

Use of acellular dermal matrices in laryngotracheal and pharyngeal reconstruction: systematic review

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Abstract

Background: Acellular dermal matrices are increasingly used in laryngotracheal and pharyngeal reconstruction, but specific indications and the type of acellular dermal matrix used vary. The authors systematically reviewed outcomes relating to acellular dermal matrix use in head and neck reconstruction.

Methods: Electronic databases were searched through 1 May 2016 for literature on acellular dermal matrix use in laryngotracheal and pharyngeal reconstruction. Studies were appraised for surgical indications, outcomes and study design.

Results: Eleven publications with 170 cases were included. Eight articles reported on acellular dermal matrix use in oncological reconstruction. Most studies were case series; no high-level evidence studies were identified. Graft extrusion was more common in non-oncological applications. In general, post-oncological reconstruction with an acellular dermal matrix demonstrated complication rates similar to those reported without an acellular dermal matrix.

Conclusion: Evidence in support of acellular dermal matrix use in head and neck reconstruction is generally poor. Prospective comparative studies are required to define the indications, safety and effectiveness of acellular dermal matrices in laryngotracheal and pharyngeal reconstruction.

Key words: Acellular Dermal Matrix; Laryngectomy; Pharyngectomy; Hypopharyngeal Cancer; Reconstruction; Radiotherapy; Tonsillectomy; Velopharyngeal Insufficiency

Introduction

Acellular dermal matrix allografts are increasingly used in otorhinolaryngology in cases of large soft tissue defects for which primary closure without tension is not feasible, or where regional or free flaps are inadequate without additional soft tissue augmentation. The use of an acellular dermal matrix provides a robust collagen framework for mucosal epithelialisation and neovascularisation, while reducing potential donor site morbidity.

Sheet acellular dermal matrices such as AlloDerm (LifeCell, Branchburg, New Jersey, USA) typically comprise a decellularised dermal layer of collagen and a basement membrane. Acellular dermal matrices may either be allografts derived from human cadavers or xenografts from other mammalian skin. Additionally, acellular dermal matrices may be available in either aseptic freeze-dried forms that require 20–30 minutes of reconstitution, or sterile ‘ready-to-use’ forms that require 2–3 minutes of rehydration or less. Sheet acellular dermal matrices may be peeled,

layered, cut, shaped, rolled or folded to tailor the graft to the contour of the surrounding host tissue.¹

Soft tissue reconstruction or repair of the larynx, trachea, nasopharynx, oropharynx and hypopharynx traditionally involves local or pedicled flaps, or free autologous tissue transfer (cartilage, bone, dermis, fat). Although the acellular dermal matrix has been described for other head and neck surgical applications, such as soft tissue augmentation in hemifacial atrophy,² palatoplasty,³ tympanoplasty,⁴ rhinoplasty⁵ and prevention of post-parotidectomy Frey syndrome,⁶ indications for their use in reconstruction of the larynx, trachea and pharynx, beyond the injection of a micronised acellular dermal matrix for vocal fold paralysis,⁷ are evolving.

This systematic review aimed to investigate: current uses of sheet acellular dermal matrices in laryngotracheal and pharyngeal reconstruction, including examination of surgical indications, graft thickness and dimensions; use of aseptic versus sterile varieties of acellular dermal matrix; concomitant flaps used; and incidence of associated peri-operative complications.

Materials and methods

A systematic review, aligned with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses ('PRISMA') standards, was performed of published literature on cases in which acellular dermal matrices were used in tracheolaryngeal and pharyngeal reconstruction. All sources were searched through 1 May 2016.

Search strategy

A literature search of the PubMed, Medline, Embase and Web of Science databases was conducted. The following Boolean search (using Medical Subject Headings (MeSHs)) was performed in PubMed: (((Alloderm OR "acellular dermal matrix")) OR ("Acellular Dermis" OR "Alloderm")) AND ((("Larynx"[MeSH] OR "Pharynx"[MeSH] OR "Nasopharynx"[MeSH] OR "Oropharynx"[MeSH] OR "Hypopharynx"[MeSH] OR "Trachea"[MeSH] OR "Glottis"[MeSH] OR "Esophagus"[MeSH] OR laryngeal OR pharyngeal OR tracheal OR laryngotracheal OR hypopharyngeal OR nasopharyngeal OR oropharyngeal OR esophageal OR thyroid)). Similar search terms were applied to Medline and Embase. Search results were limited to articles that analysed human subjects and were written in the English language. Abstracts were analysed and the full-text articles were obtained for literature that fulfilled the inclusion criteria. Additional articles were identified by conducting a screen of the references of the included full-text articles.

