Review article

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The role of biologics in pelvic floor surgery

M. Ahmad*, P. Sileri†, L. Franceschilli† and M. Mercer-Jones*

*Department of Colorectal Surgery, Queen Elizabeth Hospital, Gateshead, UK, †University of Rome Tor Vergata, Rome, Italy and ‡Department of Colorectal Surgery, Churchill Hospital/John Radcliffe Hospital, Oxford, UK

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Abstract

The advent of laparoscopic surgery and with it Laparoscopic Ventral Mesh Rectopexy (LVMR) has revolutionised the management of internal/external rectal and vaginal vault prolapse. These procedures have traditionally been performed with synthetic meshes. Biologics have gained a prominent role over the last decade in LVMR as well as perineal procedures for rectocoele and cystocoele repair. We examine the existing literature on the use of biologics in pelvic floor surgery comparing this with literature on synthetic mesh for the key outcomes of infection rates, bowel/sexual function and recurrence.

Keywords Rectopexy, biologic, rectocoele, prolapse, cystocoele

What is new in this paper?

This paper is the first synopsis of the published literature on the use of biologics in the surgical treatment of pelvic floor dysfunction.

Introduction

In the last decade, there has been a significant shift in the debate about the best treatment for external rectal prolapse from abdominal *vs* perineal approaches to ventral *vs* posterior (resection) rectopexy to laparoscopic *vs* open and now synthetic mesh *vs* biologics in ventral rectopexy. It is now accepted that the abdominal approach is superior to the perineal approach in terms of recurrence. The advent of laparoscopic surgery has reduced the morbidity of abdominal rectopexy and there is now evidence to show it is safe in the elderly [1]. Recognition of internal rectal prolapse as a pathological condition contributing to the syndrome of obstructed defaecation (ODS), and successful surgical treatment with laparoscopic ventral mesh rectopexy (LVMR) means that this operation is being performed increasingly on a younger cohort of patients.

Synthetic mesh was introduced into pelvic floor surgery to reduce the high recurrence rate of up to 30%. Concerns about mesh erosion, infection and dyspareunia then led to the introduction of biologic meshes into pelvic floor surgery. The ideal mesh is one that is flexible, shows good tissue integration, has low infection rates, is biocompatible, chemically inert, non-carcinogenic and non-allergenic [2]. It should also be cost-effective and readily available.

There has also been a debate between advocates of cross-linked vs non-cross linked biological meshes. Biological meshes work by acting as a collagen scaffold that attracts fibroblasts and endothelial cells. A process of remodeling ensues in which there is some degradation of the biologic graft and regeneration of host tissue. The balance of these two processes determines how much of the graft is left. Some biologic meshes have additional cross-links induced during the manufacturing process in an attempt to slow down degradation. It is the cross-linked type in the form of dermal porcine collagen that has seen the greatest use in surgery for pelvic floor dysfunction.

There is currently no consensus on the role of biologics in the surgical management of pelvic organ prolapse and obstructed defaecation. Biologics have been traditionally used in infected fields in the context of complex abdominal hernia or abdominal reconstruction and have an established role in these cases. More recently they have been used to close the perineum following extra-levator abdomino-perineal excision (elAPE) of the rectum.

The literature on biologics in pelvic floor surgery is limited to case series (Table 1). There is a paucity of randomized trials comparing synthetic to biologic mesh or cross-linked *vs* non-cross-linked biological mesh. This

Correspondence to: Mr Mark Mercer-Jones MB, BS, FRCS, Consultant Colorectal Surgeon, Queen Elizabeth Hospital, Gateshead, UK.
E-mail: mark.mercer-jones@ghnt.nhs.uk

Table 1 Published series of LVMR with synthetic and biologic mesh.

Authors	Year	*N*	Follow-up (months)	Median age (years)	Indication	Graft	Functional outcome		Recurrence
							ODS	FI	
Wahed *et al.*	2011	65	12	62	IRP, ERP, VP	Permacol	95% improved or same	95% improved or same	3.1
Sileri *et al.*	2012	34	12	59	IRP	Permacol	82% improved	73% improved	5
Wong *et al.*	2011	84	29	64	IRP	Polyester	37% improved	4% improved	7.1
Collinson *et al.*	2010	72	12	58	IRP	Polypropylene	86% improved	85% improved	5
Slawik *et al.*	2008	80	54	59	ERP, IRP, SRU	Polypropylene	80% improved	91% improved	0 (full thickness prolapse)
Auguste *et al.*	2006	54		53	ERP	Synthetic	47% improved	69% improved	7.4%
D'Hoore & Penninckx	2004	42	61	50	ERP, IRP	Marlex	84% improved	91% improved	4%

review presents a synopsis of the existing literature on the use of biologics in the surgical treatment of external/internal rectal prolapse, rectocoele and other forms of pelvic floor dysfunction.

