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Review Article

Biologic grafts for ventral hernia repair: a systematic review

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Ventral hernia repair;
Biologic graft;
Xenograft;
Allograft;
Infection

Abstract

BACKGROUND: Biologic grafts hold promise of a durable repair for ventral hernias with the potential for fewer complications than synthetic mesh. This systematic review was performed to evaluate the effectiveness and safety of biologic grafts for ventral hernia repair.

METHODS: MEDLINE, Embase, and Cochrane Central Register of Controlled Trials were searched for studies on biologic grafts for the repair of ventral hernias. Outcomes are presented as weighted pooled proportions.

RESULTS: Twenty-five retrospective studies were included. Recurrence depended on wound class, with an overall rate of 13.8% (95% confidence interval [CI], 7.6–21.3). The recurrence rate in contaminated/dirty repairs was 23.1% (95% CI, 11.3–37.6). Abdominal wall laxity occurred in 10.5% (95% CI, 3.7–20.3) of patients. The surgical morbidity rate was 46.3% (95% CI, 33.3–59.6). Infection occurred in 15.9% (95% CI, 9.8–23.2) of patients but only led to graft removal in 4.9% of cases.

CONCLUSIONS: No randomized trials are available to properly evaluate biologic grafts for ventral hernia repair. The current evidence suggests that biologic grafts perform similarly to other surgical options. Biologic grafts are associated with a high salvage rate when faced with infection.
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Incisional hernia is a common complication after laparotomy, occurring in 10% to 20% of cases.[1,2] Since the introduction of synthetic prostheses, repair of the defect with polypropylene mesh or expanded polytetrafluorethylene has become the mainstay of treatment showing good short- and long-term results.[3,4] The drawback of prosthetics is adhesion formation to the viscera, which may cause bowel obstruction or erosion into the viscera.[5] Surgeons are also reluctant to implant synthetic prostheses in complex hernias because of an increased risk of infection and mesh extrusion. Complicated hernias have not been properly defined but usually include repairs combined with bowel surgery or in the presence of enterocutaneous fistulas, multiple recurrent hernias, previous or current (mesh) infection, and hernias after trauma or tumor resection.

Biologic grafts have been introduced as an alternative to synthetic mesh. They consist of an extracellular collagen matrix. The graft is incorporated into the surrounding tissue by ingrowth of fibrocollagenous tissue and blood vessels. During incorporation, the graft is gradually degraded and theoretically remodeled into a neofascia to withstand the mechanical forces of the abdominal wall.[6] Commercially available biologic grafts used for ventral hernia repair are

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derived from human and porcine dermis, porcine small intestinal submucosa, and bovine pericardium. After harvesting, all tissues undergo decellularization aimed at the prevention of a foreign-body response. Some biologic grafts are dehydrated during processing to extend shelf-life, reduce extensibility, make them easier to handle, and limit the loss of growth factors during storage. A minority of biologic grafts undergo additional cross-linking. During this process, extra bonds are added between the polymers of the collagen matrix aimed at controlling the enzymatic degradation of the graft, which is claimed to be beneficial in a contaminated environment.

Because of their biocompatible nature, biologic grafts hold promise of a durable repair and lower infection propensity compared with synthetic mesh. The aim of this systematic review was to summarize and evaluate the use of biologic prostheses for ventral hernia repair under clean and contaminated conditions with a focus on recurrence and complications.

Methods

Search methods for the identification of studies

Electronic databases were searched to identify relevant studies. No restrictions were set on language or publication status. By using PubMed and Ovid, the search covered databases MEDLINE (including In-Process & Other Non-Indexed Citations, 1950–present), EMBASE (1980–present), and the Cochrane Central Register of Controlled Trials. Current registered trials were also identified in the *meta*Register of Controlled Trials. Considering the scarcity of studies on the biological materials, a high sensitivity with a consequently low precision was chosen for the search strategy. The following search terms were used: hernia, abdominal-wall defect, reconstruction, and repair. These were combined with terms for the brand names (ie, Alloderm [LifeCell Corp, Branchburg, NJ], Collamend [Davol Inc., Warwick, RI], FlexHD [Ethicon, Somerville, NJ], Peri-guard [Synovis, St. Paul, MN], Permacol [Covidien, Mansfield, MA], Pelvicol [Bard, Olen, Belgium], Strattice [LifeCell Corp, Branchburg, NJ], Surgisis [Cook Surgical, Bloomington, IN], Tutomesh [Taureon GmbH, Lienen, Germany], Veritas [Synovis, St. Paul, MN] and Xenmatrix [Davol Inc., Warwick, RI]) and the generic names (ie, human acellular dermal matrix/allograft, acellular dermis, small intestinal submucosa, porcine dermal matrix/graft, porcine dermis, and bovine pericardium) of the various collagen-based prostheses. All terms were searched for as free text and, where possible, mapped to Medline subject headings. Preliminary screening of titles and abstracts was undertaken. Then, full-text articles of eligible studies were retrieved for evaluation. The reference lists of all included and excluded studies were manually scanned for additional studies missed in the electronic search. To prevent double counts of data, different studies by the same authors were scanned for uniqueness with regard to the included patients. The most recent study with the longest follow-up was chosen in the case of overlap. The last search was performed on November 16, 2010. The characteristics and costs of the biologic grafts used in ventral hernia repair were sought in the literature, on the manufacturers' web sites, and via telephone contact with the manufacturer and/or distributor. Costs presented are based on standard sheet sizes and exclude any form of discount.

