Canadian Agency for Drugs and Technologies in Health

RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL

TITLE: Biological Mesh: A Review of Clinical Indications, Clinical Effectiveness, Cost-Effectiveness, and Clinical Practice Guidelines

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CONTEXT AND POLICY ISSUES:

A variety of products are available for use as surgical reconstructive materials including biological mesh, absorbable synthetic mesh, and non-absorbable synthetic mesh. Biological meshes are acellular extracts obtained from human (allografts) or non-human (xenografts) sources. Common sources of biological mesh include human dermis or fascia lata, porcine dermis or intestine, and bovine dermis or pericardium (Table 1).[1]

Table 1: Examples of commercially available biological mesh products*

Biological Mesh	Source	Manufacturer/Vendor
AlloDerm	Human dermis	LifeCell
FlexHD	Human dermis	Musco
GraftJacket	Human dermis	Wright Medical Technology
DermaMatrix	Human dermis	Synthes
Repliform	Human dermis	Boston Scientific
Suspend	Human fascia lata	Mentor
Tutoplast	Human fascia lata	Tutogen
Permacol	Porcine dermis	Covidien
CollaMend	Porcine dermis	Bard
XenMatriX	Porcine dermis	Brennen Medical
Strattice	Porcine dermis	LifeCell
Pelvicol	Porcine dermis	Bard
Pelvisoft	Porcine dermis	Bard
ForteGen	Porcine intestine	Organogenesis
Surgisis	Porcine intestine	Cook
SurgiMend	Bovine dermis	TEI Biosciences
Veritas Collagen Matrix	Bovine pericardium	Synovis
Tutopatch	Bovine pericardium	Tutogen
UroPatch	Bovine pericardium	YAMA

*Table compiled from a variety of sources[2-5]

There is uncertainty concerning the optimal use of biological mesh in surgical procedures. This rapid review summarizes the existing clinical and cost-effectiveness evidence, as well as the evidenced-based guidelines regarding the use of biological mesh products.

RESEARCH QUESTIONS:

1. What is the clinical effectiveness of biological mesh products?

2. What is the cost-effectiveness of biological mesh products?

3. What are the clinical indications for biological mesh products?

4. What are the evidence-based guidelines regarding the use of biological mesh products?

KEY MESSAGE:

There is insufficient evidence to clearly establish the place in therapy of biological mesh products.

METHODS:

A limited literature search was conducted on key health technology assessment resources, including OVID MEDLINE, PubMed, The Cochrane Library (Issue 10, 2010), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI (Health Devices Gold), EuroScan, international health technology agencies, and a focused Internet search. The search was limited to English language articles published between January 1, 2005 and October 6, 2010. Filters were applied to limit the retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic studies and guidelines.

Studies were considered for inclusion if they assessed the clinical or cost-effectiveness of any biological mesh material used in a surgical procedure involving humans. The included systematic reviews investigated a wide range of research questions regarding the usage of biological and synthetic mesh products. For the purposes of this rapid review, only results from comparisons of biological and synthetic mesh are summarized. HTIS reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials (RCTs), economic evaluations, and evidence-based guidelines.

SUMMARY OF FINDINGS:

There were four relevant systematic reviews[6-9] and one relevant health technology assessment[10] identified from the literature review. Sung et al (2008),[7] Maher et al (2010),[8] and Jia et al (2007)[9] conducted systematic reviews to investigate the use of biological mesh in surgery for vaginal wall prolapse and Gapski et al (2005)[6] conducted a systematic review and meta-analysis to evaluate the efficacy of using biological mesh in mucogingival surgery. Esfandiari et al (2009)[10] conducted a health technology assessment for the use of biological mesh in breast reconstruction surgery. The literature searched identified four RCTs[11-14] that also evaluated the use of biological mesh for vaginal wall prolapse. However, Meschia et al (2007)[11], Paraiso et al (2006)[12], and Natale et al (2009)[13] were included in the systematic reviews and,

therefore, are not summarized individually in this rapid review. Additional included RCTs investigated the use of biological mesh in surgery for inguinal hernia,[15] urethroplasty,[16] decompressive hemicraniectomy,[4] mucogingival surgery,[17-22] and the treatment of diabetic foot ulcers.[3] One evidence-based clinical practice guideline[23] concerning the use of biological grafts, synthetic grafts, and native tissue in transvaginal repair was included. There were no relevant economic evaluations identified in the literature search. A total of 130 potentially relevant non-randomized studies were identified in the literature search; however, these studies have not been individually summarized in this rapid review. A list of these studies is available elsewhere.[24]