Method

A literature search of published articles describing the use of biologic mesh/graft in the surgical treatment of pelvic organ prolapse and obstructed defaecation was conducted. The key comparators between synthetic mesh and biologics were functional outcome (Wexner Constipation Scores, FISI, dyspareunia), mesh-related complications (erosion/infection) and recurrence.

Inclusion criteria were studies that described the use of biologic material in the repair of external/full thickness/internal rectal prolapse, internal intussusception, vaginal vault prolapse, cystocoele, rectocoele, anterior and posterior colporrhapy. Other search terms were laparoscopic ventral rectopexy, sacrocolpopexy.

Results: abdominal

Laparoscopic ventral mesh rectopexy

Laparoscopic ventral mesh rectopexy has gained wide acceptance as the surgical treatment of choice for external rectal prolapse and internal intussusception associated with obstructive defaecation. We examined publications that describe the use of biological and synthetic mesh in LVMR.

Bowel function

The first reported series of 65 patients (median follow-up 12 months) describing the use of Permacol™ (cross-linked porcine dermal mesh) in LVMR for internal and external rectal prolapse and vaginal vault prolapse, showed results equivalent to synthetic mesh in the key functional outcomes of constipation and incontinence. There were statistically significant improvements in Wexner Constipation Scores (WCS) and Vaizey scores at 1 year ($P < 0.0001$ and $P = 0.0002$ respectively). There were two cases of symptom but not clinical recurrence in the internal rectal prolapse group (3.1%) at a median follow up of 1 year. Symptoms in this UK series, were rated as much better or better by 93% at 6 months and this was sustained at 1 year [3]. Updated data from this series ($n = 101$, median follow-up 30 months; range 6–51 months) shows sustained improvement in constipation (see Fig. 1). Mean WCS was 3.8 (SD ± 4.2) and mean Vaizey scores of 1.1 (SD ± 2.2) in patients with at least 1-year follow-up. Figure 2 shows a breakdown of the updated series by indication for LVMR.

The second published series from Italy (mean follow-up 12 months) described 34 consecutive patients that underwent LVMR with Permacol for internal rectal prolapse [4]. Nine patients (26%) had mixed ODS and faecal incontinence. Constipation scores (median Wexner

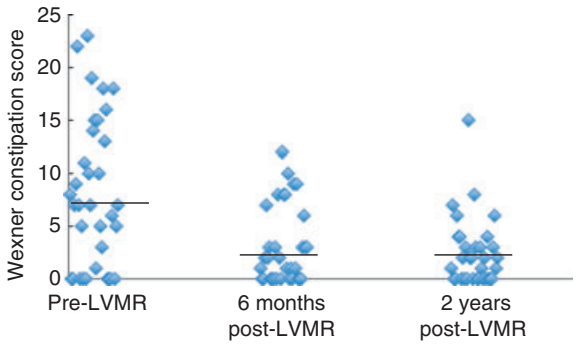

Figure 1 Wexner constipation scores pre-surgery, 6 months and 2 years after LVMR.

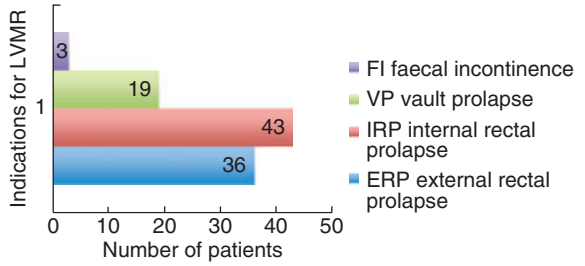

Figure 2 Indications for LMVR in gateshead series.

score 15) and FI (median FISI score 12) improved significantly at 3 months (Wexner 5, FISI 5, both $P < 0.001$). Two patients experienced prolapse persistence or recurrence. No patients had worsened bowel or sexual function.

