surgery* (2010) **147**(1):72–8. doi:10.1016/j.surg.2009.05.018
34. McGee MF, Champagne BJ, Stulberg JJ, Reynolds H, Marderstein E, Delaney CP. Tract length predicts sucessful closure with anal fistula plug in cryptoglandular fistulas. *Dis Colon Rectum* (2010) **53**:1116–20. doi:10.1007/DCR.0b013e3181d972a9
35. Lupinacci RM, Vallet C, Parc Y, Chafai N, Tiret E. Treatment of fistula-in-ano with the surgisis® AFP™ anal fistula plug. *Gastroenterol Clin Biol* (2010) **34**:549–53. doi:10.1016/j.gcb.2009.06.021
36. El-Gazzaz G, Zutshi M, Hull T. A retrospective review of chronic anal fistulae treated by anal fistulae plug. *Colorectal Dis* (2010) **12**:442–7. doi:10.1111/j.1463-1318.2009.01802.x
37. Christoforidis D, Pieh MC, Madoff RD, Mellgren AF. Treatment of transsphincteric anal fistulas by endorectal advancement flap or collagen fistula plug: a comparative study. *Dis Colon Rectum* (2009) **52**:18–22. doi:10.1007/DCR.0b013e31819756ac
38. Chung W, Kazemi P, Ko D, Sun C, Brown CJ, Raval M, et al. Anal fistula plug and fibrin glue versus conventional treatment in repair of complex anal fistulas. *Am J Surg* (2009) **197**:604–8. doi:10.1016/j.amjsurg.2008.12.013
39. Wang JY, Garcia-Aguilar J, Sternberg JA, Abel ME, Varma MG. Treatment of transsphincteric anal fistulas: are fistula plugs an acceptable alternative? *Dis Colon Rectum* (2009) **52**:692–7. doi:10.1007/DCR.0b013e31819d473f
40. Chung W, Ko D, Sun C, Raval MJ, Brown CL, Phang PT. Outcomes of anal fistula surgery in patients with inflammatory bowel disease. *Am J Surg* (2010) **199**(5):609–13. doi:10.1016/j.amjsurg.2010.01.007
41. A ba-bai-ke-re MM, When H, Huang HG, Chu H, Lu M, Chang ZS, et al. Randomized controlled trial of minimally invasive surgery using acellular dermal matrix for complex anorectal fistula. *World J Gastroenterol* (2010) **16**:3279–86. doi:10.3748/wjg.v16.i26.3279
42. Fisher OM, Raptis DA, Vetter D, Novak A, Dindo D, Hahnloser D, et al. An outcome and cost analysis of anal fistula plug insertion vs endorectal advancement flap for complex anal fistulae. *Colorectal Dis* (2014) **17**:619–26. doi:10.1111/codi.12888
43. Safar B, Jobanputra S, Sands D, Weiss EG, Nogueras JJ, Wexner SD. Anal fistula plug: initial experience and outcomes. *Dis Colon Rectum* (2009) **52**:248–52. doi:10.1007/DCT.0b013e31819c96ac
44. Owen G, Keshava A, Stewart P, Patterson J, Chapuis P, Bokey E, et al. Plugs unplugged. Anal fistula plug: the Concord experience*. *ANZ J Surg* (2010) **80**:341–3. doi:10.111/j.1445-2197.2010.05278.x
45. Lenisa L, Espin-Basany E, Rusconi A, Mascheroni L, Escoll-Rufino J, Lozoya-Trujillo R, et al. Anal fistula plug is a valid alternative option for the treatment of complex anal fistula in the long term. *Int J Colorectal Dis* (2010) **25**:1487–93. doi:10.1007/s00384-010-0957-y
46. Kleif J, Hagen K, Wille-Jørgensen P. Acceptable results using plug for the treatment of complex anal fistulas. *Dan Med Bull* (2011) **58**(3):A4254.
47. Chan S, McCullough J, Schizas A, Vasas P, Engledow A, Windsor A, et al. Initial experience of treating anal fistula with the surgisis anal fistula plug. *Tech Coloproctol* (2012) **16**:201–6. doi:10.1007/s10151-012-0810-0
48. Tan KK, Kaur G, Byrne CM, Young CJ, Wright C, Solomon MJ. Long-term outcome of the anal fistula plug for anal fistula of cryptoglandular origin. *Colorectal Dis* (2013) **15**:1510–4. doi:10.1111/codi.12391
49. Cintron JR, Abcarian H, Chaudhry V, Singer M, Hunt S, Birnbaum E, et al. Treatment of fistula-in-ano using a porcine small intestinal submucosa anal fistula plug. *Tech Coloproctol* (2013) **17**:187–91. doi:10.1007/s10151-012-0897-3
50. Blom J, Husberg-Sellberg B, Lindelius A, Gustafsson UM, Carlens S, Oppelstrup H, et al. Results of collagen plug occlusion of anal fistula: a multicenter study of 126 patients. *Colorectal Dis* (2014) **16**:626–30. doi:10.1111/codi.12585
51. Adamina M, Ross T, Guenin MO, Warschkow R, Rodger C, Cohen Z, et al. Anal fistula plug: a prospective evaluation of success, continence and quality of life in the treatment of complex fistulae. *Colorectal Dis* (2014) **16**:547–54. doi:10.1111/codi.12594
52. Köckerling F, Rosen von T, Jacob D. Modified plug repair with limited sphincter sparing fistulectomy in the treatment of complex anal fistulas. *Front Surg* (2014) **1**:17. doi:10.3389/fsurg.2014.00017
53. Song WL, Wang ZJ, Zheng Y, Yang XQ, Peng YP. A anorectal fistula treatment with acellular extracellular matrix: a new technique. *World J Gastroenterol* (2008) **14**(30):4791–4. doi:10.3748/wjg.14.4791
54. Hammond TM, Porrett TR, Scott SM, Williams NS, Lunniss PJ. Management of idiopathic and fistula using cross-linked collagen: a prospective phase 1 study. *Colorectal Dis* (2010) **13**:94–104. doi:10.1111/j.1463-1318.2009.02087.x
55. Han JG, Wang ZJ, Zhao C, Zheng Y, Zhao B, Yi BQ, et al. Long-term outcomes of human acellular dermal matrix plug in closure of complex anal fistulas with a single tract. *Dis Colon Rectum* (2011) **54**:1412–8. doi:10.1097/DCR.0b013e31822c5398
56. Sarzo G, Finco C, Mungo B, Gruppo M, Cadrobbi R, Polese L, et al. Anal fistula repair with acellular dermal matrix plug: description of a novel technique and early results. *J Surg* (2013) **1**(1):1–6 and non-Crohn's related fistula-in-ano. *Dis Colon Rectum* **55**:351–58. doi:10.1097/DCR.0b013e318239dle4
57. Cirocchi R, Trastulli S, Morelli U, Desiderio J, Boselli C, Parisi A, et al. The treatment of anal fistulas with biologically derived products: is innovation