Table 2: Summary of available literature for biological mesh

Indication	Available Literature				
	HTA	SR	RCT	E	EBG
Pelvic organ prolapse	——	3[7-9]	4[11-14]	——	1[23]
Breast reconstruction	1[10]	——	——	——	——
Inguinal hernia	——	——	1[15]	——	——
Urethroplasty	——	——	1[16]	——	——
Diabetic foot ulcers	——	——	1[3]	——	——
Decompressive hemicraniectomy	——	——	1[4]	——	——
Mucogingival surgery	——	1[6]	6[17-22]	——	——

HTA – health technology assessment; SR – systematic review; RCT – randomized controlled trial; E – economic evaluation; EBG – evidence-based guideline

Health technology assessments

Biological mesh for breast reconstruction

Esfandiari et al (2009)[10] conducted a health technology assessment of the use of biological mesh (AlloDerm and DermaMatrix) in breast reconstruction surgery. A systematic review of the literature was conducted using multiple databases and without language restriction. The primary limitations of this review were the failure to report selection criteria, methodology for data extraction, and methods used to assess the risk of bias of the included studies. Furthermore, results from the individual studies included in this assessment were poorly reported, making it difficult to assess the precision of any outcome data. It was noted that studies with a sample size of fewer than 20 patients were excluded. There were no meta-analyses performed in this review.

A total of 10 studies were included in the review, none of which involved random allocation of patients. Seven cohort studies reported on the usage of AlloDerm for expander-based, single- and two-stage breast reconstruction (sample size range: 24 to 49), six of which were uncontrolled and one used matched controls. Additional cohort studies compared AlloDerm to DermaMatrix for two-stage breast reconstruction (n = 30); assessed the use of AlloDerm in nipple reconstruction (n = 30; uncontrolled); and assessed the use of AlloDerm in the repair of rectus fascia (n = 54; uncontrolled). The available data from these studies was limited by sample sizes, lack of random allocation, and generally poor reporting in the systematic review. The authors concluded that there was no significant difference in the perioperative complication rates and number of tissue expansions with or without the use of AlloDerm. With respect to revision rates, two studies using AlloDerm reported a rate of 4%; however, the revision rates without AlloDerm showed substantial variation, ranging from 2.2% to 36%. One study reported that there was no difference between AlloDerm to DermaMatrix with respect to intraoperative expander volume, incremental volume of expansion and final expanded volume-to-expander

volume to ratio. With respect to the cost-effectiveness of AlloDerm and DermaMatrix, the authors concluded that data on long-term efficacy, safety and cost impact is required to quantify any benefit or complications. Overall, the findings of this review should be interpreted with caution due to its limitations and no clear conclusions can be made regarding the use of biological mesh for breast reconstruction.

Systematic reviews and meta-analyses

Biological mesh for pelvic organ prolapse

Maher et al (2009)[8] conducted a systematic review to assess the outcomes of surgery in the management of pelvic organ prolapse. They investigated a total of nine comparisons, one which was head-to-head comparison of type of graft (synthetic mesh or biological graft). The Cochrane Incontinence Review Groups specialized register of controlled trials was used to identify relevant literature. This consists of a collection of trials identified from the Cochrane Central Register of Controlled Trials, MEDLINE, CINAHL and hand searching of journals and conference proceedings. Eligible studies consisted of RCTs and controlled clinical trials of women seeking treatment for symptomatic primary or recurrent pelvic organ prolapse, in which a surgical intervention for pelvic organ prolapse was provided to at least one trial arm. Study selection, data extraction, and risk of bias assessment were conducted independently by two reviewers. Overall, this review was conducted using a rigorous methodology with a low risk of bias. The authors categorized studies according to: 1) vaginal compartment (i.e., anterior, posterior, and upper vagina including cervix, uterus and vault); and 2) graft type (i.e., biologic, synthetic absorbable, or synthetic non-absorbable). There were no meta-analyses conducted for the available comparisons of different surgical meshes.

