Review article

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Biological materials in colorectal surgery: current applications and potential for the future

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Abstract

Biological materials are increasingly used in abdominal surgery for ventral, pelvic and perineal reconstructions, especially in contaminated fields. Future applications are multi-fold and include prevention and one-step closure of infected areas. This includes prevention of abdominal, parastomal and pelvic hernia, but could also include prevention of separation of multiple anastomoses, suture- or staple-lines. Further indications could be a containment of infected and/or inflammatory areas and protection of vital implants such as vascular grafts. Reinforcement patches of high-risk anastomoses or unresectable perforation sites are possibilities at least. Current applications are based mostly on case series and better data is urgently needed. Clinical benefits need to be assessed in prospective studies to provide reliable proof of efficacy with a sufficient follow-up. Only superior results compared with standard treatment will justify the higher costs of these materials. To date, the use of biological materials is not standard and applications should be limited to case-by-case decision.

Keywords Biological mesh, reconstruction, colorectal, hernia, contamination

What is new in this paper?

Comprehensive overview on current and potential future applications of biological materials in colorectal surgery based on a critical appraisal of the available evidence in the literature.

Introduction

The introduction of mesh materials for reinforcement has revolutionized hernia and reconstructive surgery by reducing recurrence rates. The down-side of synthetic materials are chronic inflammation, long-term material behaviour such as stiffness, erosion/extrusion and chronic mesh infections. Autografts can provide excellent alternatives for specific indications but are limited by donor site morbidity [1].

Biologic meshes have been developed to fill this gap and to provide an alternative especially for large defects and in the contaminated field [1–5]. These materials are obtained from human (*allograft*) or animal sources (*xenograft*). The harvested tissue is freed from cellular debris and processed to become acellular, sterile and non-immunogenic. The final product is a porous connective tissue scaffold. Additional chemical cross-links results in slower degradation and a stronger collagen network associated with slower incorporation and remodeling [1,6].

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Host response depends among other factors on pore size and absorbability and can be categorized into:

1 Resorption – replacement by host connective tissue.

2 Incorporation – infiltration by host cells, revascularization, collagen deposition.

3 Encapsulation – with connective tissue formation around the material.

Complete resorption might impair long-term stability while encapsulation predisposes to risks of infection and erosion. Therefore, choice of the appropriate material depends on the individual indication [1,2,5].

Biological meshes have been increasingly used after abdominoperineal excision (APE) and hernia repair in contaminated settings [5,7]. Promising results have been published but available studies are small, heterogeneous and with limited follow-up [3,7]. It seems therefore useful to give an overview on current applications of biological materials in colorectal surgery and to provide an outlook on potential future indications.

Method

Relevant articles were searched by screening main electronic databases including Medline (searched through

PubMed) using the MeSH terms '(biological (mesh OR material) AND ((general OR visceral OR abdominal OR colorectal) surg*)'. Over 1000 hits were assessed for eligibility and relevant articles were obtained. Missing publications were searched for by cross-referencing. Only articles published in English were considered and no time limits were applied. Reviews, meta-analyses, randomized trials and large cohort studies were privileged for the purpose of this review. Final selection was performed by the authors to limit the reference list to the most important and relevant studies to the topic of this review. Although we tried our best, we can give no guarantee of a complete list of available products (Table 1) and of published studies (Table 2).

Results

While the number of publications on biomaterials increased steadily over the years, overall quality of available studies remains modest at best. Types of materials and their applications are summarized in Tables 1 and 2, respectively.

Biological materials and classification

The idea of biological meshes is to use the collagen network of human (allografts), porcine or bovine (xenografts) tissues instead of synthetic material. Biological meshes are harvested from dermis, fascia lata, intestine or pericardium, limiting the availability and explaining partially the costs. Processing techniques vary but typically involve harvesting, decellularization, preservation and terminal sterilization aiming to obtain an acellular and non-immunogenic final product field [1–5]. Details on processing are difficult to obtain and their clinical relevance has yet to be ascertained definitively. Only additional cross-linking seems to be of interest for the surgeon.