Selection criteria

Literature not in English-language publications was excluded. Animal, cadaveric, histological, radiological and *in vitro* bioengineering studies were also excluded. In addition, studies with unobtainable full text, or with insufficient or aggregate data,⁸ or those involving anatomical locations outside of the trachea, nasopharynx, posterior oropharynx or hypopharynx (i.e. inferior to the oesophageal inlet, or cervical skin overlying the pharynx, or hard and soft palate), were excluded. Literature on injectable micronised dermal fillers were also excluded, as these are almost exclusively intended for medialisation laryngoplasty and have been sufficiently reviewed elsewhere.^{9–11} Articles on the use of acellular dermal matrices in palatal repair were excluded for similar reasons.^{12,13} Searches were conducted independently by two investigators (AH and MB) to ensure that all appropriate articles were included in this analysis. Any discrepancies regarding the inclusion of articles were resolved among all authors.

Data extraction

Data extracted included author, publication year, study type, sample size, clinical indication, concomitant procedures and therapies (chemoradiotherapy), and peri-

operative complications. Characteristics of the acellular dermal matrix product used were also recorded, including source (allograft vs xenograft), thickness and shape. Conflict disclosures and level of evidence were also documented based on the Oxford Center for Evidence-Based Medicine.

Results

Our initial search of the PubMed, Web of Science, Medline and Embase databases identified a total of 67 articles (Figure 1). A total of 11 articles and 170 cases were included in this review (Table I).^{14–24} There were seven case series,^{16–19,21–23} three case reports^{14,15,24} and one prospective study²⁰ included in the analysis, with an aggregate level of evidence of 4 based on the Oxford Center for Evidence-Based Medicine. The sole prospective study included was performed with the financial support of the acellular dermal matrix manufacturer.²⁰ Conflicts of interest were not disclosed in 2 of the 11 studies.^{17,19}

Graft characteristics

Of the 11 studies included, 7 detailed the use of AlloDerm,^{14–20} 3 described the use of Heal-All Oral Biofilm (Zhenghai Biotech, Yantai, China)^{21–23} and 1 study outlined the use of Permacol (Covidien, Dublin, Ireland).²⁴ AlloDerm is an acellular dermis derived from human cadaveric tissue, and is available in freeze-dried or ready-to-use forms. Heal-All is a freeze-dried heterogeneous dermal product purified from bovine skin, and is composed of cross-linked type I and III collagen. Permacol is a ready-to-use, decellularised porcine dermis, comprising cross-linked type I and III collagen and small amounts of elastin, and was initially indicated for abdominal wall defect closure.

Only 6 of the 11 studies provided an indication of graft thickness (Table II).^{17,19,21–24} Thin acellular dermal matrices (0.30–0.69 mm) were used for hemi-tracheal reconstruction, total laryngectomy and partial hypopharyngectomy. Medium thickness grafts (0.53–1.02 mm) were implanted to bulk up the medial one-third of vocal folds for glottic insufficiency. Thicker implants (0.9–1.5 mm) were used in complex pharyngeal fistula closure and partial pharyngoplasty for advanced carcinomas of the piriform sinuses, tongue base and lateral pharyngeal walls. There were no reports of dermal matrix rolling or folding for volume augmentation.

Seven studies reported the dimensions of their implants,^{15–18,21–23} which ranged from 0.5 cm wide strips when used as a sling to narrow the velopharyngeal space in velopharyngeal insufficiency,¹⁶ to 1.5 × 1.5 cm squares for vocal fold augmentation,¹⁷ to 6 × 8 cm sheets used for total laryngo-hypopharyngeal reconstruction.²⁴ Only five studies specified defect sizes;^{15,18,21,23,24} these were within the documented dimensions of their overlying acellular dermal matrix grafts (Table II).