Three RCTs were included that directly compared two types of mesh. One RCT (n = 82) compared a non-absorbable synthetic mesh (Prolene Soft) with a biological mesh (Pelvicol) and reported no statistically significant differences between the two groups (i.e., prolapse symptoms, objective failure, urgency, detrusor overactivity or overactive bladder, de novo overactive bladder symptoms, postoperative voiding dysfunction symptoms, urodynamic voiding dysfunction, bowel function or constipation, dyspareunia, and postoperative complications) However, the authors noted that there was considerable uncertainty around the results (i.e., confidence intervals were wide). Another trial (n = 190) compared non-absorbable synthetic mesh (Gynemesh) with a biological mesh (Pelvicol). The authors reported that there was a statistically significant difference in objective success which favoured Gynemesh over Pelvicol (RR 0.64, 95% CI 0.43, 0.96); however, Gynemesh was also associated with significantly higher daytime urinary frequency (RR 4.24, 95% CI 1.83, 9.84). The final trial (n = 134) compared Pelvicol against an absorbable synthetic mesh (Vicryl) and reported that fewer women were objectively assessed as having a recurrence of prolapse with Pelvicol in comparison with Vicryl (RR 3.22, 95% CI 1.38, 7.52). Overall, the authors reported that there was insufficient evidence to accurately evaluate the different types of sutures, mesh and grafts.

Sung et al (2008)[7] conducted a systematic review to evaluate graft use in transvaginal pelvic organ prolapse repair. One of the objectives of this review was to assess and compare the anatomic and symptomatic efficacy of different mesh materials in transvaginal pelvic organ prolapse repair. A systemic literature review was performed using Medline (1950 to 2007) without language restriction. Randomized and non-randomized studies were eligible for inclusion if they reported anatomic, symptomatic or adverse event outcomes on any type of graft material in transvaginal pelvic organ prolapse repair. To evaluate the efficacy of different grafts,

studies that involved head-to-head comparisons between graft materials were included. The authors categorized studies according to: 1) vaginal compartment (i.e., anterior, posterior, apical, or multiple); 2) graft type (i.e., biologic, synthetic absorbable, or synthetic non-absorbable); and 3) outcome (i.e., anatomic or symptomatic). Methodological quality of each study was assessed using a modified version of the Agency for Healthcare Research and Quality grading system. Data extraction was performed in duplicate; however, it is unclear if duplicate reviewers were used in study selection and the risk of bias assessment. An additional limitation of this review is the use of a single database for the literature search, as two databases has been cited as the minimum for a high quality systematic review.[25]

Two studies compared a biological mesh with a synthetic mesh for surgical repair in the anterior compartment. One prospective cohort study compared Pelvicol (n = 19) with Vicryl (n = 24) and reported no difference in recurrence of prolapse. The other study compared Pelvicol (n = 56), polypropylene grafts (n = 25), and traditional repair (n = 18) and also reported no significant difference between any of the treatment groups in the recurrence of prolapse. It should be noted that this study did not report inclusion criteria and was based on retrospective comparisons. Furthermore, the authors of this review stated that both studies lacked adequate statistical power to conduct a meaningful comparison. There were no studies that compared different types of mesh for surgery of posterior, apical, and multiple compartments. Overall, the authors concluded that the available evidence was insufficient to properly assess anatomical and symptomatic graft use in any compartment of transvaginal pelvic organ prolapse. The findings of this review were used in formulating the clinical practice guidelines of the Society of Gynecologic Surgeons.[23]

Jia et al (2007)[9] conducted systematic reviews to investigate the use of biological mesh in surgery for vaginal wall prolapse. The review was conducted on behalf of the National Institute for Health and Clinical Excellence's (NICE) Interventional Procedures Programme. The findings from this review are also available as brief Interventional Procedure Guidance summaries.[26-31] One of the objectives of this review was to assess the efficacy and safety between different types of mesh and grafts. This review involved a comprehensive literature search from 1980 to 2007 to identify English language publications for the repair of anterior and posterior pelvic organ prolapse. Randomized controlled trials, non-randomized comparative studies, case series (n ≥ 50 women), and population-based registry reports were eligible for inclusion. Studies were required to have a mean follow-up time of at least one year to be included in the efficacy analysis. Those less than one year were only included for safety outcomes. There were no restrictions on the type of mesh or technique of using mesh. Studies with the following characteristics were excluded: case reports; conference abstracts published prior to 2005; animal studies; reports of studies reproduced in later publications; studies which reported anterior and/or posterior prolapse repair, in addition to cervix, uterus, or vaginal vault prolapse repair without separating the results; and studies involving women with prolapse due to pelvic trauma, congenital disease, or prolapse after the creation of neovagina.
A risk of bias assessment was performed on studies reported as full-text publications using a 13-item checklist for RCTs[32] and an 18-item checklist for non-randomized studies[32,33] Study selection, data extraction, and the risk of bias assessment were performed by a single reviewer. The data was analyzed according to the following subgroups: anterior vaginal wall prolapse repair; posterior vaginal wall prolapse repair; and anterior and/or posterior vaginal wall repair (when results were not reported separately).