better than convertional surgical treatment? An update. *Tech Coloproctol* (2013) **17**:259–73. doi:10.1007/s10151-012-0948-9
58. Ozturk E. Treatment of recurrent anal fistula using an autologous cartilage plug: a pilot study. *Tech Coloproctol* (2015) **19**:301–7. doi:10.1007/s10151-015-1299-0
59. Stamos MJ, Snyder M, Robb BW, Ky A, Singer M, Stewart DB, et al. Prospective multicenter study of a synthetic bioabsorbable anal fistula plug to treat cryptoglandular transsphincteric anal fistulas. *Dis Colon Rectum* (2015) **58**:344–51. doi:10.1097/DCR0000000000000288
60. de la Portilla F, Rada R, Jiménez-Rodriguez R, Diaz-Pavon JM, Sanchez-Gil JM. Evaluation of a new synthetic plug in the treatment of anal fistulas: results of a pilot study. *Dis Colon Rectum* (2011) **54**:1419–22. doi:10.1097/DCR.0b013e31822c4d59
61. Ommer A, Schmidt C, Rolfs T, Walz MK. Gore Bio-A Fistelplug zur Behandlung hoher Analfisteln. *Coloproctology* (2012) **34**:24–30. doi:10.1007/s00053-011-0245-5
62. Ratto C, Litta F, Parello A, Donisi L, Zaccone G, De Simone V. Gore Bio-A® fistula Plug: a new sphincter-sparing procedure for complex anal fistula. *Colorectal Dis* (2012) **14**:e264–9. doi:10.1111/j.1463-1318.2012.02964.x
63. Ommer A, Herold A, Joos A, Schmidt C, Weyand G, Bussen D. Gore BioA fistula plug in the treatment of high anal fistulas – initial results from a German multicenter-study. *Ger Med Sci* (2012) **10**:Doc13. doi:10.3205/000164
64. Heydari A, Attinà GM, Merolla E, Piccoli M, Fazlalizadeh R, Melotti G. Bioabsorbable synthetic plug in the treatment of anal fistulas. *Dis Colon Rectum* (2013) **56**:774–9. doi:10.1097/DCR.0b013e3182839824

