Review

Biological meshes for abdominal hernia: Lack of evidence-based recommendations for clinical use

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ABSTRACT

Background: In the clinical literature on abdominal hernia repair, no sound criteria have been established to support the use of biological meshes as opposed to synthetic ones. Furthermore, the information on biological meshes is quite scarce, and so their place in therapy has not yet been defined.

Methods: The treatment of primary and incisional ventral hernia was the target intervention evaluated in our analysis. Our study consisted of the following phases: a) identification of the biologic meshes available on the market; b) literature search focused on efficacy and safety of these meshes; c) Analysis of the findings derived from the literature search. The information collected this way was reviewed narratively, and presented according to standard meta-analysis. The main end-points of our analysis included infection of surgical wound at 1 month and recurrence at 12 months.

Results: Our clinical literature comprised 11 trials that evaluated 5 biological meshes: Permacol (706 patients), Strattice (324 patients), Surgisis (44 patients), Tutumesh (38 patients) and Xenmatrix (22 patients). These studies generally showed a poor methodological quality. Surgical wound infection showed a wide between-study variability (95% CI: 12.0% to 23.9%). Also the 12-month relapse rate demonstrated a wide 95% CI (from 6.2% to 24.7%). A significantly lower rate of recurrence at 12 months was found for Permacol compared with Strattice (rate difference: −14.2%; 95% CI: −22.1% to −6.2%).

Discussion: Our analysis provided an overview of 5 biological meshes currently available on the market. The different types of meshes showed a marked statistical variability in the clinical outcomes. Hence, nearly all comparisons between different meshes in the two clinical end-points did not reach statistical significance. One exception was represented by the finding that cross-linked meshes had a significantly lower recurrence rate at 12 months than non-cross-linked meshes.

1. Introduction

To date, no wide consensus has been reached about the type of mesh to be used for reconstructing the abdominal wall [1–4]. The choice of a biological mesh as opposed to a synthetic mesh generally tends to be guided by the type of surgical wound, but sound information on this point is lacking. Some studies have suggested that biological meshes, compared to synthetic ones, can better withstand infections and so, these meshes are believed to be more suitable for contaminated wounds [1–5]. On the other hand, from a recent meta-analysis that compared biological to synthetic meshes in contaminated fields, biological meshes did not add any additional benefit in terms of incidence of surgical site infections or incidence of relapses [1]. Unfortunately, the evidence from this meta-analysis is weak, mainly because of the poor methodological quality of the original clinical trials that were included. For example, the main limitations of these clinical trials were the adoption of uncontrolled designs, the short follow-up, and the inclusion of small cohorts of patients [1].

In all, the current clinical literature does not allow to support the use of a biological mesh over a synthetic mesh, and therefore no consensus has been achieved about the place in therapy that can be recognized to biological meshes [6]. Even less definite are the indications for choosing a particular biological mesh among the variety of biological meshes currently available. In particular, it is difficult to make
the decision of using a porcine rather than a bovine mesh, or a cross-linked mesh as opposed to a non-cross-linked one [1,4,7].

The aim of this paper is not to focus on the comparison of biologic meshes with synthetic meshes, but to investigate the differences, if any, among the various biological products for the treatment of abdominal hernias.

2. Methods

2.1. Study design

The treatment of primary and incisional ventral hernia was the target intervention evaluated in our analysis. Our study consisted of the following phases: a) Identification of the biologic meshes available on the market; b) Literature search focused on efficacy and safety of biologic meshes; c) Analysis of findings derived from the literature search.

2.2. Identification of biologic meshes available on the market

The biological meshes available on the market were extracted from the national database on medical devices of the Ministry of Health.

2.3. Literature search

Our search was based on PubMed and Embase and covered the last 20 years. The keywords reflected the name of the meshes identified through the national database. Therefore, our search terms were: “hernia AND (permacol OR strattice OR veritas OR xenmatrix OR surgisis OR forteva OR dura-guard OR peri-guard OR periguard OR vasuguard OR biopip OR surgimen)”. Included studies were those that satisfied each of the following criteria: 1) Treatment of primary and incisional abdominal hernia; 2) Meshes derived from porcine dermis or porcine intestinal submucosa or bovine pericardium or bovine dermis or fetal that may or may not involve “cross-linking of collagen” within the prosthetic; 3) End-point: 30-day follow-up surgical site infection and/or relapse rate after follow-up of at least 12 months. The flow of our literature search was summarized according to the PRISMA diagram [8].