Non-cross-linked meshes are progressively infiltrated and replaced by host cell and connective tissue (incorpo-

Table 1 Biological materials – type, origin, characteristics.

			Available literature (comparing number of patients)		
Origin	Crosslinking	Mesh type	> 100	99–30	< 30
Allografts					
Dermis	No	Alloderm®	2	13	8
	No	Allomax™	–	–	–
	n.a.	DermaMatrix™	–	–	–
	No	DuraDerm™	–	1	–
	No	FlexHD®	–	–	–
Fascia lata	No	Tutoplast®	–	–	–
Xenografts					
Porcine					
Dermis	Yes	CollaMend™	–	–	2
	No	InteXen®	–	–	–
	Yes	Pelvicol™	–	5	2
	No	Pelvisoft®	–	1	–
	Yes	Permacol™	1	2	13
	No	Perigee™	–	–	–
	No	Strattice™	–	–	2
	No	XenMatriX™	–	1	1
	Yes		–	–	–
Intestine	No	Surgisis®	1	5	11
	Yes	FortaGen®	–	–	1
Bovine					
Dermis	No	SurgiMend®	–	–	–
Pericardium	No	Tutopatch®	–	–	1
	n.a.	UroPatch™	–	–	–
	No	Veritas®	–	–	1

List of biological meshes used in abdominal surgery, with information about origin, crosslinking and available literature adapted from [3,4,7].
The number of published series including more than 100 patients, between 99 and 30 patients, or < 30 patients. Most papers include a small number of patients, and only few more than 30 or 100 patients.

Table 2 Summary for current applications of biological material in colorectal surgery.

Indication	Studies (contaminated)	Median no. of patients (range)	Follow-up median (range)	Success (%)*	Complications
Pelvic reconstruction	14 (0)[1,3,5]	35 (14–98)	16 (12–36)	0–100	Mesh extrusion –21% pain –30%
Ventral hernia	12 (7)[1,2,5]	44 (8–74)	16 (12–57)	47–100	Seroma 6–91% infection 1–8%
Inguinal hernia	11 (0)[1,3,5]	30 (11–60)	18 (12–60)	91–100	Seroma 9–25% pain 2–9%
Abdominal wall defects	5 (1)[2,3,4]	23 (9–37)	18 (16–30)	65–96	Seroma 4–7% infection 4–10%
Perineal reconstr. after elAPE	5 (5)[1,3]	12 (8–30)	10 (8–20)	90–100	Wound compl. 28%
Parastomal hernia repair	2 (2)[1,4]	*n* = 15	50/52	92	Seroma, pain
Enterocutaneous fistula	1 (1)[5]	*n* = 11	16	91	Seroma 27% infection 18%

Current applications for biological materials in abdominal surgery with clinical outcomes adapted from [3,7,14]. The most frequently used materials were [1]Surgisis®, [2]Alloderm®, [3]Permacol™, [4]Tutopatch®, and [5]other as referenced.
Limitation: Several studies report on mixed collectives and indications with unspecified individual outcome data.
*Success was defined as healing and free of recurrence.

ration) with reports on laxity of ventral repairs as long-term complication. Biological meshes can be additionally cross-linked by instilling chemicals, in order to create additional covalent bonds in the collagen network. This process delays degradation by collagenases and aims to obtain a permanently stable material, allowing a long-term repair [1,6]. Depending upon the degree of these additional covalent bonds, cross-linked implants may become functionally non-porous and host cellular infiltration may not occur. The material is not replaced, but encapsulated by a connective tissue envelope. However, resorption of cross-linked biological mesh over time has been reported: a woman was re-operated 1 year after a cross-linked material posterior repair, and no residual material was found [8]. It has been speculated that seroma formation and risks for infection might be higher with cross-linked prostheses although other literature counters this.