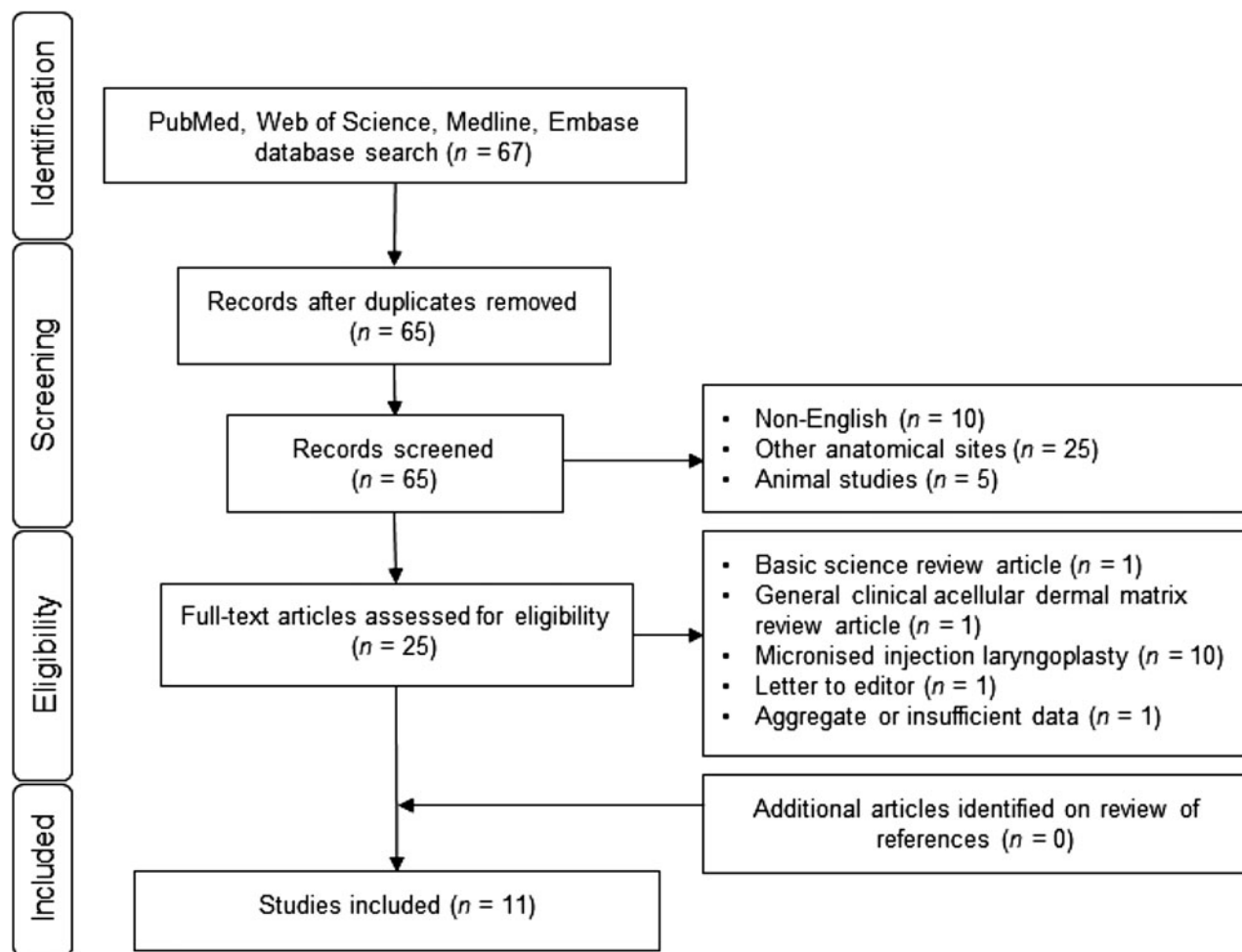


FIG. 1

Study selection flow diagram in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement.

The most commonly used flaps for coverage were the pectoralis major myocutaneous flap for circumferential laryngectomies and/or hypopharyngectomies,^{18,23} and strap muscle flaps for partial tracheal and hypopharyngeal reconstruction.^{21,22} Closure using local pharyngeal mucosal or tonsillar wall myomucosal flaps were also described in two studies in which tension-free closure was possible.^{14,16} Supraclavicular artery island and sternocleidomastoid flaps were also described for

closure.²⁴ No flaps were used for vocal fold augmentation or for coverage of exposed post-tonsillectomy defects.^{17,20} One study described the use of an AlloDerm-wrapped Montgomery T-tube as a tracheal prosthetic stent for structural support.¹⁵

Clinical indications

The majority of reports examined the use of acellular dermal matrices in primary reconstruction following

TABLE I
STUDIES MEETING CRITERIA FOR SYSTEMATIC REVIEW

Study	Year of publication	Level of evidence	Study design	Sample size (n)	Conflict disclosures
Kucur <i>et al.</i> ¹⁴	2015	4	Case report	1	None
Cheng <i>et al.</i> ¹⁵	2015	5	Case report	1	None
Kelly <i>et al.</i> ¹⁶	2012	4	Case series	16	None
Tan <i>et al.</i> ¹⁷	2011	4	Case series	20	Not reported
Zhang <i>et al.</i> ¹⁸	2010	4	Case series	7	None
Sinha <i>et al.</i> ¹⁹	2001	4	Case series	14	Not reported
Scalfani <i>et al.</i> ²⁰	2001	3b	Prospective double-blinded study	10	Financial support from manufacturer
Li <i>et al.</i> ²¹	2017	5	Case series	2	None
He <i>et al.</i> ²²	2015	4	Case series	93	None
Yin <i>et al.</i> ²³	2015	4	Case series	5	None
Persichetti <i>et al.</i> ²⁴	2013	5	Case report	1	None

