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A Critical Review of Biologic Mesh Use in Ventral Hernia Repairs under Contaminated Conditions

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Abstract

Purpose—We used an evidence-based approach to determine if the promotions and claims of superiority of biologic mesh over synthetic mesh use in ventral hernia repairs (VHRs) under contaminated conditions were sound and valid.

Methods—We searched the Medline database to specifically identify review articles relating to biologic mesh and VHR and critically reviewed these studies using an evidence-based approach.

Results—For the past forty-five years, four clinical reviews and one systematic review have included biologic meshes as part of a larger discussion on available prosthetics for VHR. All reviews supported biologic mesh use, especially in the setting of contaminated fields. Yet the primary literature included in these reviews and served as the basis for these conclusions consisted entirely of case series and case reports, which have the lowest level of evidence in determining scientific validity. Furthermore the FDA has neither cleared nor approved this particular use.

Conclusions—The cumulative data regarding biologic mesh use in VHRs under contaminated conditions does not support the claim that it is better than synthetic mesh used under the same conditions. The highly promoted and at least moderately utilized practice of placing biologic mesh in contamination is being done outside of the original intended use, and a re-evaluation of or possible moratorium on biologic mesh use in hernia surgery is seriously warranted. Alternatively, an industry-sponsored national registry of patients in whom ventral hernia repairs involved biologic mesh would substantively add to our understanding regarding how these intriguing biomaterials are being used and their overall clinical efficacy.

Keywords

hernia; incisional; mesh; prosthesis; mesh

INTRODUCTION

For as long as the human abdomen has been surgically explored, incisional hernias likely accompanied successful long-term wound closures. And for the vast majority of this history, incisional hernias have been repaired primarily. [1] The high rates of hernia recurrence, and the associated high morbidity and mortality, eventually led to the discovery that excessive forces across the healing wound played a significant role in these incisional failures. In response, tension-free surgical techniques were developed. [2] As part of that effort prosthetics in the form of mesh were first used in hernia repair in the early twentieth century, initially in various metal materials, then synthetic plastics, and most recently biologic materials. [1]

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Despite advances in hernia repair materials since Usher introduced polypropylene mesh over 50 years ago, [2] complication and recurrence rates were still high after ventral hernias repairs (VHRs). [3] Each iteration of mesh material was thought to be the answer to the shortcomings of the previous material. But despite marked improvements both in recurrence rates and complications, as the prosthetic options increased and became more complex, they were accompanied by a new set of problems. For example, the various metal prostheses significantly decreased hernia recurrence rates compared to those from primary closures, but also caused chronic sinus formation and patient discomfort from mesh fracturing. [3] Synthetic plastic meshes proved more stable in the long-term and reduced the complications associated with metallic mesh, but they also contributed to intra-abdominal adhesion formation, enteric fistulas, and surgical site infections. [4]

In response to these complications, biologic materials were introduced as surgical meshes in 2003, purporting better ability to integrate into the natural healing environment, match the tensile strength of their predecessors, and resist contamination.[1, 2, 5] It is this last quality, the ability to be used in infected or potentially infected fields, which has been the most highly promoted in the literature.[6, 7, 2, 1]

We critically reviewed the literature using an evidence-based approach to determine if these promotions and claims of superiority were valid. Given that biologic mesh has been used predominantly in VHRs,[5] which have the highest potential for concomitant contamination, we specifically examined the literature that described biologic mesh use under these conditions to determine three things: first, whether cumulative data regarding biologic mesh use on VHRs under contaminated conditions supports the claim that biologic mesh is better than synthetic mesh used in the same conditions; second, whether the predominant use and promotion of biologic mesh in the literature is taking place in or outside of the original intended use; third, whether a re-evaluation or possible moratorium on biologic mesh use in hernia surgery is seriously warranted.

In this review, we first outline the various types of biologic meshes currently being used for VHR, describe the FDA's regulatory requirements for biologic meshes, and outline the basic principles of how scientific literature is evaluated using an evidence-based approach. We then present our review of the biologic mesh literature and discuss the implications for current clinical practice.