There were a total of 49 unique studies included in the review. These studies consisted of 17 RCTs, seven non-randomized studies, one prospective registry of cases, and 24 case series.

The authors reported that a majority of RCTs described appropriate methodology for randomization and allocation concealment, and all studies used an intention-to-treat analysis. Two RCTs and one non-randomized study compared different types of mesh for surgical repair of the anterior compartment. Evidence from direct and indirect comparisons (Table 3) suggested that non-absorbable synthetic mesh had a significantly lower objective failure rate than biological grafts. One RCT reported that biological mesh was superior to absorbable synthetic mesh (RR 3.22; 95% CI 1.38, 7.52); however, the difference was not significant in the indirect comparison that involved all studies (OR 0.64; 95% CrI 0.36, 1.06). Another RCT reported that more women using absorbable synthetic mesh required reoperation compared with those using absorbable biological grafts. There were no RCTs or non-randomized studies that compared different types of mesh for posterior and combined posterior/anterior repair; hence, the authors concluded that there was insufficient evidence to draw conclusions for these procedures. A summary of direct and indirect comparisons is provided in Table 3.

Table 3: Summary of findings from Jia et al (2007)[9]

Comparison	Study (N)	RR (95% CI)
Objective failure of anterior repair		
Absorbable synthetic mesh vs. biological graft	1 RCT (125)	RR: 3.22 (1.38, 7.52)
Non-absorbable synthetic mesh vs. biological graft	1 RCT (180)	RR: 0.65 (0.44, 0.96)
Erosion of mesh/graft after anterior repair		
Non-absorbable synthetic mesh vs. biological graft	1 RCT	RR: 0.08 (0, 1.44)
Required reoperation after anterior repair		
Absorbable synthetic mesh vs. biological graft	1 RCT	RR: 4.74 (1.43, 15.69)
Comparison	**Study (N)**	**OR (95% CrI)**
Objective failure of anterior repair		
Absorbable synthetic mesh vs. biological graft	*All studies (1341)	OR: 0.64 (0.36, 1.06)
Non-absorbable synthetic mesh vs. biological graft	*All studies (1589)	OR: 0.37 (0.23, 0.59)

* Indirect comparison analyses included 12 RCTs, 3 non-randomized studies, and 8 case series.
CI – confidence interval; CrI – credible interval; N – total sample size; OR – odds ratio; RCT – randomized controlled trial; RR – relative risk

Biological mesh for mucogingival surgery

Gapski et al (2005)[6] conducted a systematic review and meta-analysis to evaluate the efficacy of mucogingival surgery with and without the use of biological mesh. A literature search was performed using multiple databases from 1990 to 2004. Eligible studies consisted of RCTs that were at least three months in duration and published in English. Mucogingival surgeries for root coverage or augmentation of keratinized tissue were the interventions of interest. Study selection, data extraction, and risk of bias assessment were performed in duplicate. The risk of bias assessment consisted of evaluating randomization, blinding, inclusion of control comparisons, and differences in baseline characteristics. It was not reported if the investigators considered allocation concealment, use of intention-to-treat analysis, equal treatment between groups, and patient disposition in their assessment of internal validity. The methodology used to pool data was appropriate.

A total of eight studies were included in the review (results summarized in Table 4). Four RCTs compared biological mesh-based root coverage with a connective tissue graft. Pooling of these studies resulted in no statistically significant differences between the two approaches for recession coverage (P = 0.39), probing depths (P = 0.89), or increase in keratinized tissue (P = 0.11). Two RCTs compared biological mesh-based root coverage with coronally-advanced flap

and reported no statistically significance differences with regard to recession coverage (P = 0.28), probing depths (P = 0.99), clinical attachment (P = 0.18), and keratinization (P = 0.19). Finally, two RCTs compared biological mesh-based root coverage with free gingival graft and, similar to the other approaches, there was no statistically significant difference in keratinization. As shown in Table 4, there was a high level of statistical heterogeneity ($I^2 \geq 75\%$) in several of the meta-analyses. A fundamental principle of meta-analysis requires that studies be sufficiently similar to pool their findings. A high I^2 is an indication that that there may be important variability between the included studies and, therefore, the results may not be an accurate reflection of the true effect size. The individual studies included in these meta-analyses were limited by the duration (less than 12 months), sample size (range: 12 to 44), and poor internal validity. Overall, the authors felt that it was difficult to draw conclusions from this systematic review.