TABLE II
DESCRIPTION OF ACELLULAR DERMAL MATRICES, DEFECTS AND FLAP TYPES IN INCLUDED STUDIES

Tissue origin & product	Study	Packaging type	Graft shape	Graft size (cm)	Graft thickness (mm)	Defect size (cm)	Reinforcing flap
<i>Allogeneic</i>							
AlloDerm	Kucur <i>et al.</i> ¹⁴	NR	Sheet	NR	NR	NR	Pharyngeal mucosa
AlloDerm	Cheng <i>et al.</i> ¹⁵	NR	Tube	2.5 in length	NR	2.5	None; 3D printed Montgomery T-tube prosthesis
AlloDerm	Kelly <i>et al.</i> ¹⁶	NR	Strip	0.5 in width	NR	NR	Pharyngeal mucosa or posterior tonsillar wall myomucosal flap
AlloDerm	Tan <i>et al.</i> ¹⁷	NR	Sheet	1.5 × 1.5	0.53–1.02	NR	None
AlloDerm	Zhang <i>et al.</i> ¹⁸	Freeze-dried	Sheet	3 × 4; 4 × 6	NR	(1) Posterior pharyngeal wall resection: 4 (2) Total resection: full circumference	Pectoralis major myocutaneous flap
AlloDerm	Simha <i>et al.</i> ¹⁹	Freeze-dried	Sheet	NR	0.9	Varied	SCM flap in 10 of 14 patients
AlloDerm	Solafani <i>et al.</i> ²⁰	NR	Sheet	NR	NR	NR	None
<i>Xenogeneic</i>							
Heal-All	Li <i>et al.</i> ²¹	Freeze-dried	Sheet	3 × 4	0.30–0.69	Patient A: 2–3 tracheal rings in length & half of tracheal circumference (2.5 × 3.5) Patient B: 2.5 × 3	Sternohyoid strap
Heal-All	He <i>et al.</i> ²²	Freeze-dried	Sheet	2 × 2.5; 4 × 3	0.30–0.69	NR	Platysmal flap (larynx); strap muscle flap (hypopharynx)
Heal-All	Yin <i>et al.</i> ²³	Freeze-dried	Sheet	4 × 6; 6 × 8	0.30–0.39	6–8	Pectoralis major myocutaneous flap
Permacol	Persichetti <i>et al.</i> ²⁴	Ready-to-use	Sheet	NR	0.5–1.5	3 × 3 fistula	Supraclavicular artery island flap

NR = not reported; 3D = three-dimensional; SCM = sternocleidomastoid

squamous cell carcinoma resection (Table III). AlloDerm was used for mucosal flap reinforcement post-oropharyngectomy, and for reconstruction of partial and total laryngo-hypopharyngectomy defects resulting from resection of stage II–IVa squamous cell carcinomas. Similarly, Heal-All was described for closure augmentation of hemi-circumferential tracheal defects following adenoid cystic carcinoma resection, and following partial and total laryngo-hypopharyngectomies for stage I–IVa carcinomas. Two instances of acellular dermal matrix use in secondary oncological reconstructions were identified. These included: repeat tracheoplasty and Montgomery T-tube framing with AlloDerm implantation after failed sternocleidomastoid flap reconstruction of a post-medullary thyroid cancer resection defect,¹⁵ and Permacol implantation for complex oropharyngeal fistula closure in a patient with recurrent fistulisation and necrotising fasciitis secondary to chemoradiotherapy.²⁴

Non-malignancy applications included revision sling pharyngoplasty for tertiary treatment of persistent velopharyngeal insufficiency¹⁶ and vocal fold augmentation for glottic insufficiency.¹⁷ The single prospective study identified examined rates of post-tonsillectomy pain in bilateral cases in which the tonsillar bed was treated with or without the use of an acellular dermal matrix.²⁰ There were no reports of nasopharyngeal or thyroidectomy-associated applications of acellular dermal matrices. Only 1 of 11 studies explored acellular dermal matrix use in the paediatric population.¹⁶

Graft complications

Follow-up duration varied widely between reports. For cases in which an acellular dermal matrix was used during primary post-oncological reconstruction, follow up ranged from 3 to 42 months.^{14,18,19,21–23}

The two reports on acellular dermal matrix use in secondary reconstruction had an average follow-up duration of two to three months.^{15,24} In the 3 non-oncological studies, post-operative follow-up duration ranged from 2 weeks, for post-tonsillectomy pain assessment,²⁰ to 40 months, for clinical speech outcomes and evidence of improved glottic closure.^{16,17}