LITERATURE SEARCH

Our intent was not to conduct a complete systematic review of biologic mesh use for hernia repair. Instead, we searched the Medline database to specifically identify review articles relating to biologic mesh and VHR. We chose to primarily explore review articles because they are so widely read and cited as up-to-date summaries of the literature. We restricted the search to the English language and review articles, from the inception of the database in 1966 to March 2011, and utilized the search terms "ventral hernia", "ventral hernia repair", "incisional hernia", "incisional hernia repair", and "biologic mesh". We then selected relevant articles that specifically addressed our topic from the reference lists of these reviews and included them in our analysis.

TYPES OF BIOLOGIC MESH

Biologic meshes come from human, porcine, or bovine sources. The different types of meshes derived from these sources are categorized into acellular dermis, fetal dermis, small intestine submucosa, and pericardium. [6] Acellular dermis is harvested from human, pig or fetal bovine skin, which then undergoes epidermal and dermal cellular removal, leaving only a collagen and elastin matrix behind. [8] Further processing can increase the cross-linking

between collagen fibers in order to decrease their susceptibility to collagenase degradation. [9] The human-derived acellular dermis meshes currently on the market are Alloderm®, Allomax™, and FlexHD®. The porcine-derived dermal meshes are Permacol™, Collamend™, Strattice™, and XenMatrix™. Surgimend™ is uniquely derived from fetal bovine skin, however, there were no peer-reviewed reports of its clinical use available for review. All of the meshes derived from small intestine submucosa are of porcine origin, and while they all undergo a decellularization similar to that of the dermal meshes, none have increased cross-linking. Those on the market are Surgisis®, SIS Gold, and LyoSIS. All of the pericardial meshes—Peri-Guard®, Veritas®, and Tutomesh®—come from bovine sources. These too undergo a decellularization process to produce a collagen matrix, but like the small intestine submucosa meshes, are not cross-linked. [9]

The end product of all of the various biologic meshes is a matrix composed of collagen and elastin. The matrix acts as a scaffold to allow native tissue and neo-vascularization to infiltrate the healing wound in a manner that resembles uninjured tissue, as opposed to what occurs during scar formation. It is also believed that with increased vascularization comes increased resistance to infection. [6]

FDA INDICATIONS FOR BIOLOGIC MESH

The FDA requires products that will be classified as medical devices meet certain regulatory requirements based on the risk associated with their intended use. They are then stratified into classes I, II, or III, with class I having the lowest risk to public safety and class III having the highest.[10] This regulatory requirement, or 510(k) *clearance*, determines that a product either has (a) the same intended use and characteristics of a product already on the market or (b) the same use but different characteristics, while effectively showing that the different characteristics are as safe and/or effective as what already exists. Under most circumstances, clinical trials are not needed to meet these requirements. [11] However, to obtain FDA *approval* the product must go through a premarket approval (PMA) process, which does require evidence from a human clinical trial documenting both safety and efficacy. In other words, *clearance* requires that a product be shown to be at least as good as what is already on the market, whereas *approval* requires proof that a product's claims are accurate.

The FDA views xenograft meshes as general surgical meshes, which are "intended to reinforce soft tissue or bone where weakness exists". [12] They have been grouped as class II products, requiring them to undergo the 510(k) *clearance* process. In obtaining this *clearance*, xenografts are held to the "substantially equivalent" safety and efficacy threshold of what is already on the market. Interestingly, the FDA views allografts as human tissue for transplantation and not as medical devices. This distinction causes them to be regulated through the FDA's Center for Biological Evaluation and Research [13], which has even fewer regulatory requirements than both the 510(k) and PMA processes. Essentially, this means that allografts have not needed the same burden of proof as xenografts to show safety and efficacy in order to be marketable as a general surgical mesh. In fact, allografts did not acquire FDA *approval* nor *clearance* to be marketed or used as a surgical mesh at all. So in summary, whereas the xenografts have obtained *clearance* to be used as a general surgical mesh where the allografts have not, neither has been cleared nor approved for use in contaminated settings. Nevertheless, both xenografts and allografts are being used as surgical meshes, and specifically, as surgical meshes in contaminated settings

EVIDENCE-BASED MEDICINE

The term "evidence-based medicine" (EBM) was coined in the 1980's to help define a newly developing framework being used to negotiate disparate research findings and sound

clinical practice. This framework, which has been defined as “the process of systematically finding, appraising, and using contemporaneous research findings as the basis for clinical decisions”, is now widely used across many, if not all, medical disciplines. [14] By implementing EBM, clinicians utilize the current best evidence to make the best decisions for their patients. [15]