Table 4: Results of meta-analyses from Gapski et al (2005)[6]

Outcomes	WMD (95% CI)	P-value	I^2 (%)	N
biological mesh-based root coverage vs. Connective tissue graft				
Recession coverage (mm)	0.41 (-1.33, 0.52)	0.39	85.6	120
Probing depths (mm)	0.02 (-0.28, 0.24)	0.89	20.6	120
Keratinization (mm)	0.52 (-0.12, 1.16)	0.11	20.6	50
biological mesh-based root coverage vs. Coronally advanced flap				
Recession coverage (mm)	0.62 (-0.74, 0.51)	0.28	83.6	NR
Probing depths (mm)	0.00 (-0.36, 0.35)	0.99	0.0	NR
Clinical attachment (mm)	0.56 (-1.33, 0.21)	0.18	45.2	42
Keratinization (mm)	0.31 (-0.78, 0.15)	0.19	0.0	NR
biological mesh-based root coverage vs. Free gingival graft				
Keratinization (mm)	1.51 (-1.41, 4.43)	0.31	94.5	NR

CI – Confidence Interval, mm – millimeter, NR – not reported, N – total sample size, WMD – weighted mean difference

Randomized controlled trials

Biological mesh for pelvic organ prolapse

One RCT[14] not captured in the included systematic reviews[7-9] was identified that investigated the use of biological mesh for pelvic organ prolapse. Hviid et al (2010)[14] compared the use Pelvicol (n = 30) with conventional repair of the anterior vaginal wall (n = 31). Patients with stage II or higher defects in the anterior vaginal compartment were eligible for inclusion. Patients with any of the following were excluded: defects in the posterior or apical compartment or decent of the uterus; less than 18 years of age; any previous pelvic surgery; or history of collagen or endocrine diseases. Methods for randomization and allocation concealment were appropriate and clearly reported in the publication. Baseline characteristics were comparable between the two groups, including Pelvic Organ Prolapse Quantification (POPQ) stages.

Following the surgery, there was no significant difference between the two groups with respect to POPQ stages, objective recurrence, bleeding during operation, quality of life, urinary incontinence, and length of hospital stay. The procedure involving Pelvicol was of longer duration than the conventional procedure (32 min vs. 23 min; P = 0.001). Overall, the authors concluded that both procedures are safe and effective and that their data does not support the use of Pelvicol for primary anterior vaginal repair.

Biological mesh for inguinal hernia

Ansaloni et al (2009)[15] conducted a double-blind RCT to compare Lichtenstein repair of inguinal hernia using polypropylene mesh (n = 35) or Surgisis biological mesh (n = 35). The inclusion criteria were specified as follows: men with non-complicated primary inguinal hernia; at least 18 years of age; American Society of Anestheseologists score I through III; and provision of informed consent. Patients with recurrent hernia, any condition preventing a correct evaluation of pain, hypersensitivity to any study drug or findings of a pathology other than inguinal hernia were excluded from the trial. The primary limitations with this study were the failure to report methods for randomization, allocation concealment, and blinding. Baseline characteristics were similar between the two treatment groups with no significant differences reported. The primary end point of the study was the degree of postsurgical pain as measured by a simple verbal scale (SVS) and a 100-mm visual analogue scale (VAS). Secondary outcomes included the degree of discomfort; the incidence of anesthesia/paresthesia; recurrence rate; and the incidence of surgical site infection or any other complication. This study was entirely funded by the Hospital where the investigators are employed.

The difference between groups in the incidence of postsurgical pain was not statistically significant at any point during the three year follow-up period. The authors reported that there was a statistically significant lower degree of pain in the patients who received the Surgisis mesh in the following outcomes and time points: pain at rest (1, 3, and 6 months), on coughing (1, 3, and 6 months) and on movement (1, 3, 6, 12, 24, and 36 months). Patients who received Surgisis mesh were also more likely to experience a temperature above 38 ºC. There were no statistically significant differences in pain localization, pain irradiation, or the incidence of anesthesia/paresthesia. Overall, the authors concluded that the use of Surgisis mesh in ingunal hernia repair was a safe and effective intervention.

Biological mesh for urethroplasty

Jamal et al (2010)[16] conducted an RCT comparing primary closure (n = 10) vs. AlloDerm closure (n = 10) of buccal mucosal graft harvest site for substitution urethroplasty. The investigators allocated patients by alternating the closure technique in successive patients. This is a poor method of randomization as the investigator would be fully aware which treatment the patient is to receive (i.e., allocation has not been concealed) and may use this knowledge to bias the selection patients. There were no statistically significant differences between the two groups in oral pain, analgesic use, neurosensory deficits, or mastication following surgery (measured at 3 weeks and 3, 6, and 12 months). The only statistically significant difference in outcome was an increase in cheek swelling at three weeks (80% of the AlloDerm group vs. 30% of the primary closure group; P = 0.01). The absence of statistical significance may be a reflection of inadequate statistical power due to the sample size of this trial. Overall, the authors concluded that AlloDerm was an effective treatment; however, it offers no significant advantages in comparison with primary closure. The authors also noted that in the absence of a larger, long-term trial they advocate for the use of primary closure.