We found reports on over 20 different biological meshes. Most papers relate to Alloderm®, Permacol™, Surgisis® and Pelvicol™. Most of the publications are retrospective study, including small number of patients [3,7]. Only few prospective randomized studies have been published. Current applications are summarized in Table 2 and detailed in the following paragraphs.

Abdominal wall repair

Biological meshes have been documented for different abdominal repairs, especially in potentially contaminated fields [4]. Documented abdominal wall indications include incisional, ventral, inguinal and parastomal hernia repair, and abdominal reconstruction [3,4,7]. The reported recurrence rate after abdominal hernia repair in non-contaminated field ranges from 0% to 27% [9]. Most common post-operative complications seem to be seroma and local pain [3].

In potentially contaminated settings, biological mesh can be an interesting alternative to synthetic mesh in hernia repair. Biomaterials seem to have lower recurrence rate in these conditions, ranging from 0% to 46% [10]. However, for complex hernia repair or when used for bridging repair, acellular human dermis has higher recurrence rates reported as: 80% [11], 73% [12], 67% [13]. Recurrence rate and complications are to be interpreted with caution since most studies are retrospective, with variable indications, material, methods and follow up duration. Furthermore, many studies are hampered by a lack of information about the size of the defect.

Enterocutaneous fistula (ECF)

For complex Crohn's ECF there is often a significant portion of the abdominal wall that needs to be resected. The Mayo Clinic reported on 11 patients where a human acellular dermal matrix (hADM) was used to reconstruct the defect [14]. After a mean follow-up of 1 year ± 118 - days, 10 of 11 patients remained free of ECF while on a general oral diet. Only two of the 11 patients stayed on medical therapy. Although hADM is an expensive material ($4100 for a single 12 × 12 cm sheet), these results justify its use because refractory ECF and the associated long-term cost of dealing with the complications in this high-risk population is far greater.

Pelvic hernia repair and prevention

A recent review summarized 14 articles on the use of biological mesh for treatment of cystocoeles, rectocoeles and genital organ prolapse [3]. Two cohort studies approached 100 subjects (98 and 94) and median follow-up was 16 months. Recurrence and healing rates vary both from 0 to 100% (Table 2). Rare but typical adverse advents were vaginal wound complications and mesh protrusion, pain issues, and functional problems like fecal incontinence und urinary retention. These heterogeneous results and the lack of comparative studies (biological *vs* synthetic mesh) hinder firm conclusion.

Pelvic reconstruction after abdominoperineal resection (APR)

Perineal wound breakdown is the most frequent complication after standard APE and occurs in 35–65% of the patients [15]. Miles' original technique of extralevator APE (elAPE) has recently been revived to decrease the incidence of positive circumferential resection margins and thus local recurrence. This radical resection leaves only the ischioanal fat and skin to close the perineal wound in an area that has frequently been radiated prior to surgery. Therefore, myo- or fascio-cutaneous flaps have been advocated as optimal solution for filling of the defect and preventing wound complication.

A recent systematic review summarized 11 small cohort studies comparing 255 patients (seven studies) with flap reconstruction against 85 patients (five studies) with biological mesh repair after elAPE. Perineal wound complications occurred in 28% and 32% of patients after bio-mesh and flap repair, respectively; perineal hernia was infrequent in either group (3.5% *vs* 3.9%) [7]. Arguments for the use of biological material were shorter operating time and lack of donor site morbidity with earlier mobilization. Overall, study quality was low and lacking control groups and insufficient follow-up make definitive conclusion difficult.

Future applications

Biological meshes are of interest for enforcement of hernia repairs when the use of synthetic material appears to be inappropriate due to risks of infection or erosion. A typical indication would be ventral or parastomal hernia repair and even prophylaxis after concomitant bowel resection. Williams *et al.* suggested recently an elegant stapled (SMART) technique for prevention of parastomal hernia using a Permacol™ mesh [16]. The procedure is appealing especially for laparoscopic procedures. Reports with clinical outcome data are awaited (Table 3).

Small bowel obstruction after prior pelvic surgery can be extremely tedious for the surgeon and dangerous for the patient. Prophylactic mesh placement could prevent

Table 3 Potential future applications of biological meshes.