EBM incorporates the use of various ranking scales, or levels of evidence, to assess the validity of the evidence found in the literature [16-18] and even though negotiating between these scales can be confusing because of the different terminology and schemes used, they are consistent about how high and low quality evidence is defined and how that influences clinical practice recommendations. The highest-rated type of data comes from randomized controlled trials and systematic reviews of those trials, whereas the opinions of experts have the lowest rating. Not surprisingly, higher levels of evidence (LOE) translate into strong recommendations, whereas recommendations based on data with low LOE are essentially weak. Of particular interest to our review of biologic mesh use for VHR, case reports and case series consistently fall on the lower end of this spectrum.

LITERATURE REVIEW

Over 10 years ago, Luijendijk et al showed that mesh was better than suture when closing incisional hernias. [19] Since then, there has been considerable debate as to what kind of mesh and which technique is optimal in VHR. [20] In line with all mesh prostheses, the purpose of biologic mesh is to assist in tension-free closures of incisional wounds. Biologic mesh is also promoted as being able to integrate better than synthetic mesh into the healing matrix and resist infection; essentially expanding its potential use in areas where synthetic mesh is otherwise contraindicated. [2] Attempting to take advantage of these characteristics, an increasing number of surgeons are using biologics for clean and contaminated hernia repairs of all types. [5, 21] In examining the literature, we focused specifically on biologic mesh use in VHR under contaminated conditions, because VHR is the most commonly used indication, [5] and because the use of biologic mesh in contamination is the most highly promoted indication.

Clinical Reviews of Case Reports and Case Series

To date, there have been four clinical reviews [6, 2, 1, 7] and one systematic review [5] that included biologic meshes as part of a larger discussion on available prosthetics for VHR. All four clinical reviews—by Grey et al in 2008 [2], Bachman et al in 2008 [6], Breuing et al in 2010 [7], and Shankaran et al in 2011 [1]—concluded that biologic mesh use should be incorporated in a surgeon’s armamentarium, especially in the setting of contaminated fields. Yet, the primary literature that served as the basis for this conclusion consisted entirely of case series that varied widely in terms of sample size, mesh material used, how the mesh material was placed, and how the results were reported (Table 1). For example, among the primary articles cited in the clinical reviews, sample sizes ranged widely, from five to 240 patients. Alloderm usage predominated, with Surgisis following closely behind, and only two articles using Permacol were reported. Various methods of mesh placement were reported, including onlay, inlay, interposition, and component separation. The most consistently reported complication across all four clinical reviews was surgical site infection (SSI), the rate of which ranged from 0% to 60%. The hernia recurrence rate ranged from 0% to 50%. The follow-up period ranged from 6 months to 18 months.

Grey et al’s 2008 review [2] initially took a historical view of inguinal and ventral hernia repair, followed by a broad review of the various kinds of prosthetic materials that have been in use since their inception. At the end of this discussion, biologic prostheses were introduced with the stated benefit of being able to be used in contaminated fields, with three

primary articles cited in support of this position. One of these three covered only inguinal hernias and was not included in our analysis. The two others, by Kim et al [22] and Patton et al [23] were both case series from individual institutions, had mean ages of the patients in the mid-fifties, and near equal male/female gender distributions. Kim et al's inclusion criteria was Alloderm use in high-risk VHRs; high-risk being defined as having an active abdominal wall infection, a co-existing enterocutaneous fistula, skin coverage that was questionable, and being considered high-risk for post-operative infection. [22] Patton et al's inclusion criterion was simply Alloderm use in VHRs in the setting of contamination or potentially contaminated fields. [23] Kim et al reported an average BMI score of 31 (range, 17-58) and a most common co-morbidity of diabetes, whereas Patton et al reported neither BMI nor co-morbidities. But Patton et al did mention correlations, or the lack thereof, between infection rate and hernia recurrence, indication for surgery, mesh placement, whereas Kim et al did not report on correlations. [22,23]