Biological mesh for diabetic foot ulcers

Reyzelman et al (2009)[3] conducted a 12-week RCT to compare healing of foot ulcers in patients receiving GraftJacket regenerative tissue matrix (n = 47) compared with standard of care wound management (n = 39) (i.e., moist-wound therapy with alginates, foams, hydrocolloids or hydrogels at the discretion of the treating physician. Eligible patients included adults with type 1

or type 2 diabetes, a grade 1 or 2 diabetic foot ulcer (1 to 25 cm^2) absence of infection based on Infectious Disease Society of America criteria and adequate circulation to the affected extremity. Patients with any of the following criteria were excluded: hemoglobin A1c greater than 12% within the previous 90 days; serum creatinine levels ≥ 3.0 mg/dl; sensitivity to gentamicin, cefoxilin, linocmycin, polymyxin B or vancomycin; ulcers probing to bone; or treatment with biomedical or topical growth factors within the previous 30 days. The manufacturer of the GraftJacket product (Wright Medical Technology, Inc.) paid for the clinical trial and conducted the statistical analysis.

The authors failed to report whether the trial was blinded or open-label. The methodology used for randomization and allocation concealment was not provided. The proportion of patients who withdrew from the study was acceptable (i.e., less than 20% and comparable between two the treatment arms) and patient disposition was well reported in the publication. Baseline characteristics were similar between the two treatment groups. The primary outcome was the duration of time that the wound persisted (i.e., had not yet healed) and the secondary outcome was the mean time to healing. There were statistically significant differences in the proportion of healed ulcers (P = 0.0289) and in non healing rate (P = 0.0075) both of which favoured the use GraftJacket over the standard of care. There was no statistically significant difference in the mean time to wound healing observed between the two treatment groups. Overall, the authors concluded that their findings support the use of GraftJacket therapy in the treatment of diabetic foot ulcers.

Biological mesh for decompressive hemicraniectomy

Horaczek et al (2008)[4] conducted an RCT to investigate the application of a bovine collagen matrix (Duragen) as an onlay graft to reduce operating time during hemicraniectomy and to facilitate dural dissection during second-stage cranioplasty. The study compared surgery with and without the use Duragen. Eligible patients were those admitted to two major neurosurgical centers and qualified for decompressive hemicraniectomy for either ischemic or traumatic intracranial hypertension. Methods for randomization were appropriate and clearly reported; however, it was not immediately clear if allocation was properly concealed from the investigators. The envelopes containing the allocated treatment were reported as being sealed, but it was not specifically stated that the envelopes were opaque. Baseline characteristics were similar between the collagen and control treatment groups. The funding source for this study was not explicitly stated; however, the first author is listed as a consultant for Integra Life Sciences, the manufacturer of Duragen.

Eighteen patients were randomized to receive the Duragen bovine collagen and 16 to surgery without the use of this product. Statistically significant differences favouring the use of Duragen were reported for the following outcomes: time for dural closure; total operation time for the first operation; time required for reimplantation of the bone; total operation time for both operations; and the total time required for dural separation (summarized in Table 5). The authors concluded that their findings demonstrated that surgery time was significantly reduced for both hemicraniectomy and cranioplasty when Duragen bovine collagen matrix was used as a separation layer between brain and muscle.

Table 5: Summary of findings from Horaczek et al (2008)[4]

Outcome	Collagen (mean ± SD)	Control (mean ± SD)	P value
First operation			
Time for dural closure (min)	3.8 ± 1.4	23.9 ± 18.3	P < 0.01
Total operation time (min)	96.2 ± 32.1	122.8 ± 43.4	P < 0.05
Second operation			
Time for reimplantation of the bone (min)	112 ± 49.1	139.3 ± 56.8	P < 0.05
Both operations			
Total time (min)	208.2 ± 70.2	263.7 ± 59.0	P < 0.05
Dural separation (min)	27.3 ± 13.5	88.3 ± 28.7	P < 0.05