Inclusion and exclusion criteria

Studies including men and women over the age of 18 who underwent definitive repair of all types (ie, incisional, epigastric, Spiegel [lateral ventral], and [para-]umbilical) of ventral hernias were selected. In addition, the reconstruction of large defects created during surgery (eg, transverse rectus abdominus myocutaneous (TRAM) flap reconstruction and tumor resection) or trauma were included. The biological prosthesis had to be the sole graft material used to repair the defect. Studies on biologic grafts placed as reinforcement or as a bridging material were included. Studies with less than 7 patients were excluded.

The methodological quality and the risk of bias of each individual remaining study were assessed by subjecting it to a modified version of the methodological index for non-randomized studies tool 7 (Table 1). This instrument was constructed and validated for the appraisal of nonrandomized trials in surgery.[7] In the modified version, a score of 2 on each item results in a maximum score of 14. Studies that scored a 0 on items 2, 5, or 7 or had a total score of less than 8 were excluded from analysis of the primary outcome. All articles selected for inclusion during the search process were scored independently by 2 authors (NJS and RPB). Disagreement was resolved by discussion and consensus.

Primary and secondary outcomes

The primary outcome of this systematic review was recurrence as defined by the authors in the individual reports including only studies with a follow-up of at least 12 months. Secondary outcome measures were counted irrespectively of follow-up duration and included mortality, laxity of the repair, surgical site infection, deep (fascial) wound dehiscence, seroma and haematoma formation, enterocutaneous fistula, and the total number of surgical complications.

Data extraction and subgroup formation

All data were extracted using a predesigned data form. The demographic variables age, body mass index (BMI), size of defect, comorbidities, American Society of Anesthesiologists (ASA) score, the indication for surgery and wound class, and the surgical technique (ie, open or laparoscopic, reinforcement or bridging, and anatomic position) were noted. Reinforcement repair is defined as the placement of a graft to augment approximated native

Table 1 Modified MINORS

Item	Criteria	Option	Score
1	A clearly stated aim	Not reported	0
		Partially reported, no clear aim	1
		Clear aim	2
2	Minimum of 5 patients included	No	0
		Yes	2
3	Inclusion of consecutive patients	Not reported	0
		Patients in a certain time period	1
		Consecutive patients + characteristics	2
4	Diagnostic modality of follow-up	Not reported/unclear/telephone used	0
		Clinical examination	1
		Clinical examination + CT/Ultrasound	2
5	Surgical methods (ie, anatomic placement of prosthesis, surgical technique, bridge/reinforcement used)	Not reported	0
		Incomplete	1
		Reported clearly, appropriate to aim	2
6	Endpoints clearly stated in methods section	Not reported/unclear	0
		Stated but inadequate	1
		Clearly stated	2
7	Endpoints appropriate to aim	Not reported	0
		Recurrences only	1
		Recurrences and postoperative complications	2
		Maximum score	14

fascia, whereas in bridging there is no (complete) approximation of native fascia. The anatomic position of the prosthesis was defined as subcutaneous on top of the anterior rectus fascia ("onlay"), between the rectus muscle and the posterior rectus fascia ("preperitoneal underlay" or the Rives-Stoppa technique), behind the posterior rectus sheath ("intraperitoneal underlay" or modified Rives-Stoppa technique), or within the defect and sutured directly to the fascial edges ("interpositional" or "inlay").

Certain assumptions were made while extracting information because of the lack of consistency of reporting and terminology in the reports. Only complications explicitly noted in the methods or results section were counted. Laxity, diastasis, and "bulging" were all grouped as laxity of the repair. Superficial wound dehiscence was counted as a wound infection. The total number of surgical complications per study was calculated by adding up all reported surgical complications. In case additional data were needed, authors were contacted.

Subgroups were formed for wound class (ie, clean/clean-contaminated, contaminated/dirty, or complicated), biologic graft (ie, Alloderm, Permacol, or Surgisis), and surgical technique (ie, reinforcement or bridging). Where necessary, patients from a single study were divided between different subgroups. Wound classification was performed according to the US National Research Council group.[8] Patients classified by the authors were grouped accordingly. If this was not done by the authors, the indications for surgery were reviewed to determine the wound classes. The classes clean and clean-contaminated were grouped together, and contaminated and dirty were grouped together. The third group (complicated) consisted of patients who could not be stratified into the first 2 groups (ie, clean/clean-contaminated and contaminated/dirty) and/or had complex, complicated, or potentially contaminated hernias as noted by the authors.

In the wound class subgroups, data allowed for the extraction of the outcomes recurrence, infection, and total surgical morbidity. Biologic grafts subgroups were analyzed with regard to the following outcomes: recurrence, laxity, seroma, and total surgical morbidity. Surgical techniques were analyzed with regard to recurrence and laxity.