Updated data from the Italian series that now includes 57 patients shows functional outcomes similar to the published data. Median Wexner constipation scores preoperatively were 15.1 compared to 5 at 12 months. Faecal incontinence also improved from a median FISI score of 9 to 2.5.

Sexual function

Twenty seven per cent of patients in the Italian series reported dyspareunia preoperatively compared to 7.5% at 6 months (one new onset) and 5% at 12 months (the one new onset patient had resolved). These results are supported by a paper from Abet *et al.* [5] who assessed sexual function in a cohort of patients that had LVMR with synthetic mesh using a questionnaire and found no *de novo* dyspareunia. The levels of dyspareunia post-operatively were also comparable to the general population. Eleven patients (16.9%) in the UK series reported dyspareunia prior to surgery. At 6 months follow up 3/40 had dyspareunia (7.5%). This was a new symptom in one of these patients and the other two were pre-existing. Two patients with initial dyspareunia had symptoms at 1 year but stated these were the same as before their surgery. These results correlate with the Italian series.

Mesh-related complications

There were no cases of mesh erosion or mesh-related infection in the two published series describing the use of Permacol™. There was one mesh related seroma that required laparoscopic de-roofing 2 years after LVMR. Rectal erosion has however been reported in laparoscopic ventral rectopexy with synthetic mesh [6].

Non-mesh related complications

The published UK series described a general complication rate of 12.3% (8/65 patients). Most of these were minor complications and only one required a return to theatre following readmission for a port site hernia. The overall complication rate was 23.5% (8/34 patients) in the Italian series. Only one patient required a return to theatre for adhesiolysis in this series.

Recurrence

The difficulty here is gauging the relevance of asymptomatic clinical recurrence. The overall recurrence rate in the UK series was 3.1%. Subset analysis shows a recurrence rate in the external rectal prolapse patients of 2.8% (1/36), which compared favourably to another series describing the use of synthetic mesh in LVMR for external rectal prolapse [7]. The published data from the Italian series included only patients that had LVMR with Permacol™ for internal intussusception with a recurrence rate of 5% (median follow up 12 months), which again compares favourably with 3.7% from another series of patients with internal intussusception describing the use of synthetic mesh [8]. Interestingly, current data from the Italian series shows an increase in recurrence rate to 19% with a minimum follow-up of 1 year. Recurrence rate was 10.5% at 1 year and performing a Kaplan Meier curve the risk of recurrence at 3 years follow-up was close to 18%. The maximum peak of recurrences occurred between 24 and 36 months after surgery, remaining stable thereafter. Six out of 11 recurrences were observed in the first 20 patients and the learning curve might be responsible for these. It is also possible that early recurrences or persistence of anatomical abnormalities are secondary to technical failures, though a mesh-related problem cannot be excluded. In the Gateshead series there has been only one external rectal prolapse recurrence and this suggests that this is not a mesh-related problem.

On further analysis, 8 out of eleven patients with recurrences had previous hysterectomy. Nine out of 11 patients had redundant colon and 5 had concomitant sigmoidopexy (overall sigmopidopexy was performed in 12/57 patients). These were all symptomatic recurrences and confirmed by defaecating proctogram. Eight of these patients have had STARR (one posterior and the others circumferential) and the others are awaiting surgery.

Another series from Spain described a high recurrence rate of 21% in sacrocolpopexy and LVMR using biological grafts. This was however a heterogeneous series covering disorders in all three pelvic floor compartments and few patients actually had LVMR. Further analysis showed all these patients had middle/anterior compartment symptoms and only 9% required re-intervention [9]. This paper raises the question of how clinical recurrence is assessed. There appears to be poor correlation between clinical recurrence and symptomatic recurrence.

Laparoscopic sacrocolpopexy

A review by the UK National Institute for Clinical Excellence (NICE) compared sacrocolpopexy with synthetic non-absorbable mesh to biological graft and found mesh erosion occurred in 4% of women treated by synthetic mesh compared with 0% of women who received a biological graft (1-year follow-up) [10]. Reoperation for mesh-related complications was up to 9% (follow-up of 4–20 months).

The same review showed an objective failure rate ranging from 0 to 6% for mesh sacrocolpopexy at an average follow up of 2 years. The incidence of subjective failure was however much higher (range 3–31%) with 2–14% requiring further surgery. This is in keeping with data from LVMR series that show lower re-intervention rates compared to the actual subjective (symptom) recurrence rate. Of the 19 patients in the UK series that had vault prolapse (Median follow-up 27 months; range 10–41 months), there have been no objective failures (0% recurrence rate for vault prolapse).