Graft exposure or extrusion was not reported in any of the oncological reconstruction cases. In the largest series reported, graft mucosalisation was reported to be complete by three to six months post-operatively.²² Three studies reported no complications.^{14,15,24} Two studies reported mild stricture or stenosis, which either resolved with dilation or remained stable.^{18,21} Rates of infection and secondary fistulisation in the included studies (which used acellular dermal matrices) did not differ significantly from previously reported complication rates in studies where acellular dermal matrices were not used.^{19,22,23} Not surprisingly, scarring, atresia and fistula incidence rates were reported to be higher in patients who received prior radiotherapy.²³

TABLE III
INDICATIONS AND COMPLICATIONS IN INCLUDED STUDIES

Study	Cases (n)	Outcome measures	Surgical procedure	Indication	Peri-operative CRT	Graft complications	Notes
Kucur <i>et al.</i> ¹⁴	1	Safety; presence of post-op pharyngeal-cutaneous fistula	Transoral oropharyngectomy	Stage IVb oropharyngeal SCC	None reported	None	
Cheng <i>et al.</i> ¹⁵	1	Clinical speech outcomes; presence of granulation tissue	Repeat cervical tracheoplasty	Tracheal anastomotic dehiscence post-flap reconstruction for recurrent medullary thyroid cancer	None reported	None	Previous cervical tracheoplasty using SCM flap. Resulted in post-op infection, dehiscence & flap necrosis
Kelly <i>et al.</i> ¹⁶	16	Nasalance of speech	Revision sling pharyngoplasty	Persistent velopharyngeal insufficiency	N/A	2 cases of post-op graft dehiscence & upper respiratory tract infection (12.5%)	10 patients were primarily treated via sphincter pharyngoplasty; 6 patients via pharyngeal flaps
Tan <i>et al.</i> ¹⁷	20	Vocal fold augmentation at 12 mths; clinical speech outcomes; glottic closure	Mini-thyrotomy, or transoral cordotomy with vocal fold augmentation	Glottic insufficiency secondary to trauma, previous surgery or sulcus vocalis	N/A	1 case of early resorption of AlloDerm graft requiring revision mini-thyrotomy; 1 case of early incision dehiscence & extrusion of AlloDerm graft; 3 cases of AlloDerm resorption over 1 year post-op, requiring revision laryngoplasties	17 patients were treated via mini-thyrotomy, 2 via transoral cordotomy & 1 via both; satisfactory long-term vocal fold augmentation in 71%
Zhang <i>et al.</i> ¹⁸	7	Graft survival; presence of pharyngeal fistula or stenosis; healing within 10 days post-op; epithelialisation; diet resumption	Total laryngectomy & hypo-pharyngectomy (5 of 7 patients), or tumour resection from posterior pharyngeal wall (2 of 7 patients)	Stage II–IVa hypopharyngeal SCC	All patients received neoadjuvant chemotherapy; 6 of 7 patients received 60 Gy adjuvant external-beam RT	Mild stenosis of hypopharynx post-AlloDerm grafting, in all patients, resolved after dilation; reduced sensation & slight contracture of graft patches noted at 3 mths post-op	No graft failures or fistulas; good epithelialisation & mucosal integration at 3 mths
Sinha <i>et al.</i> ¹⁹	14	Graft survival, contracture, & integration; clinical speech outcomes; diet resumption	Partial pharyngectomy	Stage III–IV oropharyngeal or hypopharyngeal SCC	None received chemotherapy. 1 patient received pre-op external-beam RT; 11 patients received post-op external-beam RT	2 post-op pharyngeal fistulas (14.3%) (with & without SCM flap); both fistulas resolved conservatively. Neither patient received pre-op external-beam RT	Good graft mucosalisation by 3–6 wks post-op; no graft contractures, infections or pharyngeal stenosis. 10 patients had an SCM flap, 4 had no SCM flap
Sclafani <i>et al.</i> ²⁰	10	Post-tonsillectomy pain (e.g. odynophagia, otalgia, nocturnal pain)	Bilateral tonsillectomy	Recurrent adult tonsillitis refractory to antibiotics	N/A	2 cases of partial AlloDerm graft sloughing within 7 days post-op (20%); both grafts were subsequently explanted	No incidences of bleeding or infection; reduced total pain significantly by 50% on post-op day 7
Li <i>et al.</i> ²¹	2	Graft survival & epithelialisation; complications [†]	Hemi-circumferential tracheal resection	Tracheal adenoid cystic carcinoma	Patient A received 50 Gy adjuvant external-beam RT at 6 wks post-op; patient B received 60 Gy adjuvant external-beam RT at 6 wks post-op	Patient A presented with mild tracheal stricture at 1 mth post-op, with no progression to stenosis at 33 mths post-op	No incidences of bleeding, fistula or infection; total graft mucosalisation at 2 mths post-op