Bachman et al's 2008 review [6], unlike Grey et al's, introduced the concept of biologic mesh very early into their discussion of the historical and contemporary use of prosthetic mesh use in ventral hernia repairs. [6] Like Grey et al, they affirmed the successes of biologics in contaminated fields, but cited seven primary articles in support of the claim. [24-30] All seven were case series from single institutions, with total sample sizes ranging from 5 to 75 patients, and average patient ages ranging from the fifties to the early seventies. Only two of the articles reported co-morbidities, and the most common of those were diabetes and coronary artery disease. [24, 25] Six of the seven articles mentioned gender distribution, four of which had nearly a balance between the genders represented. [24, 27, 29, 30] One of the seven articles did not have the stated aim of investigating biologics in the setting of contamination but nevertheless indicated which cases were. [28] A range of conclusions was reached: Only three articles reported looking for correlations, and of those, one article found a non-significant trend in infection being associated with recurrence [24], another found that wounds not primarily closed during repair, even with the biologic prosthesis, predicted recurrence [25], and the third found positive correlations between wound class and re-operating, complications, and recurrence. [28]

Breuing et al's 2010 article [7] reviewed the literature and offered a set of new recommendations, including a grading system for how to best repair ventral hernias. Biologic mesh was included as part of the discussion of prosthetic material selection, but only animal studies were cited to support the claims that biologic mesh characteristics carried benefits specific to contaminated environments. The human studies put forth as evidence for stating that permanent synthetic meshes were not recommended but that biologics should be, were already discussed above, [22-24] and were case series from single institutions.

The most recent clinical review from Shankaran et al in 2011 included a short history of hernia repair, followed by a long discussion of various aspects of mesh use, including mesh mechanics and different methods of using mesh, culminating in the types of mesh that are available. [1] The authors primarily used six articles to support the idea that biologic mesh can be used in contaminated fields. [22, 23, 31-34] Two of these articles were discussed above as part of Grey et al's review, [22, 23] and were case series from single institutions. The four remaining articles were also case series, one of which was from a multi-institution collaboration. [31] The sample sizes ranged widely from 9 to 240. Only two of the four series had a primary aim of examining hernia repair in the setting of contamination, [31, 32] whereas the two others simply looked at their institution's track record with a particular biologic mesh and included cases that were in or were potentially in contaminated fields. [33, 34] The average age of patients in these series was the fifties and sixties, two series had near equal gender distributions [31, 33], and when reported, the BMIs were all above 30.

[31, 34, 32] The most common co-morbidities were diabetes and hypertension. [29-32] Only one series reported an American Society of Anesthesiologist (ASA) mean score of 3.2. [32] Only one series reported correlative findings, which were that BMI >30, SSI, and concurrent ostomy repair were associated with hernia recurrence, whereas the level of pre-operative contamination was not. [31]

The one systematic review, reported by Hiles et al in 2009, included a total of 80 articles on biologic mesh use in hernia repair, 36 of which focused on or included incisional and/or VHRs, and 23 of those included cases done in contaminated fields. [5] Many of the primary articles included in that systematic review have already been mentioned in our description of the four clinical reviews above. The 12 remaining articles are described here and summarized in Table 2. Of these 12 articles, eight were case series and four were case reports. Like the clinical reviews, these articles reported a predominance of Alloderm use, various methods of placing the mesh, and average follow-up times that ranged widely from 6 to 29 months. In contrast to the primary articles included in the four clinical reviews, these 12 primary articles had significantly fewer patients, ranging from 1 to 37 (as opposed to 5-240). Of the six case series that reported on gender distribution, four had a male majority. [30, 35-37] Three of the four case reports were of females. [38-40]

In Hiles et al's systematic review, the indications for surgical management varied as well. In one article, the surgical indication was simply VHR; sterility of the field was not mentioned and the overwhelming majority of cases were non-contaminated, yet the introduction and discussion mentioned the potential benefits of using biologic mesh in a contaminated setting. [41] Another article reported indications of either incisional hernia repair or transverse rectus abdominis musculocutanous flap reconstruction. [42] A third article's patient population was composed of cancer patients who underwent chest wall, abdominal wall, or pelvic reconstructive surgery following either tumor resections or fistula takedowns. [37] In all three articles, only a handful of cases were considered VHRs in the setting of contamination or potential contamination. The remaining articles reported fairly common hernia repair indications that included contamination. Co-morbidities were rarely reported. Average patient age mostly ranged from the forties to the sixties, though one case report was of a 28-year-old woman who was being treated for a contaminated gynecologic wound. [40] Surgical site infection rates were not reported in one article [43], and recurrence rates ranged from 0% to 32%. Of the two articles that reported correlations, both concluded that there was no association between pre-operative infection or mesh exposure and subsequent hernia recurrence. [42, 43] As was the case in all of the clinical reviews described above, Hiles et al concluded that biologic grafts can be used successfully in infected fields. [5]