Results: perineal approach

Transperineal rectocoele repair

This approach was popularized in the decades leading up to the development of laparoscopic colorectal surgery and LVMR particularly. There is no reliable data about the proportion of surgeons that still offer this approach to their patients. There is data, however, to suggest that the infection rate using Permacol™ is less (0%) compared with synthetic mesh (13%). These results are from the same unit using the same technique with different meshes. They were neither randomised nor controlled [11,12]. Synthetic absorbable mesh appears to have a lower mesh erosion rate as exemplified by a series from Turkey of 83 consecutive patients with a published erosion rate of 0% following transperineal rectocoele repair using polyglycolic acid mesh [13].

Transvaginal rectocoele repair

A NICE review (2008) of posterior vaginal repair for rectocoele revealed a 0% erosion rate for biological grafts (Permacol™ was used in the one trial that included biologic grafts), 4% for combined synthetic/biologic and 7% for synthetic only [10]. Evidence from this review also showed objective recurrence rate of 12.7% for procedures without mesh/graft, 8.6% for absorbable synthetic mesh, 20.4% biological graft, and 6.5% for non-absorbable synthetic mesh. Interestingly, there was no significant difference in the re-intervention rates between the four groups.

Cystocoele repair

A meta-analysis of four RCTs showed a significantly lower objective recurrence rate (12%) with biological mesh were compared to 23% without mesh [10]. Three of these trials used Permacol while one used solvent-derived fascia lata. Mesh erosion with biological grafts was 0% compared to 6% with synthetic mesh though this was not statistically significant. Figure *3* shows an anterior repair being performed with Permacol™.

Conclusion

Although there were no randomized trials comparing synthetic to biological mesh, the available evidence suggests biological grafts are safe and effective in the surgical treatment of pelvic floor prolapse. The results in the key outcomes of complications particularly mesh erosion; recurrence, patient satisfaction, constipation and incontinence are comparable to synthetic mesh.

One of the challenges we found in analysing the available evidence is the variability between published series in patient selection and outcomes measured. It is difficult comparing the efficacy of the various procedures used in pelvic floor surgery in terms of mesh *vs* no mesh and biological *vs* synthetic mesh, as the comparators used are different. Similar difficulty is encountered when comparing objective and subjective recurrence rates between the studies because the assessment tools vary. LVMR is however performed using similar techniques in all the published series we evaluated and this strengthens our analysis.

One of the drawbacks of biological mesh is difficulty handling the mesh in laparoscopic surgery. The authors have found that aiming for the natural fenestrations in the porcine graft (Permacol™) with the needlepoint helps overcome this. A useful tip published by one of the

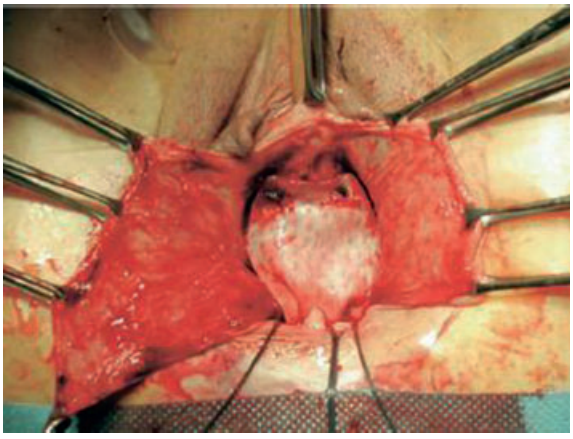

Figure 3 Permacol in anterior vaginal repair.

authors suggests using a sterile belt hole puncher to make holes in the graft prior to insertion into the peritoneal cavity [14].

The main drawback of biological grafts is the higher cost when compared to synthetic mesh. Biological grafts have gained an established role in surgery that involves infected fields and we believe their use in pelvic floor surgery could mitigate the potentially disastrous effects of pelvic sepsis when synthetic mesh is sutured to the rectum.

Conflicts of interest

M. Mercer-Jones and P. Sileri have received honoraria for lecturing on the use of porcine collagen from Covidien. M. Ahmad and L. Franceschilli have declared no potential conflicts.

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