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

frontiers in Surgery

MINI REVIEW
published: 15 September 2015
doi: 10.3389/fsurg.2015.00048

Biological meshes for inguinal hernia repair – review of the literature

Ferdinand Köckerling[1], Nasra N. Alam[2], Sunil K. Narang[2], Ian R. Daniels[2] and Neil J. Smart[2]*

[1] *Department of Surgery, Center for Minimally Invasive Surgery, Academic Teaching Hospital of Charité Medical School, Vivantes Hospital, Berlin, Germany,* [2] *Exeter Surgical Health Services Research Unit (HeSRU), Royal Devon and Exeter Hospital, Exeter, UK*

Introduction: Biological meshes are a potential alternative to the synthetic meshes to avoid complications and are used in a contaminated field for incarcerated inguinal hernias. The clinical experiences gained with biological meshes for repair of inguinal hernias are presented in this review.

Materials and methods: In a literature search of the Medline database using the key word "Biological mesh," 2,277 citations were found. There remained 14 studies in which biological meshes had been used to repair inguinal hernias.

Results: In prospective randomized trials, the use of polypropylene vs. biological meshes was compared in open inguinal hernia repair. There was no difference in the recurrence rate, but differences were observed in the postsurgical pain incidence in favor of the biological mesh. In the remaining retrospective studies, the recurrence rates were also acceptable. The biological mesh was used successfully in a potentially contaminated setting.

Conclusion: Inguinal hernias can be repaired with biological meshes with reasonable recurrence rate, also as an alternative in a potentially contaminated field.

Keywords: biological mesh, inguinal hernia, contaminated field, recurrence, pain

OPEN ACCESS

Edited by:
Hakan Kulacoglu, Rize University, Turkey

Reviewed by:
Kun-Ming Chan, Linkou Chang Gung Memorial Hospital, Taiwan
Ulf Gunnarsson, Karolinska Institutet, Sweden

****Correspondence:***
Ferdinand Köckerling, Department of Surgery, Center for Minimally Invasive Surgery, Academic Teaching Hospital of Charité Medical School, Vivantes Hospital, Neue Bergstraße 6, Berlin D-13585, Germany
ferdinand.koeckerling@vivantes.de

Specialty section:
This article was submitted to Visceral Surgery, a section of the journal Frontiers in Surgery

Received: *22 July 2015*
Accepted: *01 September 2015*
Published: *15 September 2015*

Citation:
Köckerling F, Alam NN, Narang SK, Daniels IR and Smart NJ (2015) Biological meshes for inguinal hernia repair – review of the literature Front. Surg. 2:48. doi: 10.3389/fsurg.2015.00048

Introduction

The Guidelines of the European Hernia Society state, based on evidence level 1 A, that operation techniques using mesh result in fewer recurrences than techniques, which do not use mesh (1). Although mesh repair appears to reduce the likelihood of chronic groin pain rather than increase it (1), mesh can cause considerable pain and stiffness around the groin and affect physical functioning (2). This has led to various types of mesh being engineered, with a growing interest in lighter weight polypropylene (PP) meshes (2), absorbable meshes (3), and biological meshes. For open inguinal hernia repair the use of light-weight PP meshes was not associated with an increased risk of hernia recurrence. Light-weight PP meshes reduce the incidence of chronic groin pain as well as the risk of developing other groin symptoms (4). To avoid complications, the use of absorbable meshes – such as those made of lactic acid polymer or lactic and glycolic acid copolymers – has been proposed. This exposes the patient to inevitable hernia recurrence because the inflammatory response, through a hydrolytic reaction, completely digests the implanted prosthetic material (3, 5).