DISCUSSION

The published reviews on biologic mesh use for VHR under contaminated conditions all conclude by supporting the continued use of these meshes for that purpose. But a closer look at the primary studies contained in these reviews indicates that such positive conclusions are not warranted, for several reasons. First, all of the primary studies included in these reviews are either case series or case reports, all of which are considered a low level of evidence. Second, the way data is reported is inconsistent, which is not surprising given the fact that with rare exceptions, reporting guidelines for case series are not standardized. This inconsistency makes it difficult, if not impossible to compare studies, and drawing conclusions from them premature. For instance, although 80% of the primary articles used in these reviews reported the number of patients who had each type of mesh placement (onlay, inlay, underlay, etc), the numbers of each type varied widely between studies. Interpreting outcomes when a potentially significant variable such as mesh placement is not represented more evenly is problematic. Third, some articles found that interpositional mesh placement

was associated with hernia recurrence [23, 35, 43], while others did not [24, 31, 32, 41], which adds to the confusion. Fourth, only six articles utilized the standardized Centers for Disease Control and Prevention (CDC) wound classification system (clean, clean-contaminated, contaminated, dirty) [22-24, 34, 28, 31, 33]; the rest either did not define what was meant by "contamination" or listed a few scenarios that the authors considered "unclean". Of those that did use the CDC system, one article [24] made "clean-contaminated" one group and considered the "contaminated" and "dirty" as a second group, whereas another article [28] analyzed each of the four CDC subgroups separately. Arbitrary designation of contamination, or not using a standard classification system for such an important definition, leaves open the possibility for provider bias in what is considered a contaminated field, and thus, can affect how the data is interpreted. Fifth, one article chose to distinguish between a recurring hernia and mesh "laxity" that presents with bulging [35], while another article used the same definition of mesh laxity to define a recurrence [43], which raises the question of how other authors were defining what a hernia recurrence actually was, especially when using Alloderm, which is known to have a high eventration rate. [44]

In examining the primary articles in light of their source material, other issues also became apparent. One was related to the follow-up times—of the 25 primary articles used in the reviews, only 10 had mean follow-up periods longer than one year. For example, four of the six articles cited by Shankaran et al [1] had average follow-up times of less than one year. In addition, of the 10 articles on synthetic mesh that these primary studies used for the comparison with biologic mesh, two were animal studies [45, 46] and the eight others all had follow-up periods of more than two years. [19, 47, 3, 48-52] This was the pattern in all of the review articles we examined, and since most of the literature on biologic mesh use for VHR provides only a short-term picture, comparisons with synthetic mesh are problematic because of different follow-up times. Because recurrences can take place after short-term follow-up, the recurrence rates found in this population are likely underestimated. [47] Finally, many of the primary articles on biologic mesh for hernia repair comment that synthetic mesh is contraindicated in contaminated conditions and go on to mention how biologic mesh can address this difficult issue. But, as is noted in Shankaran et al's review, the complication rates from the biologic mesh literature are in fact comparable to those of synthetic mesh. [1] What is really supposed to distinguish biologic from synthetic meshes, Shankaran et al argue, is the recurrence rate, and the six primary articles cited as support for biologic mesh use in contamination had recurrence rates ranging from 10 to 30%. [22, 23, 31-34] Yet, the sources cited in those six primary articles to support their statements that synthetic mesh use is contraindicated in contamination reported recurrence rates for synthetic mesh that range between 1% to 55%, [3, 19, 47- 49, 51, 53] and just one reported a recurrence rate above 32%. [53] Therefore, quite possibly, the recurrence rates for biologic and synthetic mesh are not that dissimilar after all.