Statistical analysis

Weighted pooled proportions with 95% confidence intervals (CIs) using the random-effects (DerSimonian-Laird) model were calculated for all primary and secondary outcomes and are presented for subgroups and the whole group. Differences in weighted pooled proportions were analyzed using the chi-square test and only performed on outcomes that could be stratified by wound class. A P value $< .05$ was considered statistically significant. The odds ratio (OR) with the 95% CI was calculated to quantify statistically significant different outcomes. The heterogeneity of the wound class subgroups was quantified using I^2. Analysis of outcome differences between grafts was not undertaken because insufficient data left subgroups that were too small or empty after stratification by both wound class and graft type. Univariate regression analysis was performed to explore the relationship between recurrence and the outcomes infection and overall surgical complications. Median scores were calculated for the modified Methodological Index of Non-Randomised Studies (MINORS) indices and for the reported means of months follow-up, age, BMI, and the size of the hernia defect. Univariate analyses were

performed using SPSS 16 (SPSS Inc, Chicago, IL).[9] All other analyses were performed using StatsDirect statistical software (StatsDirect Ltd., Cheshire, England).[10]

Results

Systematic review

The search strategy yielded a total of 1,152 titles and abstracts (Fig. 1). A total of 27 studies[11–37] were included in the systematic review. Seventeen studies provided sufficient follow-up and were included for primary outcome analysis, and 25 studies were included for secondary outcome analysis. Although various studies reported on using prospectively collected data, none of them elaborated on how data were collected according to a protocol rendering them qualitatively indistinguishable from the retrospective studies. The median modified MINORS score of the included studies was 11 (range 8–14) (Table 2).

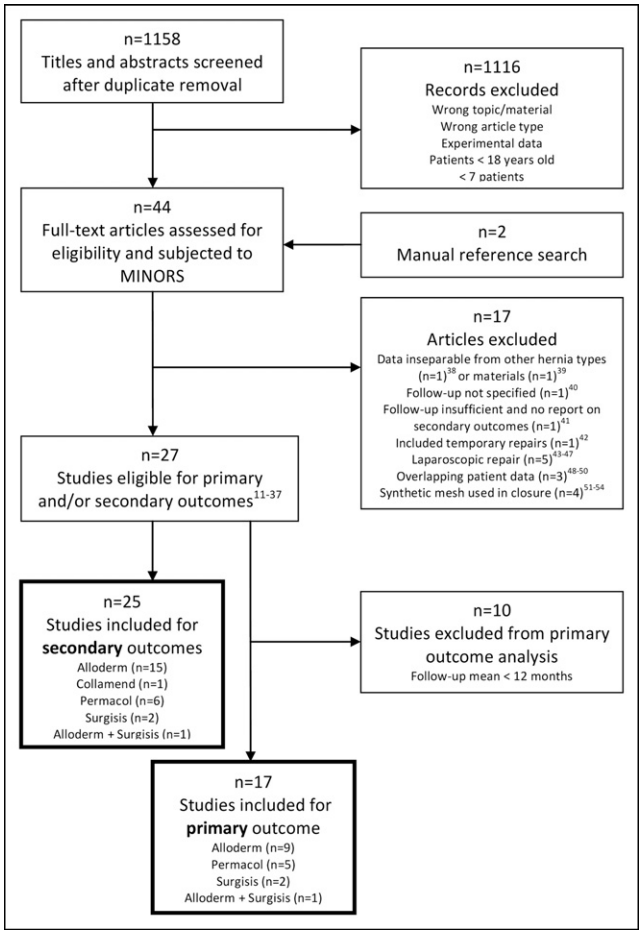


Figure 1 Search flow chart in accordance with Preferred Reporting Items for *Systematic Reviews* and Meta-Analyses. Search performed in databases Cochrane Central Register of Controlled Trials, Embase, MEDLINE, and MEDLINE In-Process & Other Non-Indexed Citations using PubMed and Ovid. "Articles excluded" box includes information from references.[38–54]

Most studies reported age (82%) and BMI (52%), whereas less than half reported the ASA score (44%) and the size of the defect (40%). The median of reported means were 54.5 years, 32.0 kg/m^2, and 150.0 cm^2 for age, BMI, and the size of the defect, respectively. All reported median ASA scores were 3. No differences between subgroups were found for age ($P = .108$) or BMI ($P = .123$).

Alloderm, Permacol, and Surgisis

Three biologic grafts were found almost exclusively in the ventral hernia literature and were included for primary outcome analysis: Alloderm, Permacol, and Surgisis. Alloderm is an allograft derived from human cadaveric dermis and is available in sizes up to 16 × 20 cm and costs $35.31 per cm^2. Varying thicknesses are available including .79 to 2.03 mm ("Thick") and 2.06 to 3.30 mm ("X-Thick"). To prevent physical and chemical alterations because of sterilization, after decellularization Alloderm is not sterilized but instead treated with antibiotic agents and packaged aseptically. Alloderm needs to be stored refrigerated, undergo a 2-step rehydration (10-40 minutes depending on the thickness), and be prestretched for hernia repair to prevent otherwise expected laxity.

Permacol is derived from porcine dermis and has the largest grafts available with sizes up to 28 × 40 cm costing $18.97 per cm^2. Grafts are available with thickness varying from .5 mm to 1.5 mm. After decellularization, Permacol is sterilized by gamma radiation and is packaged in a hydrated state that makes it usable straight away without any preparation. Permacol undergoes additional cross-linking during processing by hexamethylene diisocyanate aimed at decreasing its biodegradability, which might be accelerated in contaminated wounds.

Surgisis is made from porcine small intestinal submucosa and is available in sizes up to 20 × 30 cm. The cost per cm^2 graft is $20.00. Material harvested from small intestinal submucosa is thin, but Surgisis undergoes lamination to make it thick enough (up to 2.0 mm) for hernia repair. This graft undergoes ethylene oxide sterilization and is packed dehydrated, making rehydration necessary before implantation. Surgisis has been found to retain certain proteoglycans, glycosaminoglycans, and angiogenic growth factors that potentially stimulate cell attachment and vascularisation.