Another potential alternative to the synthetic meshes is biological meshes which, unlike absorbable meshes, are not completely degraded; instead, these induce a remodeling process, i.e., the biological mesh is incorporated into the host through the reproduction of new site-specific

tissue. The clinical experiences gained with biological meshes for repair of inguinal hernias are presented below.

Materials and Methods

A literature search of the Medline database was performed using the PubMed search engine. The following key words were used: Biological mesh; inguinal hernia OR Groin hernia AND Biological mesh OR Biomesh OR Biological. 2,277 citations were found. After checking the title and abstracts, there remained seven prospective randomized trials (RCTs) (5–11). In one of these seven RCTs (**Table 1**), the results were reported for a smaller sample size (6) from the entire study (5) at an earlier follow-up time point. For two RCTs, only an abstract is available (8, 9). Recently, two meta-analyses were also published reporting on three and four RCTs, respectively (12, 13). Furthermore, there are five retrospective case series available (14–18), in which biological meshes had been used to repair inguinal hernias and the corresponding follow-up results reported (**Table 2**). These are also described below.

Results

In a prospective randomized double-blind trial (5, 6), Lichtenstein's inguinal hernia repair was compared using a PP or a small intestine submucosa (SIS) mesh. Seventy male patients underwent Lichtenstein's hernioplasty, with 35 patients in the SIS group and 35 patients in the PP group. At 3 years after surgery, there were two deaths (5.7%) in the PP group and one death (2.9%) in the SIS group (NS). Only one recurrence (2.9%) was seen in the PP group (NS). Although a significant decrease in the postsurgical pain incidence was never observed among patients in the SIS group, a significantly lower degree of pain was detected at rest and on coughing at 1, 3, and 6 months and on movement at 1, 3, and 6 months and 1, 2, and 3 years. A significant decrease in the postsurgical incidence and degree of discomfort when coughing and moving were observed among patients in the SIS group at 3 and 6 months and at 1, 2, and 3 years after surgery. The authors concluded that SIS hernioplasty seems to be a safe and effective procedure.

TABLE 1 | Characteristics and outcomes of RCTs on inguinal hernia repair with the use of biologic vs. polypropylene mesh.

Reference	Study design	Patients characteristic	Mesh material	Intervention details	Follow-up	Outcome	Conflict of interest	LoE
(8) Abstract only	Prospective blinded randomized trial	$n = 140$ primary inguinal hernias	Collagen mesh vs. polypropylene	Open procedures	12 months	One recurrence in each group	NR	1b
(6)	Prospective double-blinded randomized trial	$n = 20$ primary inguinal hernias	SIS vs. polypropylene	Lichtenstein in general or spinal anesthesia	6 months	No recurrence, no wound infection, no post-hemioplasty acute and chronic pain/discomfort, parenteral/oral analgesic consumption were lower in surgisis group	NR	1b
(7)	Prospective randomized trial	$n = 45$ male patients with inguinal hernia	SIS vs. polypropylene vs. polylactic and polypropylene	Lichtenstein in local anesthesia	Mean: 12 months (1–16)	No recurrence, postoperative pain lower with SIS, full recovery shorter with SIS	NR	1b
(9) Abstract only	Prospective blinded randomized trial	$n = 201$	Porcine dermal collagen vs. polypropylene	Open procedure	24 months	No difference in recurrence rate, collagen repairs had improved pain scores	NR	1b
(5)	Double-blinded RCT	$n = 70$ primary inguinal hernia	SIS vs. polypropylene	Lichtenstein in general or spinal anesthesia	36 months	One recurrence in the PP group; significant lower pain degree for the SIS group	NR	1b
(10)	Prospective, double-blinded, single-center randomized trial	$n = 100$	Biodesign Inguinal Hernia Matrix (IHM) vs. polypropylene	Lichtenstein in local anesthesia	12 months	Three recurrences in the IHM group vs. 0 in the polypropylene group ($p = 0.11$). Persistent pain trended higher in the polypropylene group	Grant from producer of IHM	1b
(11)	Prospective, double-blinded, multicenter randomized trial	$n = 172$	Strattice vs. Ultrapro	Lichtenstein in local or general anesthesia	3 months	No recurrence, no wound complication, impairment caused by the hernia decreased significantly in both groups, less postoperative pain days 1 and 3 in the Strattice group	Grant form producer of Strattice	1b

TABLE 2 | Characteristics and outcomes of studies reporting on inguinal hernia repair with the use of biologic mesh.