Min – minutes; SD – standard deviation

Biological mesh for mucogingival surgery

Six RCTs[17-22] addressed the use of biological mesh in the treatment of gingival recession and were published after the systematic review by Gapski et al (2005).[6] A relatively small number of procedures were performed in each study, with the number of gingival recessions ranging from 14 to 48. The largest RCT[22] (n = 48) compared the use of AlloDerm against a combination of a connective tissue graft and coronally-positioned flap. The authors reported no statistically significant differences between these two treatment groups for any of the outcomes studied. Two studies[19,20] compared the use of AlloDerm with connective tissue graft and both reported no statistically significant differences between the two treatments for any outcome. Two RCTs[17,21] compared the use of AlloDerm in combination with a coronally-positioned flap against the use of a coronally-positioned flap alone. There were no statistically significant differences reported for the majority of outcomes in these studies, with the exception of greater improvement in recession height favouring the use of the coronally-positioned flap at 24 months (P < 0.05) and an increase in keratinized gingiva favouring AlloDerm in combination with a coronally-positioned flap (P < 0.05). One RCT[18] compared a combination of AlloDerm and a coronally-positioned flap against connective tissue graft and a coronally-positioned flap. The authors reported statistically significant differences favouring the combination of the connective tissue graft and a coronally-positioned flap for recession depth, clinical attachment level, keratinized width, and mean root coverage (all P < 0.05). These studies are limited by small sample sizes and the corresponding lack of statistical power. Furthermore, methodologies for randomization and allocation concealment were either poor or not reported. Overall, the findings from all of these studies should be interpreted with caution.

Table 6: Results of RCTs for biological mesh in mucogingival surgery

Study	Comparators (n)	Summary of key findings
De Souza et al (2008)[22]	1. AlloDerm (24) 2. CPF + CTG (24)	**Gingival recession:** No significant difference **Probing depth:** No significant difference **Clinical attachment level:** No significant difference **Keratinized tissue:** No significant difference
Mahajan et al (2007)[17]	1. AlloDerm + CPF (7) 2. CPF (7)	**Probing depth:** No significant difference **Keratinized gingiva:** No significant difference **Attached gingiva:** No significant difference
Joly et al (2007)[18]	1. AlloDerm + CPF (10) 2. CPF + CTG (10)	**Recession depth:** Favours CPF + CTG (p < 0.05) **Probing depth:** No significant difference **Clinical attachment level:** Favours CPF + CTG (p < 0.05) **Keratinized width:** Favours CPF + CTG (p < 0.05)

Study	Comparators (n)	Summary of key findings
		Keratinized thickness: No significant difference **Mean root coverage:** Favours CPF + CTG ($p < 0.05$)
De Queiroz et al (2006)[21]	1. AlloDerm + CPF (13) 2. CPF (13)	**Recession width:** No significant difference **Recession height:** Favours CPF at 24 months ($p < 0.05$) **Probing depth:** No significant difference **Keratinized gingiva:** Favours AlloDerm + CPF ($p < 0.05$) **Clinical attachment level:** No significant difference
Rahmani et al (2006)[20]	1. AlloDerm (10) 2. CTG (10)	**Recession width:** No significant difference **Probing depth:** No significant difference **Keratinized gingiva:** No significant difference **Attached gingiva:** No significant difference **Clinical attachment level:** No significant difference **Mean root coverage:** No significant difference
Haghighati et al (2009)[19]	1. AlloDerm (16) 2. CTG (16)	**Papilla width:** No significant difference **Papilla height:** No significant difference **Mean root coverage:** No significant difference

CPF – coronally positioned flap; CTG – connective tissue graft; n - number of gingiva recessions

Guidelines and recommendations

Biological mesh for pelvic organ prolapse

The Society of Gynecologic Surgeons Systematic Review Group published an evidence-based clinical practice guideline to provide recommendations concerning the use of biological grafts, synthetic grafts, and native tissue in transvaginal repair.[23] The evidence used in developing the recommendations was derived from the systematic review by Sung et al (2008).[7] The Grading of Recommendations Assessment, Development and Evaluation (GRADE) process was used in formulating the recommendations.[34] It should be noted that this guideline did not formally consider the cost or cost-effectiveness of the interventions in formulating their recommendations. Overall, the guideline was developed using a rigorous methodology, based on criteria of the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument.[35] The recommendations are provided for biological grafts, absorbable synthetic grafts, and non-absorbable synthetic grafts for each location (i.e., anterior, posterior, and multiple compartments) in Table 7.