Mortality

Mortality was reported in 19 series[11,12,14–16,18–20,22,23,27,28,30,31,33–37] including 879 patients. Thirty-six (4.1%) patients died; 20 (2.3%) died within 30 days of surgery. One study described 2 deaths after multiple attempts to repair enterocutaneous fistulas.[16] All other deaths were noted as unrelated to the ventral hernia repair (eg, multiple organ failure, congestive heart failure, and disseminated intravascular coagulation).

Table 2 Study characteristics and recurrence rates for ventral hernia repair with biologic grafts

Reference	Year	MINORS index	Graft used	No. of patients	Mean size of defect, cm^2	No. of C/D procedures (%)	No. of recurrences (%)	Follow-up (range)
Clean/Clean-Contaminated								
Buinewicz et al[14]	2004	10	Alloderm	36	86.4	0 (0)	1 (2.8)	20 (8–32)
Glasberg et al[17]	2006	12	Alloderm	54	166	0 (0)	0 (0)	18.5 (9–30)
Gupta et al[18]	2006	10	Alloderm	33	NS	0 (0)	8 (24.2)	29 (NS)
Boehmler et al[13]	2009	11	Alloderm	31	NS	0 (0)	0 (0)	20.4 (NS)
Helton et al[36]	2005	13	Surgisis	21	202	0 (0)	0 (0)	14 (2–29)
Gupta et al[18]	2006	10	Surgisis	38	NS	0 (0)	0 (0)	19 (NS)
Overall C/CC (95% CI)*			Various	213			2.9% (.2–8.3)	
Contaminated/dirty								
Buinewicz et al[14]	2004	10	Alloderm	8	86.4	8 (100)	1 (4.5)	20 (8–32)
Alaedeen et al[11]	2007	11	Alloderm	11	NS	11 (100)	2 (18.2)	14 (2–68)
Taner et al[28]	2009	13	Alloderm	11	NA	13 (100)	0 (0)	12 (±4)
Ueno et al[37]	2004	13	Surgisis	20	NS	20 (100)	6 (30.0)	15.7 (NS)
Helton et al[36]	2005	13	Surgisis	19	202	19 (100)	8 (42.1)	14 (2–29)
Gupta et al[18]	2006	10	Surgisis	3	NS	3 (100)	0 (0)	29 (NS)
Connolly et al[31]	2008	10	Permacol	12	NA	12 (100)	5 (41.7)	29 (16–84)
Overall C/D (95% CI)*			Various	84			23.1% (11.3–37.6)	
Complicated*								
Kolker et al[21]	2005	8	Alloderm	16	NS	9 (56.3)	0 (0)	16 (9–23)
Jin et al[19]	2007	10	Alloderm	37	122	16 (43.2)	12 (32.4)	22.2 (15–37)
Candage et al[15]	2008	12	Alloderm	46	NS	17 (37.0)	14 (30.4)	12.1 (NS)
Lee et al[22]	2009	11	Alloderm	68	NS	54 (79.4)	21 (30.9)	15.4 (NS)
Parker et al[34]	2006	10	Permacol	9	NS	5 (55.6)	1 (11.1)	18.2 (NS)
Shaikh et al[35]	2007	12	Permacol	20	180	5 (25.0)	3 (15)	18 (6–36)
Hsu et al[32]	2009	13	Permacol	28	150	NS	3 (10.7)	16 (10–23)
Loganathan et al[33]	2010	10	Permacol	10	NS	NS	1 (10.0)	12 (3–62)
Overall "complicated" (95% CI)†			Various	234			19.4% (11.4–29.0)	
Overall combined (95% CI)*							13.8% (7.6–21.3)	

C/CC = clean/clean-contaminated; C/D = contaminated/dirty; NA = not available; NS = not specified.

*This subgroup contains groups of patients for which the outcomes could not be stratified per wound class and/or that contained cases with unclear surgical indications that were classified by the corresponding authors as either "complex," "complicated," "potentially contaminated," or "high risk."

†Weighted pooled proportion using the random-effects (DerSimonian-Laird) model.

Surgical morbidity

Table 3 presents the surgical morbidity divided by wound class. Overall, surgical morbidity could be extracted for 1,152 patients out of 25 studies[11–18,20–26,28–37] in which 584 surgical complications (46.3%; 95% CI, 33.3–59.6) were documented. Infectious complications were reported most often. Wound infections were reported in 246 of 1,109 (15.9%; 95% CI, 9.8–23.2) patients.[12,14–18,20,22–30,32,34–37] In 12 patients (4.9%), the prostheses had to be removed.[26,29,34,36] Other infectious complications were intra-abdominal abscesses in 2.4% and miscellaneous in 2.7%.

Seroma formation was reported in 115 of 827 (14.2%, 95% CI, 9.5–19.5) patients (Table 4).[14–18,21,23,24,26,28,32,35,37] Five cases of explantation after significant seroma formation were documented in 1 report of repair with Surgisis.[17] All other seromas resolved either spontaneously or after percutaneous aspirations. Hematomas were reported 9 times in 354 patients (3.0%, 95% CI 1.4–5.3).[12,14,15,17,20,22,24,33,35]

Deep wound dehiscence necessitating operative intervention was documented in 16 of 191 patients (8.6%; 95% CI, 6.2–11.2).[12,22,24,36] The postoperative course was complicated by an enterocutaneous fistula in 59 of 756 patients (6.5%; 95% CI, 3.5–10.3).[13–16,21–23,25,27,30,32,34] Fifty-six percent was related to fistula takedown performed concomitantly with the hernia repair, 10.4% after bowel surgery, and 12.6% in patients with open wounds or after simple ventral hernia repair. Other postoperative wound-related complications were skin necrosis/breakdown (14/83 patients, 16.9%) and graft rejection/degradation (4/157, 2.5%). Medical complications were inconsistently reported.