The most salient issue regarding the biologic mesh literature for VHR in general is that it would be considered low-level evidence by evidence-based medicine standards. Published studies are overwhelmingly either case series or reports, and with respect to biologic mesh use in VHR under contaminated conditions specifically, all of the data comes from either case series or reports. According to every established criterion for determining the strength and validity of scientific data, data from these two sources is considered the weakest. Therefore, recommendations based on such data would be considered equally weak and possibly unfounded. Nevertheless, each of the reviews we discussed promotes the continued and expanded use of biologic mesh in the very setting for which the data is the weakest. Even more troubling is the fact that the vast majority of the primary articles used in these reviews attest to the weakness of their own data, and furthermore suggest longer-term follow-up [22-24,33, 34, 26-28, 42, 39] and/or better orchestrated trials, [22-24, 28, 31, 32,

34] but those explicit limitations are not inherent in the conclusions reached in the review articles.

Evidence-based medicine is not foreign to surgical subspecialties, and has a long history of being incorporated in surgical research. [54, 55] It is well recognized that randomized controlled trials can be a challenging task to undertake in the field of surgery for various reasons. But the inherent difficulty of obtaining a higher level of evidence in surgical research does not change how data from studies with a low level of evidence should be subsequently defined and interpreted. In other words, a lack of randomized controlled trials in the biologic mesh literature does not mean that the existing case studies and series can be interpreted as anything more than what they are. A similar problem exists with adverse events and xenograft use in VHRs. According to Harth and Rosen, [56] who examined the FDA's adverse event database, most of the xenograft data came from industry-sponsored trials, most of the studies were done in clean cases, and there was little evidence for xenograft use in contaminated fields. In a response to Harth and Rosen, Segan, who works for Covidien, the manufacturer of Permacol™, discredits the authors' use of the FDA adverse event database as a comparative or evaluative tool based on the database's inherent biases and shortcomings. [11] But he too states that an evidence gap exists and that none of the current biologic meshes in use have received FDA clearance or approval for use in an infected field.

One last issue of concern regarding the implementation and use of biologic meshes is cost. These meshes can be up to 10 times more expensive than synthetic meshes. [6] Out of the five review articles discussed here, three either included charts illustrating examples of what these prostheses cost [6,1] and/or briefly discussed how cost should be an important deciding factor when choosing which mesh to use. [1, 7] But only one actually stated that biologic meshes are more expensive than synthetics. [1] Of the 25 primary articles used by the clinical review articles, only nine mention cost in their discussion sections. But of those nine, all of them conclude that biologic mesh materials are substantially more expensive than other prosthetics available. [25, 26, 28-30, 32, 33, 43, 40] The fact that the vast majority of the reviews and primary articles have not paid special attention to this important issue does not lessen its importance. Specific cost data is not always obtainable because of hospital-manufacturer contracts, but it is undeniable that on average, the price for biologic mesh material is significantly more than for standard mesh. [2, 25, 26, 28-30, 32, 33, 40, 43] Given the economic strains that the health care field is currently under, along with the overall weakness of the available data on biologic meshes, we think it is absolutely necessary for a rigorous and truthful cost-benefit analysis to be undertaken if they are to remain in use. Accordingly, we are in the process of conducting a multi-site, FDA supported randomized controlled trial designed to compare the use of biologic versus synthetic prosthetics for repair of complex VHRs in the setting of wound contamination. Study outcome variables include hernia recurrence and relative costs of treatment.

In conclusion, our review highlights four important issues that surgeons should consider seriously when evaluating the biologic mesh literature and when considering using biologic mesh in practice. First, the cumulative data regarding biologic mesh use on VHRs under contaminated conditions does not support the claim that it is better than synthetic mesh used in the same conditions. Second, the highly promoted and at least moderately utilized practice of placing biologic mesh in contamination is being done outside of the original intended use, and in some instances, equates to off-label use of a medical device. Third, although not the focus of this review, it became apparent that biologic mesh use even in non-contaminated conditions is questionable when their reported results are viewed in light of their exorbitant costs. And fourth, as a result, a re-evaluation or possible moratorium on biologic meshes in hernia surgery is seriously warranted. Alternatively, a strong and reasonable argument can

be made for creating an industry-sponsored, publically available registry of biologic prosthetic use for VHR. This straightforward mandate, if properly constructed and implemented, would significantly expand our knowledge regarding how these intriguing biomaterials are being used and their overall clinical efficacy.