Principle	Indication	Example
Enforcement	Synchronous hernia repair within contaminated surgery	Incisional hernia and Hartmann's reversal, incarcerated hernia
	Prevention of incisional or parastomal hernia	High risk patients, poor tissue quality, definitive ostomy
'Pelvic seal'	Prevent pelvic small bowel obstruction and fistulas	Low anterior resection or abdomino-perineal resection
	To allow for pelvic irradiation: Adjuvant or neoadjuvant	Malignancies: colorectal, urological, gynaecological
Separation	Partition of multiple anasto moses, suture-/staple-lines	Combined colorectal, urological, gynaecological procedures
	Surgery at high risk for fistula formation	Crohn's: multiple anastomoses, stricturoplasties, ECFsurgery
'Firewall'	Containment of inflammation or uncontrolled perforation	Necrotizing pancreatitis, pancreatic fistula
	Protection of vital structures from detrimental infection	Cover of vascular grafts from contaminated areas
'Patch', 'wrap'	Closure of 'difficult' (tissue, mobilisation) perforation sites	ECF with laparostomy, perforation and peritoneal. carcinomatosis, duodenal perforation
	Enforcement of high-risk anastomoses, staple-lines	IBD surgery, emergency colectomies, immunosuppression, malnutrition

small bowel loops from dropping deep into the pelvis and adhering to de-peritonealized surfaces or suture- and staple lines. Fistula formation might be prevented and pelvic irradiation would remain an option.

Biological meshes might be considered to separate several anastomoses from each other or from suture- and staple-lines to prevent fistula formation. Combined colorectal, gynecological and urological procedures can be considered as well as multiple resections in inflammatory settings such as Crohn's disease. Separation of structures can be of interest in the presence of pancreatitis and/or pancreatic fistula. A close-by bowel anastomosis is at high risk for leak and containment of the inflammatory compartment could protect the anastomosis and help to direct inflammation and fistula in a controlled manner to the outside. Vital grafts like vascular prostheses can be separated from infected areas of the abdominal cavity by interposition of a biological mesh.

Patch repair of intestinal perforation is an imaginable option when direct suture appears insufficient due to poor tissue quality and resection is impossible, for example, in patients with long-standing open abdomen treatment and an undissectible block of small bowel. Other examples are malignant perforations with extensive peritoneal carcinomatosis and large duodenal defects. With the same rationale, biological meshes can be tried for reinforcement of anastomoses and staple lines to prevent leakage or blow-out of a long Hartmann's stump in high-risk situations including emergency surgery for inflammatory bowel disease or abdominal sepsis.

Current limitations

The available evidence for the use of biological material is weak due to methodological shortcomings. Available studies are small and there are hardly any randomized trials. Patients' follow-up is mostly short and the reported outcome measures are variable, incomplete and not well defined. A plethora of different mesh types has been used for as many different indications. Therefore, comparison and (statistical) summary on these studies in systematic reviews is problematic at least if not impossible. Considerable interests from the industry side cannot be neglected and although industry-supported studies are needed and welcome, conflicts of interests must be cautioned.

Biological materials are relatively new products and hence long-term outcome is lacking. The true recurrence rate after hernia repair and long-term stability after reconstruction using biological meshes is therefore unknown; long-term complication rates such as mesh erosion or adhesion formation need to be reported. Finally, higher costs limit the wide-spread use. Health care economic analyses including not only the product cost, but also the potential savings by reducing the number of re-interventions (in infected open abdomens for example) are urgently needed.

Conclusion

Biological materials are useful elements in the armamentarium of the abdominal surgeon. Theoretical advantages compared with synthetic mesh or reconstructive flap procedures include superior incorporation, less infection and no donor site morbidity; there is a wide variety of *potential* applications in colorectal surgery. However, available data is limited and costs are still high. Therefore, clinical studies are strongly advised, and indications for the use of biological material should be well-chosen and stringent.

Conflicts of interest

None.

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