Continued

Table III Continued

Study	Cases (n)	Outcome measures	Surgical procedure	Indication	Peri-operative CRT	Graft complications	Notes
He <i>et al.</i> ²²	93	Graft survival & epithelialisation; complications [†]	Vertical partial laryngectomy	Stage I–IVa laryngeal or hypopharyngeal carcinoma	All stage III+ patients received 60–75 Gy adjuvant external-beam RT post-op	5 cases of infection (5.4%); 3 developed a laryngeal fistula & 2 developed pharyngeal fistula	94.6% cases demonstrated full mucosalisation at 3–6 mths post-op
Yin <i>et al.</i> ²³	5	Presence of pharyngeal fistula or stenosis; diet resumption	Partial hypo-pharyngectomy & partial proximal oesophageal resection	Stage IVa hypopharyngeal carcinoma	4 of 5 patients received 50–60 Gy adjuvant external-beam RT at 5–6 wks post-op	1 case of pharyngeal fistula	No pharyngeal stenosis reported
Persichetti <i>et al.</i> ²⁴	1	Graft survival & epithelialisation; mucosal integration	Anterior oropharyngeal fistula closure	Recurrent fistula & necrotising fasciitis secondary to CRT for pharyngeal SCC	CRT 2 years previously	None	No fistula relapse; good mucosal integration on histological analysis at 2 mths post-op

CRT = chemoradiotherapy; post-op = post-operative; SCC = squamous cell carcinoma; SCM = sternocleidomastoid; N/A = not applicable; mth = month; RT = radiotherapy; wk = week

Among the 20 patients who underwent sheet acellular dermal matrix vocal fold augmentation, 5 cases of resorption were detected, with 3 of these being reported more than 1 year post-operatively.¹⁷ A cumulative rate of graft extrusion or failure of 19.6 per cent was observed in non-oncological applications. There were no reports of acellular dermal matrix scarring or contractures, post-operative bleeding, delayed healing, or unsatisfactory mucosal integration in instances of successful graft takes across all 11 studies.

Discussion

The use of acellular dermal matrices in laryngotracheal and pharyngeal reconstruction is a relatively new development, and offers theoretical advantages over the use of synthetic prostheses and autologous split-thickness skin grafts. Acellular dermal matrices are commercially available in a variety of thicknesses for good epithelialisation, vascularisation and incorporation into host mucosa.¹⁸ They are thin and flexible, while myocutaneous flaps are bulkier and associated with greater risk of pharyngocutaneous fistulas and strictures.²⁵ Compared to harvesting split-thickness skin grafts or raising flaps, which may necessitate microsurgery, acellular dermal matrices generally cost less and eliminate donor site complications.^{26,27} Some surgeons describe a reduction in total operative time with the use of acellular dermal matrices;^{18,19} however, this has not been objectively assessed.

Previous reports have endorsed the use of thin acellular dermal matrices in oral mucosal reconstruction^{19,27} and partial pharyngeal reconstruction.²⁸ The application of thicker acellular dermal matrix implants in the neck had not been explored until Sinha *et al.* investigated the use of 0.9 mm thick AlloDerm in reconstructing partial pharyngeal defects, reporting a complication-free rate of 86 per cent.¹⁹ The authors suggested that extensive pharyngeal defects, such as those that are circumferential or larger than one-third of the base of the tongue, should be closed using thick grafts,¹⁹ but they did not offer data to support this statement. Although the total number of cases included in our review was limited, a trend could be identified, whereby thin acellular dermal matrices were more frequently used for partial superficial defects of the trachea, larynx and hypopharynx, while thicker implants were used in complex pharyngeal fistula closure and partial pharyngoplasty for more extensive stage III–IV carcinomas. Unfortunately, 5 of the 11 articles in our review failed to report the graft thickness used, potentially skewing our appraisal of how acellular dermal matrix thickness consideration plays into head and neck reconstruction.

Previously, Shi *et al.* documented transient mild acellular dermal matrix graft contracture in 7 of 36 patients with buccal mucosal defects (19.4 per cent), and graft failure in 2 of 36 patients who underwent hard palate closure using an acellular dermal matrix (5.6 per cent).²⁹ Our review showed a similarly high

rate of acellular dermal matrix survival in laryngotracheal and pharyngeal reconstruction, with concomitant low rates of infection, graft rejection or failure. There were no reports of delayed healing, or poor graft epithelialisation or neovascularisation, other than those secondary to graft extrusion or infection. Graft failure was observed in two cases of tonsillar fossa implantation²⁰ and in one case of medialisation laryngoplasty.¹⁷ In the former cases, graft failure may have occurred because the acellular dermal matrix was applied as an onlay, with no mucosal coverage, while in the latter case ongoing laryngeal movement could have led to more rapid resorption or extrusion. Similarly, mild and progressive acellular dermal matrix resorption was reported as early as 2.5 months following sling pharyngoplasty for persistent velopharyngeal insufficiency.¹⁶