Table 7: Recommendations regarding transvaginal repair[23]

Type of Graft	Recommendation	Strength
Anterior compartment		
Biologic graft	"It is suggested that native tissue repair remains appropriate in anterior vaginal wall repair when compared with biologic graft" (p 1126)	Weak
Absorbable synthetic graft	"It is suggested that native tissue repair remains appropriate in anterior vaginal wall repair when compared with absorbable synthetic graft" (p 1126)	Weak
Non-absorbable synthetic graft	"It is suggested that non-absorbable synthetic mesh may improve anatomic outcomes of anterior vaginal wall repair, but there are significant trade-offs in regard to the risk of adverse events" (p 1126)	Weak
Posterior compartment		
Biologic graft	"It is suggested that native tissue repair remains appropriate in posterior	Weak

Type of Graft	Recommendation	Strength
	vaginal wall repair when compared with biologic graft" (p 1127)	
Absorbable synthetic graft	"It is suggested that native tissue repair remains appropriate in posterior vaginal wall repair when compared with absorbable synthetic graft" (p 1127)	Weak
Non-absorbable synthetic graft	"There are no comparative studies to guide any recommendation on the use of non-absorbable synthetic mesh in posterior vaginal wall repair when compared with native tissue repair" (p 1127)	N/A
Multiple compartments		
Biologic graft	"There are no comparative studies to guide any recommendation on the use of biologic grafts in multiple compartment repair when compared with native tissue repair" (p 1128)	N/A
Absorbable synthetic graft	"There are no comparative studies to guide any recommendation on the use of absorbable synthetic graft in multiple compartment vaginal wall repair when compared with native tissue repair" (p 1128)	N/A
Non-absorbable synthetic graft	"There are no comparative studies to guide any recommendation on the use of non-absorbable synthetic graft in multiple compartment repair when compared with native tissue repair" (p 1128)	N/A

Limitations

With respect to the use of biological mesh in vaginal wall prolapse, the available systematic reviews are composed of studies that were heterogeneous with regard to study design, surgical techniques, length of follow-up, populations (e.g., recurrent or primary prolapse), sample size, and outcomes. Furthermore, the systematic reviews differed in their approach to synthesizing the data: Sung et al (2008)[7] stated that the studies were too heterogeneous to pool in a meta-analysis, whereas, Jia et al (2007)[9] conducted both pair-wise indirect comparisons by pooling data. Similar limitations were observed for the repair of gingival recessions where the individual studies that assessed the efficacy of biological mesh were limited by their duration, sample size, and poor internal validity. The systematic review and meta-analyses conducted for repair of gingival recessions revealed a high level of statistical heterogeneity and the authors were unable to draw conclusions.

Single, RCTs of limited sample size were available to assess the efficacy of biological mesh for Lichtenstein repair of inguinal hernia (n = 70),[15] urethroplasty (n = 20),[16] diabetic foot ulcers (n = 86)[3], and use in decompressive hemicraniectomy (n = 34).[4] The two studies[3,4] that supported the use of biological mesh were funded and/or written by the manufacturers of the product being investigated. Horaczek et al (2008)[4] concluded that surgery time is significantly reduced for both hemicraniectomy and cranioplasty when bovine collagen matrix is used; however, this study involved a small number of patients and there is no information concerning the overall cost-effectiveness of this procedure. Reyzelman et al (2009)[3] concluded that their findings support the use of GraftJacket therapy in the treatment of diabetic foot ulcers. Similar to the other studies, this conclusion was made independently of information regarding overall differences in cost.

Despite the use of rigorous methodology and a comprehensive systematic review, the only evidence-based guideline identified in the literature search was limited by a lack of relevant trials comparing biological and synthetic mesh. This lack of robust clinical data resulted in either weak or no recommendations. Furthermore, this guideline did not consider cost or cost-effectiveness of the interventions and there was no discussion regarding whether or not different biological products should be considered equally efficacious.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

This report identified evidence concerning the use of biological mesh for a wide range of surgical procedures, including pelvic organ prolapse, breast reconstruction, inguinal hernia, urethroplasty, diabetic foot ulcers, decompressive hemicraniectomy, and various mucogingival surgeries. There was no evidence regarding the cost-effectiveness of these products for any indications and, overall, there was insufficient clinical evidence to thoroughly assess the comparative efficacy of biological and synthetic mesh products. This was reflected in the only evidence-based guideline identified which did not recommend the use of biological mesh in surgery for pelvic organ prolapse. In addition to the complexity of having many indications and few studies, there is an abundance of different mesh products available and an absence of evidence regarding differences in safety and efficacy.

Based on the findings of the literature included in this review, there is currently insufficient evidence to clearly establish the place in therapy of biological mesh products. Further evaluations based on robust clinical data will be required in order to ascertain the cost-effectiveness of biological mesh.

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