Reference	Study design	Patients characteristic	Mesh material	Intervention details	Follow-up	Outcome	Conflict of interest	LoE
(14)	Retrospective case series	$n = 137$ male patients $n = 16$ emergency cases	Porcine dermis (Zenoderm)	Modified Notaras-technique	Mean: 48 months	Two recurrences (1.25%)	NR	4
(18)	Retrospective case series	$n = 15$ potentially or grossly contaminated field	SIS	Laparoscopic TAPP	Median: 19 months (1–30)	No recurrence	NR	4
(17)	Retrospective case series	$n = 10$ sports hernia. Professional or amateur athletes	SIS	TEP; 7 cm × 10 cm mesh size, fixation with five tacks (Protack), one patient had only fibrin glue fixation	12 months	Nine improved, one not	NR	4
(15)	Retrospective case series	$n = 38$ patients with 45 primary and 6 recurrent inguinal hernias	SIS	TEP; 7 cm × 10 cm mesh size, fibrin glue fixation	Mean: 13 months (1–30)	One recurrence (2%), three patients chronic pain (7.9%)	NR	4
(16)	Retrospective case series	$n = 11$	SIS	TAPP; Fibrin glue fixation	Mean: 14.5 ± 1 month	One recurrence	NR	4

In a prospective RCT (7), Lichtenstein inguinal hernioplasty was performed in local anesthesia, using prolene (PP) or vypro (polylactin and PP) or SIS. The median follow-up was 12 months, with a range of 1–16 months. No recurrent hernias were observed. Postoperative pain (visual analog scale) and discomfort were lower in patients with SIS. There was a tendency toward a higher incidence of pain and discomfort in the vypro and prolene group.

In an abstract as interim report, Macklin et al. (8) have treated 140 patients in a prospective RCT receiving either PP or collagen mesh. Postoperatively, there was an increase in hematoma in the PP group ($p = 0.048$). Infection and inflammation were similar postoperatively and at 3 months. There was one recurrent hernia in each group in 1 year.

Initial results showed that collagen mesh is an effective method of providing tissue repair in primary inguinal hernia.

In another abstract, Ridgway et al. (9) reported on a blinded randomized controlled trial comparing porcine dermal collagen with PP for primary inguinal hernia repair in 201 patients. Recurrence, inflammation, infection, and hematoma rates were comparable at all time intervals. Collagen repairs had improved pain scores at 2 years. The authors concluded that inguinal hernia repair using modified porcine dermal collagen can be performed successfully.

In another prospective, randomized, double-blinded, single-center study (10), the use of a Biodesign Inguinal Hernia Matrix (IHM) vs. a PP mesh for Lichtenstein operation was compared for 100 patients. The follow-up period was 1 year. Three recurrences were observed in the IHM group and none in the PP group ($p = 0.11$). There was a higher tendency toward persistent pain in the PP group (6 vs. 4%).

Likewise, in a prospective randomized, double-blinded multi-center study (11) that compared the use of Strattice vs. Ultrapro for Lichtenstein operation in 100 patients, no differences were observed in the wound complication rate after 3 months. No recurrences occurred in any of the two groups, nor any difference was seen in postoperative pain after 3 months.

On pooling, the results of the three (5, 7, 10) aforementioned RCTs, each of which used small intestinal submucosa (SIS), no difference was found in the recurrence and pain rate after 1 year (12). Only the discomfort rate was lower in the SIS group, but the seroma rate was higher. Likewise, these findings are confirmed in the meta-analysis of four (5, 7, 10, 11) RCTs (13).

In a retrospective case series Holl-Allen (14) published the results of 137 consecutive unselected male patients with inguinal hernias treated with Zenoderm as the repair material after a mean follow-up of 48 months. There have been two indirect recurrences after 11 and 14 months, representing a low recurrence rate of 1.25%.