2.4. Analysis of literature data

Incidence of infection at 30 days and/or relapse after follow-up of at least 12 months were the two end-points of our analysis. The analysis was mainly based on a descriptive approach.

2.5. Statistical testing

The two end-points of our analysis were examined through standard statistical tests. A proportion meta-analysis based on random-effect model [9] was employed to determine group-specific event estimates (with 95% confidence interval, CI) from single-arm studies employing the same brand. The unpaired t-test for independent samples in two-sample data sets and meta-regression in meta-analyses data-sets [9] were employed to assess between-group differences. Significance level was set at < 0.05.

3. Results

3.1. Identification of biologic meshes available on the market


3.2. Literature search

Our search based on PubMed and Embase is shown in Fig. 1. The 9 studies that did not meet our inclusion criteria are represented by Refs. [7,10-17], while those included by Refs. [6,18-27]. The final number of included studies was 11.

3.3. Analysis of included studies and results

Overall, our clinical literature comprised 11 trials (see Table 1) that evaluated 5 biological meshes: Permacol (for a total of 706 patients), Strattice (for a total of 324 patients), Surgisis (for a total of 44 patients), Tutomesh (for a total of 38 patients) and Xenmatrix (for a total of 22 patients).

The 11 clinical studies generally showed a poor methodological quality that made it difficult to establish a specific “place in therapy” for these products. The most critical features of the studies were the following: non-comparative design, different follow-up periods, and heterogeneous definition of the clinical end-points. The classification of the wound was based on the criteria of Centers for Disease Control (Class I, Clear; Class II, Clean-contaminated; Class III, Contaminated and IV Class, Infected) [28]) or Hernia Grading System (Hernia Working Group), which is based on the risk factors related to the patient and to the wound (grade I, low risk; grade II, co-morbidity; grade III, potentially contaminated and grade IV, infected) [5].

Fig. 2 shows incidence data for surgical wound infection, broken down by single study and mesh type. The Forest plot confirms the wide variability of this data as confirmed by the I² value of 85% and by the wide 95%CI of this outcome (from 12.0% to 22.9%). There was no significant difference in this end-point between the different groups of meshes (difference in rate for Strattice vs Permacol, −5.6%; 95%CI: −18.7% to +7.5%; p = 0.40; difference in rate for other vs Permacol, +2.0%; 95%CI: −14.3% to +18.3%; p = 0.81). As regards the cross-linked vs non-cross-linked nature of the meshes, non cross-linked products showed a lower rate of infections (difference: −3.5%; 95%CI: −14.8% to +7.9%), which did not reach statistical significance.

With regard to the 12-month relapse rate, this information was only present in 4 studies (Fig. 3); even in this case, there was a significant heterogeneity (I² = 86%) and the 95%CI was wide (from 6.2% to 24.7%). Interestingly enough, a significantly greater rate was found for Strattice compared with Permacol (rate difference: +14.2%; 95%CI: +6.2% to +22.1%; p = 0.001). Of course, the comparison between non-cross-linked (Strattice) and cross-linked (Permacol) gave the same result.

4. Discussion

Our analysis provided a quite complete overview of biological meshes currently available on the market. Despite the meta-analytical nature of our study, the different types of meshes were mainly examined through a descriptive approach because the outcomes showed a marked statistical variability, and the between-meshes comparisons (with just a single exception) remained far from suggesting any product-related differences in outcomes.

The most critical feature of the studies selected from our literature search was the non-comparative design; in fact, among the 11 included
studies, 9 were single-arm (both prospective or retrospective), and only 2 were based on a comparative design.

The quality of the clinical literature was poor, and also the amount of clinical information was quite limited. If we consider all biological meshes currently available on the market, the literature we retrieved shows that only 5 out of 9 products have been evaluated in clinical studies (namely: Pervacol, Stratific, Surgisis, Tutomesh, and Xenumatrix). In contrast, for the other 4 meshes (Fortiva, Veritas, Bioripar and Tutomesh) there was no published literature.

Compared to the other meshes, Pervacol was studied in the largest number of patients (n = 706), followed by Stratific (n = 324), Surgisis (n = 44), Tutomesh (n = 38), and Xenumatrix (n = 22).

Among all comparisons carried out within these biological meshes, we found just a single significant difference in that Pervacol (a cross-linked mesh) showed a lower recurrence rate at 12 months than Stratific (a non-cross-linked mesh). Although this is an indirect comparison that does not represent a conclusive evidence, this result suggests the resistance of biological meshes can be strengthened by cross-linking.