Based on the limited number and heterogeneity of cases included in our review, it is impossible to draw any conclusions regarding the impact of acellular dermal matrix use on post-operative stricture and stenosis rates in tracheal or pharyngeal reconstruction. The use of adjuvant external-beam radiation for pharyngeal cancer treatment further complicates the interpretation of current literature. As well as affecting native pharyngeal tissue, external-beam radiation has been shown to adversely affect angiogenesis and rates of recellularisation in animal models of acellular dermal matrix engraftment.^{30,31} Although others have pointed to a correlation between post-operative radiation and negative acellular dermal matrix graft outcomes, complication rates have not been shown to be significantly different when compared to split-thickness skin grafts in oral cavity reconstruction.²⁷ In our review, a similarly inconsistent picture emerged. Zhang *et al.* reported mild stenosis and stricture following AlloDerm reconstruction of the larynx and hypopharynx in all seven patients in their series; however, all patients had undergone pre-operative radiotherapy.¹⁸ Similarly, Yin *et al.* documented a case of pharyngeal fistula formation following acellular dermal matrix grafting in a patient with a history of hypopharyngeal scarring and atresia secondary to prior adjuvant radiotherapy.²³ Conversely, in the study by Sinha *et al.*, neither of the two patients who developed a post-operative pharyngeal fistula received pre-operative radiotherapy, while the sole patient who did receive pre-operative radiation did not develop a fistula.¹⁹

The current review points to the need for adequately powered randomised controlled trials, to effectively determine the potential benefit of acellular dermal matrix use in tracheolaryngeal and pharyngeal reconstruction. A greater understanding of how adjuvant chemoradiotherapy might alter acellular dermal matrix engraftment and subsequent morbidity in human head and neck reconstruction would help shape management guidelines with regard to post-operative recovery time prior to radiotherapy, radiation dose and schedule. Other areas for future investigation

include a comparison of various thicknesses or sources (xenogeneic vs allogeneic) of acellular dermal matrices head-to-head for similar defects, or a comparison of differences in operative time and costs for reconstructions with or without acellular dermal matrices.

Conclusion

Current literature on acellular dermal matrix use in laryngotracheal and pharyngeal reconstruction is limited to case reports, retrospective chart reviews and a single industry-funded prospective cohort study. In general, the available studies provide incomplete descriptive detail concerning: peri-operative radiation dosing and scheduling, the surgeon's experience using dermal grafts, graft thickness, and defect size. Prospective randomised studies are needed to make stronger recommendations regarding sheet acellular dermal matrix use in laryngopharyngeal reconstruction. Potential variables for future studies to investigate include graft outcomes in the setting of pre- and post-operative chemoradiotherapy, differences in operative time, and complication rates of different acellular dermal matrix forms.

References

- 1 Pushpoth S, Tambe K, Sandramouli S. The use of AlloDerm in the reconstruction of full-thickness eyelid defects. *Orbit* 2008; **27**:337–40
- 2 Ortega VG, Sastoque D. New and successful technique for the management of Parry-Romberg syndrome's soft tissue atrophy. *J Craniofac Surg* 2005; **26**:e507–10
- 3 Hudson JW, Pickett DO. A 5-year retrospective review of primary palatoplasty cases utilizing an acellular collagen interpositional graft. *J Oral Maxillofac Surg* 2015; **73**:1393
- 4 Haynes DS, Vos JD, Labadie RF. Acellular allograft dermal matrix for tympanoplasty. *Curr Opin Otolaryngol Head Neck Surg* 2015; **13**:283–6
- 5 Gryskiewicz JM. Dorsal augmentation with AlloDerm. *Semin Plast Surg* 2008; **22**:90–103
- 6 Wang W, Fan JC, Sun CJ, Chen Y, Zhao HW, Ma H *et al.* Systematic evaluation on the use of acellular dermis matrix graft in prevention Frey syndrome after parotid neoplasm surgery. *J Craniofac Surg* 2013; **24**:1526–9
- 7 Pearl AW, Woo P, Ostrowski R, Mojica J, Mandell DL, Costantino P. A preliminary report on micronized AlloDerm injection laryngoplasty. *Laryngoscope* 2002; **112**:990–6
- 8 Deneve JL, Turaga KK, Marzban SS, Puleo CA, Sarnaik AA, Gonzalez RJ *et al.* Single-institution outcome experience using AlloDerm as temporary coverage or definitive reconstruction for cutaneous and soft tissue malignancy defects. *Am Surg* 2013; **79**:476–82
- 9 Lisi C, Hawkshaw MJ, Sataloff RT. Viscosity of materials for laryngeal injection: a review of current knowledge and clinical implications. *J Voice* 2013; **27**:119–23
- 10 Remale M, Lawson G. Results with collagen injection into the vocal folds for medialization. *Curr Opin Otolaryngol Head Neck Surg* 2007; **15**:148–52
- 11 King JM, Simpson CB. Modern injection augmentation for glottic insufficiency. *Curr Opin Otolaryngol Head Neck Surg* 2007; **15**:153–8
- 12 Aldekhayel SA, Sinno H, Gilardino MS. Acellular dermal matrix in cleft palate repair: an evidence-based review. *Plast Reconstr Surg* 2012; **130**:177–82
- 13 Losee JE, Smith DM. Acellular dermal matrix in palatoplasty. *Aesthet Surg J* 2012; **31**:S108–15
- 14 Kucur C, Durmus K, Gun R, Old MO, Agrawal A, Teknos TN *et al.* Safety and efficacy of concurrent neck dissection and transoral robotic surgery. *Head Neck* 2015; **38**:e519–23
- 15 Cheng GZ, Folch E, Brik R, Gangadharan S, Mallur P, Wilson JH *et al.* Three-dimensional modeled T-tube design and