In three retrospective case series (15–18) with 10–38 patients, inguinal hernias were repaired in an endoscopic technique (TEP, TAPP) with SIS. During a mean follow-up period of 12–14.5 months, a recurrence rate of 2 and 9.1% was observed, respectively (15, 16). No improvement in symptoms was seen in one patient with a sports hernia following TEP operation with SIS (17). In another study the biological meshes (SIS) were used successfully even in a potentially contaminated setting, i.e., with incarcerated/strangulated bowel within the hernia or coincident with a laparoscopic cholecystectomy/colectomy as well as in a grossly contaminated field (i.e., gross pus or fecal spillage) (18).

Discussion

Inguinal hernias can be repaired with biological meshes, and with a reasonable recurrence rate. This applies for a period of 3 years for the Lichtenstein operation and of 1 year for the endoscopic TEP and TAPP techniques. As such, biological meshes can be used as an alternative in a potentially contaminated field for incarcerated inguinal hernia or coincident with a laparoscopic cholecystectomy or colectomy as well as in a setting grossly contaminated with pus or fecal spillage (18). However, this was a retrospective case series rather than a RCT. The RCTs identified demonstrated the equivalence of a biological mesh and the PP mesh in terms of the

recurrence rate as well as reduced pain at rest, on coughing or on movement. Because of the very small sample size, the equivalence of biological meshes and synthetic meshes with regard to recurrence rate and reduced pain must be verified in further studies. Besides, in none of the studies were the higher costs incurred for the biological meshes analyzed. Since the biological meshes do not have any major advantages over the synthetic meshes with respect to the most important assessment criteria, at present they can only be recommended for situations involving a contaminated surgical field.

References

1. Simons MP, Aufenacker T, Bay-Nielsen M, Bouillot JL, Campanelli G, Conze J, et al. European hernia society guidelines on the treatment of inguinal hernia in adult patients. *Hernia* (2009) **13**:343–403. doi:10.1007/s10029-009-0529-7
2. Currie A, Andrew H, Tonsi A, Hurley PR, Taribagil S. Lightweight versus heavyweight mesh in laparoscopic inguinal hernia repair: a meta-analysis. *Surg Endosc* (2012) **26**(8):2126–33. doi:10.1007/s00464-012-2179-6
3. Tyrell J, Silberman H, Chandrasoma P, Niland J, Shull J. Absorbable versus permanent mesh in abdominal operations. *Surg Gynecol Obstet* (1989) **168**(3):227–32.
4. Sajid MS, Leaver C, Baig MK, Sains P. Systematic review and meta-analysis of the use of lightweight versus heavyweight mesh in open inguinal hernia repair. *Br J Surg* (2011) **99**(1):29–37. doi:10.1002/bjs.7718
5. Ansaloni L, Catena F, Coccolini F, Gazzotti F, D'Alessandro L, Pinna AD. Inguinal hernia repair with porcine small intestine submucosa: 3-year follow-up results of a randomized controlled trial of Lichtenstein's repair with polypropylene mesh versus surgisis inguinal hernia matrix. *Am J Surg* (2009) **198**:303–12. doi:10.1016/j.amjsurg.2008.09.021
6. Ansaloni L, Catena F, D'Alessandro L. Prospektive randomized, double-blind, controlled trial comparing Lichtenstein's repair of inguinal hernia with polypropylene mesh versus surgisis gold soft tissue graft: preliminary results. *Acta Biomed* (2003) **74**(Suppl 2):10–4.
7. Puccio F, Solazzo M, Marciano P. Comparison of three different mesh materials in tension-free inguinal hernia repair: prolene versus vypro versus surgisis. *Int Surg* (2005) **90**(3 Suppl):21–3.
8. Macklin C, Moore P, Foster L, Peters J, Dent K. A prospective blind randomized trial comparing collagen mesh with polypropylene mesh in primary inguinal hernia repair: an interim report. *Br J Surg* (2002) **89**(Suppl 1):18. doi:10.1046/j.1365-2168.89.s.1.9_4.x
9. Ridgway DM, Mahmood F, Moore L, Bramley D, Stojkovic S, Al-Muhktar A, et al. A blinded randomised controlled trial comparing porcine dermal collagen with polypropylene for primary inguinal hernia repair. *J Am Coll Surg* (2007) **205**(3S):S69. doi:10.1016/j.jamcollsurg.2007.06.172
10. Bochicchio GV, Jain A, McGonigal K, Turner D, Ilahi O, Reese S. Biologic vs synthetic inguinal hernia repair: 1-year results of a randomized double-blinded trial. *J Am Coll Surg* (2014) **218**(4):751–7. doi:10.1016/j.jamcollsurg.2014.01.043
11. Bellows CF, Shadduck P, Helton WS, Martindale R, Stouch BC, Fitzgibbons R. Early report of a randomized comparative clinical trial of Strattice™ reconstructive tissue matrix to lightweight synthetic mesh in the repair of inguinal hernias. *Hernia* (2014) **18**:221–30. doi:10.1007/s10029-013-1076.9
12. Nie X, Xiao D, Wang W, Song Z, Yang Z, Chen Y, et al. Comparison of porcine small intestinal submucosa versus polypropylene in open inguinal hernia repair: a systematic reciew and meta-analysis. *PLoS One* (2015) **10**(8):e135073. doi:10.1371/journal.pone.0135073
13. Fang Z, Ren F, Zhou J, Tian J. Biologic mesh versus synthetic mesh in open inguinal hernia repair: system review and meta-analysis. *ANZ J Surg* (2015). doi:10.1111/ans.13234
14. Holl-Allen RTJ. Porcine dermal collagen repair of inguinal hernias. *J R Coll Surg Edinb* (1984) **29**:154–7.
15. Fine AP. Laparoscopic repair of inguinal hernia using surgisis mesh and fibrin sealant. *JSLS* (2006) **10**:461–5.
16. Agresta F, Bedin N. Transabdominal laparoscopic inguinal hernia repair: is there a place for biological mesh? *Hernia* (2008) **12**:609–12. doi:10.1007/s10029-008-0390-0
17. Edelman DS, Selesnick H. "Sports" hernia: treatment with biologic mesh (surgisis). A preliminary study. *Surg Endosc* (2006) **20**:971–3. doi:10.1007/s00464-005-0281-8
18. Franklin ME Jr, Gonzalez JJ Jr, Glass JL. Use of porcine small intestinal submucosa as a prothetic device for laparoscopic repair of hernias in contaminated fields: 2-year follow-up. *Hernia* (2004) **8**:186–9. doi:10.1007/s10029-004-0208-7