More interestingly, the overall framework of biological mesh effectiveness resulting from our study deserves some indirect comparisons with the results previously reported by Holihan et al. for synthetic meshes [29]. From these comparisons, some insight emerges concerning the respective clinical indications of these devices.

As regards the occurrence of surgical site infection at 30 days, the pooled rate of this end-point for biological meshes (17.5%; 95%CI: 12.0%–22.9%) was higher than that reported by Holihan et al. [29] for synthetic meshes (crude rate = 8.58%; pooled rate = 8.4%; 95%CI: 4.1%–12.8%; n = 9; I² = 50%). Likewise, the pooled rate of relapse at 12 months was higher for biological meshes (+14.2%; 95%CI: +6.2% to +22.1%) than that reported by Holihan et al. [29] for synthetic meshes (crude rate = 9.94%; pooled rate = 8.0%; 95%CI: 3.7%–12.4%; n = 9; I² = 6.0% (p < 0.05).

These comparisons, however, do not allow us to draw any firm conclusion about the difference in these outcomes because these findings likely reflect the different characteristics of the patient cohorts receiving these implants. In other words, one hypothesis is that the population given biological meshes was at higher risk of surgical site infection or recurrence than that given synthetic meshes.
Table 1
Summary of the 11 included studies.

<table>
<thead>
<tr>
<th>Authors (study design)</th>
<th>Clinical indication and patients characteristics</th>
<th>Type of mesh (brand-name and main characteristics)</th>
<th>Rate of surgical site infection at 30 days (n/N, %)</th>
<th>Relapse at 1 year or more (n/N, %)</th>
</tr>
</thead>
</table>
| Giordano 2015 [19] (single-arm, retrospective, multi-center) | Repair of abdominal hernia (primary or incisional)  
ASA grade: 2 or 3 in 90% of patients  
Hernia size: not reported.  
Type of wound: 37 (31.9%) clean, 43 (39.4%) clean contaminated, 21 (19.3%) contaminated, 8 (7.3%) infected. | Permacol (porcine, cross-linked) | 15/109 (13.8%) | 10/109 (9.2%) at 12 months of follow-up, 20/109 (18.3%) at 24 months of follow-up |
| Cheng 2014 [20] (comparative, retrospective, multi-center) | Repair of abdominal hernia (primary or incisional)  
ASA score: not reported  
Hernia size: not reported  
Type of wound: see next column | Permacol (porcine, cross-linked)  
Type of wound: 50 (26%) clean, 60 (35%) clean contaminated, 54 (16%) contaminated, 42 (22%) infected. | 43/195 (21.8%) | 23/195 (12%) at 28.1 months of follow-up |
| Chaud 2014 [21] (single-arm, retrospective, multi-center) | Repair of abdominal hernia (primary or incisional)  
ASA score: 2 or 3 in 50% of patients  
Hernia size: not reported.  
Type of wound: 190 (55.0%) clean, 103 (30.0%) clean contaminated, 28 (8.2%) contaminated, 22 (6.4%) contaminated. | Permacol (porcine, cross-linked) | 19/59 (32%) | 64/59 ± 5 years of follow-up |
| Abdelfatah 2015 [23] (single-arm, retrospective, single-center) | Repair of abdominal hernia (incisional)  
ASA score: high risk of infection  
Hernia size: diameter ≥10 × 7 cm  
Type of wound: 32 (49%) clean, 21 (32%) clean contaminated, 6 (12%) contaminated, 4 (6%) infected. | Permacol (porcine, cross-linked) | 2/41 (4.9%) | 0/41 at a mean follow-up of 445 days (range, 176 to 648) |
| Patel 2013 [22] (single-arm, retrospective, single-center) | Repair of abdominal complex hernia (primary or incisional)  
ASA grade: 2 or 3 in all patients  
Hernia size: median diameter 13.67 cm (range 5–30)  
Type of wound: contaminated, infected | Strattec (porcine, non cross-linked) | 2/14 (16%) | 6/14 (42%) at a median of 13 months of follow-up |
| Zerbih 2015 [24] (single-arm, prospective, single-center) | Repair of abdominal herniaa  
ASA score: not reported  
Hernia size: median diameter 14 cm (range 5–25)  
Type of wound: Infected | Strattec (porcine, non cross-linked) | 2/14 (1%) | 15/85 (19%) at 12 months of follow-up, 22 (28%) at 24 months of follow-up |
| Elini 2012 [25] (single-arm, prospective, single-center) | Repair of abdominal hernia (incisional)  
ASA score: 3 or 4  
Hernia size: 236 × 135 cm²  
Type of wound: 39 (49%) clean contaminated, 39 (49%) contaminated, 2 (2%) infected | Strattec (porcine, non cross-linked) | 17/85 (21%) | 22 (28%) at 24 months of follow-up |
| Shihany 2015 [27] (single-arm, retrospective, single-center) | Repair of abdominal hernia  
ASA score: 3 or 4  
Hernia size: 384 cm² (35–993)  
Type of wound: 36 (88%) clean contaminated and 5 (12%) contaminated | Strattec (porcine, non cross-linked) | 6/41 (15%) | 5/41 (12%) at a mean of 25 months of follow-up |
ASA score: 1 or 2  
Hernia size: 207 ± 248 cm²  
Type of wound: not reported | Strattec (porcine, non cross-linked) | 20/68 (29.9%) | 10/68 (14%) at a mean of 18 months of follow-up |
| Madini 2017 [18] (single-arm, retrospective, single-center) | Repair of abdominal hernia  
ASA score: 2 or 3 in 91% of patients  
Hernia size: 100 ± 50 cm²  
Type of wound: 16 (30%) clean contaminated, 11 (24%) contaminated, 19 (41%) dirty | Surgisis (porcine, non cross-linked) | 19/44 (41%) | 28/44 (61%) at a median of 47 months of follow-up |
| Guerado 2015 [26] (comparative, retrospective, single-center) | Repair of abdominal hernia (incisional)  
ASA score: 3.1 ± 0.9  
Hernia size: 110 ± 20 cm² (25–380)  
Type of wound: clean 13 (32%), clean contaminated 3 (8%), contaminated 23 (61%) | Tutumesh (bovine, non cross-linked) | 1/38 (3%) | 0/38 at 12 months of follow-up |
Abbreviations: ASA (American Society of Anesthesiology) score.
Note: Because of insufficient information in the trials, results are not separately reported according to the type of surgical wound.