The data allowed for the comparison of morbidity between wound classes regarding infection and total surgical morbidity using the chi-square test. Infection ($P = .0077$) and total surgical morbidity ($P < .0001$) were both dependent on wound class. Infection was significantly higher in the contaminated/dirty group than in the clean/clean-contaminated group ($P = .0016$; OR = 1.9; 95% CI, 1.24–2.91). Infection

Table 3 Pooled proportions of recurrence, infection, and total surgical morbidity divided by wound class

Complication	Wound class	No. of studies	No. of patients	Incidence	% (95% CI)*	Significance
Recurrence	C/CC	5	213	9	2.9 (.2–8.3)	
	C/D	7	84	22	23.1 (11.3–37.6)	$P < .0001$§
	Comp†	8	234	55	19.4 (11.4–29.0)	
	Overall	17‡	531	86	13.8 (7.6–21.3)	
Infection	C/CC	5	365	60	4.7 (.1–20.6)	
	C/D	7	224	61	19.3 (6.8–36.2)	$P = .0077$§
	Comp†	10	480	118	22.3 (15.3–13.3)	
	Overall	20‡	1109	246	15.9 (9.8–23.2)	
Total surgical morbidity	C/CC	5	235	74	32.5 (9.2–61.9)	
	C/D	8	160	72	52.4 (23.8–80.2)	$P < .0001$§
	Comp†	12	725	437	50.3 (33.4–67.2)	
	Overall	25	1152	584	46.3 (33.3–59.6)	

C/CC = clean/clean-contaminated; C/D = contaminated/dirty; Comp = complicated.

*Weighted pooled proportion using the random-effects (DerSimonian-Laird) model.

†This subgroup contains groups of patients for which the outcomes could not be stratified per wound class and/or that contained cases with unclear surgical indications that were classified by the corresponding authors as either "complex," "complicated," "potentially contaminated," or "high risk".

‡Does not add up because 1 or more studies were split into multiple groups.

§Statistically significant difference using the chi-square test.

was also significantly higher in the complicated group than in the clean/clean-contaminated group ($P = .004$; OR = 1.7; 95% CI, 1.16–2.39).

The contaminated/dirty subgroup showed a significantly higher total surgical morbidity rate compared with the clean/clean-contaminated subgroup ($P = .0064$; OR = 1.8; 95% CI, 1.15–2.75). The complicated subgroup also had significantly higher overall surgical morbidity compared with the clean/clean-contaminated subgroup ($P < .0001$; OR = 3.3; 95% CI, 2.39–4.58).

Recurrence

Seventeen studies[11,13–15,17–19,21,22,28,31–37] with a total enrollment of 531 patients met the inclusion criteria for the primary outcome. Overall, there were 86 recurrences (13.8%; 95% CI, 7.6–21.3; Table 3). Weighted pooled recurrence rates for each wound class are presented in Table 3 and Fig. 2. There were significantly less recurrences in the clean/clean-contaminated group compared with the contaminated/dirty group ($P < .0001$; OR = 55.9; 95% CI, 8.5–2,321.3) and the complicated group ($P < .0001$; OR = 39.0; 95% CI, 6.5–1,581.0; Table 3). No significant difference was found between the contaminated/dirty and the complicated subgroup ($P = .2233$).

To identify factors associated with recurrent hernia, univariate regression was performed. Postoperative infection ($r^2 = .325$, $P = .011$, Fig. 3) and total surgical morbidity ($r^2 = .189$, $P = .038$, Fig. 4) were revealed as significant explanatory variables for recurrent hernia.

Laxity

Laxity of the repair was documented in 8 studies[12–14,17,18,21–23] including 451 patients and occurred in 51 patients (10.5%; 95% CI, 3.7–20.3). All cases of laxity were reported with the use of Alloderm.

Surgical technique

Recurrence and/or laxity by type of closure were adequately documented in 14 studies including 380 patients.[11–15,17,19,27,28,30–32,35,37] In patients who underwent reinforcement, recurrence occurred in 14 of 161 (8.1%;

Table 4 Pooled proportions of infection, seroma, and total surgical morbidity divided by biologic graft

Complication	Material	No. of studies	No. of patients	Incidence	% (95% CI)*
Infection	Alloderm	14	926	224	17.1 (9.3–6.7)
	Permacol	4	64	3	6.1 (1.7–3.0)
	Surgisis	3	101	15	14.9 (.4–44.8)
Seroma formation	Alloderm	10	718	93	13.2 (8.8–18.4)
	Permacol	2	48	3	7.6 (1.9–16.4)
	Surgisis	2	61	19	26.0 (.3–59.2)
Total surgical morbidity	Alloderm	16	947	502	46.5 (29.7–63.7)
	Permacol	6	86	26	28.7 (17.2–41.8)
	Surgisis	3	101	46	45.7 (36.2–55.3)

*Weighted pooled proportion using the random-effects (DerSimonian-Laird) model.