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Table 1

Clinical Review Summary

Review Article	Primary Articles Cited	Study Type	Material Used	SSI Rate	Recurrence Rate	Mesh Placement	Follow Up (mean, months)	Correlations
Grey et al, 2008[2]	Kim et al, 2006[22]	Series	Alloderm	41%(12/29)	10% (3/29)	Underlay, CS	6	NR
	Patton et al, 2007[23]	Series	Alloderm	16% (11/67)	18% (12/67)	Inlay, Interposition, Onlay	10.6	Interposition/ onlay associated with recurrence
Bachman et al, 2008[6]	Diaz et al, 2006[24]	Series	Alloderm	33% (25/75)	16% (12/75)	Inlay, Interposition, Onlay, CS	9	NR
	Schuster et al, 2006[25]	Series	Alloderm	NR	50% (9/18)	Unclear	9	NR
	Catena et al, 2007[26]	Series	Permacol	0% (0/7)	0% (0/7)	Inlay, Onlay	11	NR
	Ueno et al, 2004[27]	Series	Surgisis	40% (8/20)	6/20 (30%)	Inlay, Onlay	16	NR
	Helton et al, 2005[28]	Series	Surgisis	58% (18/31)	26% (8/31)	Underlay, CS, Inlay	14	Contamination associated with SSI and/or recurrence
	Franklin et al, 2002[29]	Series	Surgisis	5% (1/19)	0% (0/19)	Onlay	15	NR
	Franklin et al, 2004[30]	Series	Surgisis	2% (1/43)	0% (0/43)	Onlay	19	NR
Breuing et al, 2010[7]	Patton et al, 2007[23]; Kim et al, 2006[22]; Diaz et al, 2006[24]	See above	See above	See above	See above	See above	See above	See above
Shankaran et al, 2010[1]	Kim et al, 2006[22]; Patton et al, 2007[23]	See above	See above	See above	See above	See above	See above	See above
	Diaz et al, 2009[31]	Series	Alloderm	40%(96/240)	17% (41/240)	Inlay, Interpositional, Onlay, CS	10	SSI associated with interpositional placement
	Alaedeen et al, 2006[32]	Series	Alloderm, Surgisis	60% (6/10)	20% (2/10)	Interpositional, CS	14	NR
	Parker et al, 2006[33]	Series	Permacol	0% (0/5)	20% (1/5)	Underlay	18	NR
	Bellows et al, 2008[34]	Series	Alloderm	25% (5/20)	30% (6/20)	Underlay	9	Wound class associated with complication

Abbreviations: CS, component separation; NR, not reported; SSI, surgical site infection

Table 2

Relevant Summary from Systematic Review by Hilar et al, 2009

Primary Article	TYPE	Material	SSI Rate	Recurrence rate	Mesh Placement	Follow up (mean, months)	Correlations
Gupta et al, 2007[41]	Series	Surgisis	0% (0/3)	0% (0/3)	Overlay, interposition, underlay	29	NR
Trevino et al, 2006[30]	Series	Surgisis	0% (0/4)	0% (0/4)	Two-layered method	10	NR
Bluebond- Langner et al, 2008[30]	Series	Alloderm	86% (6/7)	0% (0/7)	Interpositional, CS	9	Interpositional placement is associated with laxity; Infection is associated with laxity
Buinewicz et al, 2004[42]	Series	Alloderm	Not Clear	Not Clear	Onlay, interpositional, multi-layer	20	No association of contamination and recurrence.
Butler et al, 2005[37]	Series	Alloderm	0% (0/6)	0% (0/6)	Inlay	6	NR
Hirsch et al, 2004[57]	Report	Alloderm	0% (0/1)	0% (0/1)	Onlay	9	NR
Jin et al, 2007[43]	Series	Alloderm	NR	32% (12/37)	Onlay, Interpositional, Underlay, CS	22	Interpositional placement associated with recurrence
Kolker et al, 2005[36]	Series	Alloderm	0% (0/16)	0% (0/16)	Two-layered method, CS	16	NR
Tung et al, 2006[40]	Report	Alloderm	0% (0/1)	0% (0/1)	Interpositional	12	NR
Adedeji et al, 2002[38]	Report	Permacol	0% (0/1)	0% (0/1)	Onlay	12	NR
Armellino et al, 2006[58]	Series	Permacol	0% (0/6)	0% (0/6)	NR	3-24	NR
Liyanage et al, 2006[39]	Report (0/1)	Permacol	0%	0% (0/1)	Underlay	12	NR

Abbreviations: CS, component separation; NR, not reported