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

Appendix

BioMesh Study Group

Ferdinand Köckerling (Chairman), Stavros Antoniou, René Fortelny, Frank A. Granderath, Markus Heiss, Franz Mayer, Marc Miserez, Agneta Montgomery, Salvador Morales-Conde, Filip Muysoms, Alexander Petter-Puchner, Rudolph Pointner, Neil Smart, Marciej Smietanski, and Bernd Stechemesser.

Aim

The BioMesh Study Group has set itself the task of identifying how best to use biological meshes for the various indications. The first step toward achieving that goal is to compile systematic reviews of the different indications on the basis of the existing literature. The available literature sources will be evaluated in accordance with the Oxford Centre for Evidence-based Medicine-Levels of Evidence (March 2009). Next, based on the review findings corresponding Statements and Recommendations are to be formulated in a Consensus Conference for the use of biological meshes for the different indications. The findings of the Consensus Conference are then to be summarized for a joint publication. This present publication is part of the project undertaken by the BioMesh Study Group.

Advantages of publishing in Frontiers

OPEN ACCESS
Articles are free to read for greatest visibility and readership

FAST PUBLICATION
Around 90 days from submission to decision

HIGH QUALITY PEER-REVIEW
Rigorous, collaborative, and constructive peer-review

TRANSPARENT PEER-REVIEW
Editors and reviewers acknowledged by name on published articles

Frontiers
Avenue du Tribunal-Fédéral 34
1005 Lausanne | Switzerland

Visit us: www.frontiersin.org
Contact us: info@frontiersin.org | +41 21 510 17 00

REPRODUCIBILITY OF RESEARCH
Support open data and methods to enhance research reproducibility

DIGITAL PUBLISHING
Articles designed for optimal readership across devices

FOLLOW US
@frontiersin

IMPACT METRICS
Advanced article metrics track visibility across digital media

EXTENSIVE PROMOTION
Marketing and promotion of impactful research

LOOP RESEARCH NETWORK
Our network increases your article's readership