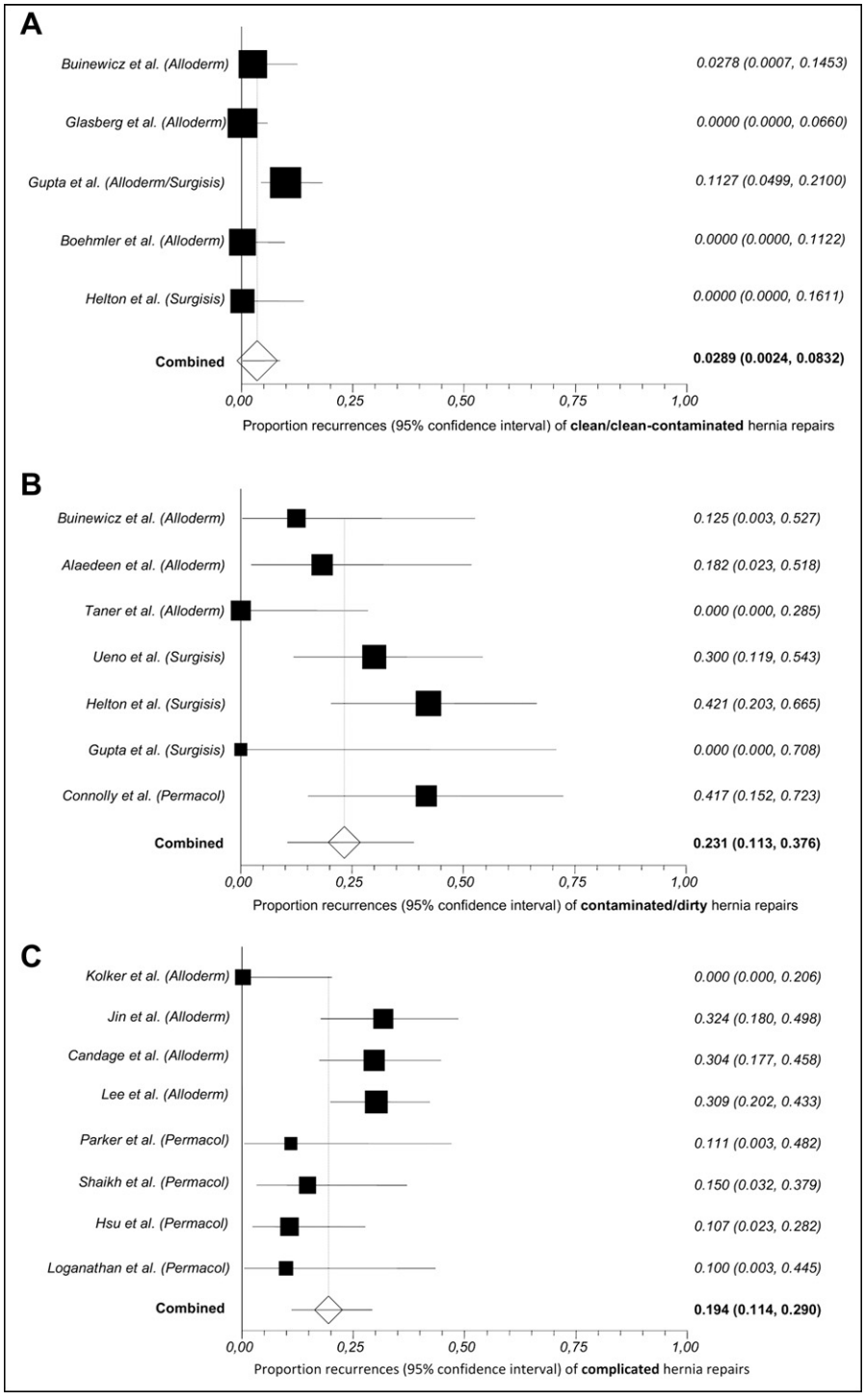


Figure 2 Meta-analysis (random-effects model) of proportions of recurrences of (A) clean/clean-contaminated (I^2 = 68.4%), (B) contaminated/dirty (I^2 = 52.9%), and (C) complicated (I^2 = 64.2%) ventral hernia repair with biologic grafts. The square size represents the weight of the study, and the horizontal line through the square represents the CI of the effect estimate.

95% CI, 2.2–17.2). Laxity was observed in 9 of 72 patients (9.7%; 95% CI, .1–32.1). Only 3 studies (75 patients) provided the mean size of defect specifically for reinforced repairs; it ranged from 86 to 180 cm^2.[14,19,35]

In patients in whom the defect was bridged, recurrence occurred in 39 of 219 (21.8%; 95% CI, 7.5–40.9). Laxity was reported in 28 of 138 patients (21.0%; 95% CI, 14.8–28.0). The mean size of defect could be extracted for bridging repairs in 7 studies (168 patients), with a median of 158.0 cm^2 (range 147–210 cm^2).[12,14,17,19,27,30,32]

Of all repairs, underlay placement of the graft was the most used technique (57.3%) followed by inlay (25.9%), onlay (14.7%), and "sandwich" placement including both onlay and underlay placement of prostheses (2.1%). About