*In this study the type of hernia (primary or incisional) is not specified or the results are not divided by type of hernia.

Fig. 2. Rates of surgical site infection at 30 days in the 11 studies in 13 cohorts included in our analysis. Pooled rates (with 95%CI) are reported according to the type of mesh (Permacol vs Strattice vs others). Squares indicate the rates for individual studies, the horizontal bars are the 95%CI, the vertical dashed line (in red) shows the meta-analytical pooled rate. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.).

Fig. 3. Rates of recurrence at 12 months in 4 studies included in our analysis. Pooled rates (with 95%CI) are reported for the overall cohorts included in the 4 studies and according to the type of mesh (Permacol vs Strattice). Squares indicate the rates for individual studies, the horizontal bars are the 95%CI, the vertical dashed line (in red) shows the meta-analytical pooled rate. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.).

In summary, the appropriate place in therapy for biological meshes remains uncertain. On the one hand, our comparisons, that are undoubtedly affected by important biases of selection, tend unexpectedly to suggest that the most commonly used outcomes could be worse with biological meshes than with synthetic ones. On the other, our analysis underscores the lack of randomized trials aimed at head-to-head comparisons of biological meshes and, more importantly, the scarce evidence surrounding the direct comparison between biological meshes and synthetic ones. With regard to this latter point, the meta-analysis by Atema et al. [11] found no difference between biological and synthetic meshes, while our findings, based on an indirect comparison, even suggest that some outcomes could be worse with biological meshes compared with synthetic meshes. Finally, our findings are in line with those of a recent consensus review that does not recommend the routine use of biologic meshes for abdominal wall reconstruction [30].

Ethical approval

Our study is a review paper that does not require any ethical approval.

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Author contribution

Sabrina Tripoll and Andrea Messori carried out the analysis of all
papers included in the present work. Claudio Martini, Ermilia Caccese
and Giorgio Tulli conducted the literature search and supervised
the writing of the manuscrit. Pierfilippi contributed to the writing
of the manuscript and reviewed the literature from his role of expert
in abdominal surgery.

Conflicts of interest

ST, EC, CM, GT, and AM declare that they have no conflict of interest;
P1 declares no conflict of interest directly related to this work but
received consulting fees from Medtronic and LifeCell in the past.

Trial registry number

Not applicable.

Guarantor

Andrea Messori is the Guarantor of the study.

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