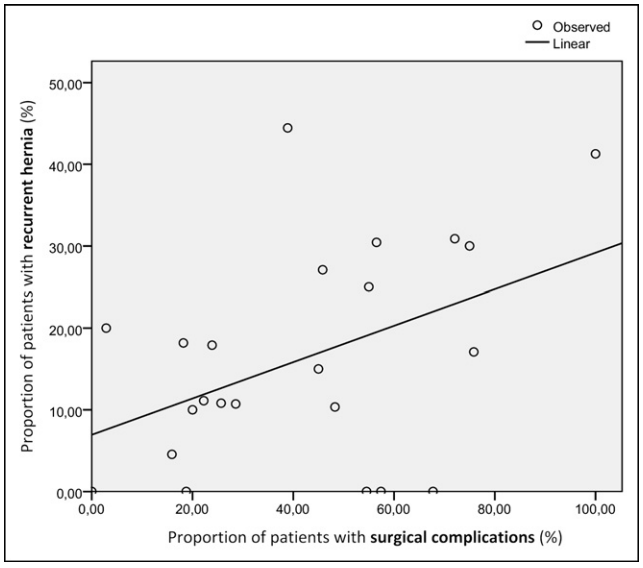


Figure 3 Univariate regression with the recurrence rate as the outcome and the infection rate as the predictor (r^2 = .325, P = .011). Circles represent observed rates in the studies, and the line represents the linear regression.

a third of the authors (31.0%) reported the additional use of the component separation technique in some or all of their patients to achieve primary fascial closure. Inadequate reporting made it impossible to relate component separation technique or the type of anatomic graft position to any study outcome.

Comments

The current systematic review evaluated postoperative morbidity and the recurrence rate after ventral hernia repair with biologic grafts. Half of the patients suffered wound-related morbidity. Infectious complications developed in a fifth of the patients but only rarely necessitated graft removal. The overall recurrence rate was 13.8% after a mean follow-up of 18 months. The recurrence rate was low (2.9%) in clean and clean-contaminated cases and increased with the extent of contamination. Nearly a quarter of the patients undergoing contaminated, dirty, or otherwise complicated repair experienced a recurrence. Overall, laxity of the repair occurred in 1 out of 10 patients.

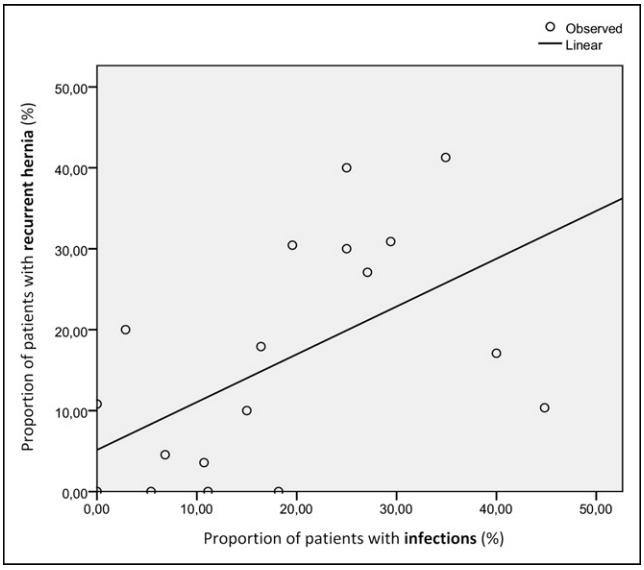


Figure 4 Univariate regression with the recurrence rate as the outcome and the overall surgical morbidity rate as the predictor (r^2 = .189, P = .038). Circles represent observed rates in the studies, and the line represents the linear regression.

Quality of studies

The quality of evidence rates a 4 (recommendation grade C) according to the Oxford Centre for Evidence-based Medicine levels of evidence.[55] The current findings are troubled by the heterogeneity of patients and hernia characteristics within and between studies. The interpretation of data was difficult because of the lack of uniformity in definitions, terminology, and reporting. Classification of hernias following the European Hernia Society guidelines was not possible.[56]

A limited follow-up is a well-recognized flaw in many studies. In this review, a study follow-up of at least 12 months was considered sufficient to provide a reliable outcome, realizing that recurrence rates are underestimated and increase up to and beyond 13 years after repair.[4,57] Despite these limitations, results of the current study are meaningful because a large number of patients who underwent ventral hernia repair using biologic grafts were included, encompassing 531 patients to determine recurrence rate and 1,152 patients for secondary outcome parameters. Also, outcome stratification by wound class made more homogenous groups.

Postoperative morbidity

Postoperative morbidity increased with wound class, overall occurring in nearly half of the patients. Because of the inability to stratify surgical complications by both wound class and biologic graft, safety comparisons between different grafts are hard to undertake. Still, certain outcomes were surprising and deserve further attention.

Seroma formation was the second most common postoperative complication, occurring in 14.2% of patients. Noteworthy is the high rate of seroma formation found with the use of Surgisis, which is also observed after laparoscopic hernia repair.[44,47] This may be because of delamination of the graft or an enhanced inflammatory response. Gupta et al[18] performed histologic analysis on grafts explanted after significant seroma formation and found that they were only partially incorporated and remodeled into fibrocollagenous tissue, allowing seroma formation between the different (unincorporated) layers of the graft. An exaggerated inflammatory response to small intestinal submucosa grafts was reported in 3 publications. Helton et al[36] observed a pronounced inflammatory response in 6 of 53

patients (11%) in whom a Surgisis graft was implanted. Fluid aspiration around the graft presented a negative culture, and the inflammatory response rapidly decreased in all patients with anti-inflammatory medication. Zheng et al (unpublished data, February 2005) observed transient noninfectious edema and pain in patients treated for rotator cuff injury with Surgisis grafts. Similar inflammatory responses were observed after implantation of small intestinal submucosa–derived products in pubourethral sling procedures.[58] Cell remnants and other immunogenic material, noncollagenous proteins, growth factors, and glycosaminoglycans found in porcine small intestinal submucosa may be responsible.[59–61]

Infection was the most common postoperative complication and increased with the extent of wound contamination, with an overall rate of 15.9% (Table 3). The high infection rates seem to refute the claims that biologic grafts are infection resistant because of their biocompatibility and direct access of immune cells. However, the majority of infections were superficial, and the biologic graft could nearly always be salvaged. Grafts were removed in only 4.9% of infected cases.

In a recent meta-analysis of incisional hernia repair with synthetic mesh, open repairs resulted in seroma formation in 15.5% and hemorrhagic complications in 5.9%. Infection not requiring mesh removal occurred in 10.1%, and infections requiring removal occurred in 3.5%, meaning a quarter of all infections required mesh removal.[62] A meta-analysis of the component separation technique for ventral hernia repair revealed an 18.9% infection rate, contributing to an overall complication rate of 23.8%.[63] Given the current evidence, biologic grafts do not seem to result in fewer surgical complications than other techniques. However, biologic grafts are associated with a high salvage rate in cases of infection. After synthetic mesh repair, mesh removal is often mandatory when infection develops.

Recurrence and laxity

Recurrence rates were also related to the extent of wound contamination. Reconstruction in a contaminated field is a major indication for the use of biologic grafts. Surprisingly, about a quarter of repairs in the included studies were performed under clean or clean-contaminated conditions. In this group, the recurrence rate was low (2.9%) and similar to recurrence rates after synthetic mesh repair found in a meta-analysis.[62]

The recurrence rates for the contaminated/dirty and complicated subgroups were 23.1% and 19.4%, respectively. Despite the reluctance to use synthetic mesh in a contaminated environment, similar results were reported after synthetic mesh repair in selected contaminated and complex ventral hernia repairs including concomitant enterostomy closure, necrotic bowel resection, enterocutaneous fistula takedown, and other elective bowel procedures.[64–70] Recurrence rates varied between 0% and 21% and morbidity between 15.8% and 26%. Given these results, there are still possible indications for synthetic mesh use in the certain compromised wound environments. However, the option of a 1-stage repair in grossly infected wounds still makes biologic grafts a potential attractive alternative to 2-stage repair with synthetic mesh. Techniques of autologous repair have been summarized and also yield similar results.[63] Of these, the component separation technique met with wide acceptance, yielding an 18.2% rate of recurrence found in a meta-analysis[63] and more recent studies showing even lower rates.[53,71] In view of the current evidence, biologic grafts have similar results to synthetic mesh or autologous repair in either clean, contaminated, or complicated ventral hernia repair.

Laxity is a common complication with the use of biologic grafts, showing an overall rate of 10.5%. Unlike hernias, which can be debilitating and coincide with a risk of strangulation, laxity does not necessarily affect a patient's functionality and it is unclear what effect it has on quality of life. However, its occurrence is considered a negative outcome.

All reported cases of laxity in this review were related to repairs with Alloderm. The high elastin/collagen ratio, insufficient prestretching, no additional cross-linking, and thin and vulnerable border regions because of the dermatome harvest from human cadavers may all be responsible for bulging. Laxity is rarely investigated with the use of synthetic mesh, and the prominent focus it receives in studies on biologic grafts may be an attention bias. However, in their study comparing human acellular dermal allograft (Alloderm) with polypropylene mesh repair of abdominal wall defects after TRAM flap harvesting, Boehmler et al[13] reported rates of bulging and other complications of 29% and 39% in the Alloderm group and 7% and 17% in the polypropylene mesh group, respectively. When taking laxity into account alongside reherniation, a quarter of all patients experienced full or partial failure of the integrity of their abdominal wall reconstruction.

Surgical technique

A relevant aspect of hernia repair, whether bridging the defect or reinforcing the closure, is the anatomic position of the prosthesis. Unfortunately, the data did not allow for pooled analysis. In individual reports, it was found that interpositional (inlay) placement of the prostheses while bridging the defect resulted in higher recurrence rates compared with methods in which an adequate overlap between the prosthesis and the adjacent fascia was created.[16,19,24,26]

Costs

A major issue surrounding biologic grafts is their high price. Depending on the choice of product, a 150 cm^2 prosthesis costs between $2,845 and $5,311. In the clinic, proper

evidence and clear indication for their use is thus paramount for the provision of not only effective but also efficient health care. Claims are made by the industry that long-term financially beneficial outcomes are to be expected with biologic grafts when taking into account less short- and long-term complications compared with other techniques.[72] These analyses are based on scant literature and should be strengthened by more evidence from properly designed trials comparing the various techniques available.

The current review did not compare biologic with synthetic prostheses. No randomized controlled trials are available yet that compare the results of both techniques. However, postoperative morbidity and recurrence rates seem to be similar between biological and synthetic prostheses in nondirty fields. Considering the high costs of biologic grafts, they are not recommended in these situations. The use of biologic grafts results in high complication and recurrence rates in contaminated and dirty fields but is associated with a high salvage rate of the prosthesis in cases of infection and potentially offers a 1-stage repair in these compromised surgical fields. Biologic grafts are not popular in Europe because of their high costs, and more convincing evidence of their performance and proper indication is awaited. The Food and Drug Administration reported adverse events with the use of biologic grafts that warrant caution and judicious decision making. Biologic grafts have not been approved for use in abdominal wall reconstruction in contaminated fields.[73] Studies with longer follow-ups are essential to properly determine the durability of biologic grafts given their biodegradable nature.

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