- insertion in a patient with tracheal dehiscence. *Chest* 2015;**148**: e106–8
- 16 Kelly DA, Plikatitis C, Blalock D, Argenta LC, David LR. AlloDerm revision for failed pharyngoplasty. *J Craniofac Surg* 2012;**23**:645–9
 - 17 Tan M, Bassiri-Tehrani M, Woo P. Allograft (AlloDerm) and autograft (temporalis fascia) implantation for glottic insufficiency: a novel approach. *J Voice* 2011;**25**:619–25
 - 18 Zhang L, Cheng JP, Zhang WC, Li W, Anniko M. Reconstruction of defects following surgery for hypopharyngeal carcinoma using artificial biological material. *Acta Otolaryngol* 2010;**130**:1293–9
 - 19 Sinha UK, Chang KE, Shih CW. Reconstruction of pharyngeal defects using AlloDerm and sternocleidomastoid muscle flap. *Laryngoscope* 2001;**111**:1910–16
 - 20 Sclafani AP, Jacono AA, Dolitsky JN. Grafting of the peritonsillar fossa with an acellular dermal graft to reduce posttonsillectomy pain. *Am J Otolaryngol* 2001;**22**:409–14
 - 21 Li P, Li S, Tang Q, He X, Yin D, Wang S *et al.* Reconstruction of human oncological tracheal defects with xenogenic acellular dermal matrix. *Auris Nasus Larynx* 2017;**44**:237–40
 - 22 He J, Tian Y, Wu P, Liao L, Quan H, Kang J *et al.* Heterogeneous bovine acellular dermal matrix for mucosal repair in reconstructive surgery for laryngeal and hypopharyngeal carcinoma. *Oncol Res Treat* 2015;**38**:282–4
 - 23 Yin D, Tang Q, Wang S, Li S, He X, Liu J *et al.* Xenogenic acellular dermal matrix in combination with pectoralis major myocutaneous flap reconstructs hypopharynx and cervical esophagus. *Eur Arch Otorhinolaryngol* 2015;**272**:3457–61
 - 24 Persichetti P, Aveta A, Segreto F. Combined use of acellular dermal matrix and supraclavicular artery island flap for oropharyngeal reconstruction. *Plast Reconstr Surg* 2013;**131**:641e–2e
 - 25 Piazza C, Taglietti V, Nicolai P. Reconstructive options after total laryngectomy with subtotal or circumferential hypopharyngectomy and cervical esophagectomy. *Curr Opin Otolaryngol Head Neck Surg* 2012;**20**:77–88
 - 26 Kontos AP, Qian Z, Urato NS, Hassanein A, Proper SA. AlloDerm grafting for large wounds after Mohs micrographic surgery. *Dermatol Surg* 2009;**35**:692–8
 - 27 Girod DA, Sykes K, Jorgensen J, Tawfik O, Tsue T. Acellular dermis compared to skin grafts in oral cavity reconstruction. *Laryngoscope* 2009;**119**:2141–9
 - 28 Chiu ES, Friedlander PL. Reply: combined use of acellular dermal matrix and supraclavicular artery island flap for oropharyngeal reconstruction. *Plast Reconstr Surg* 2013;**131**:642e–3e
 - 29 Shi LJ, Wang Y, Yang C, Jiang WW. Application of acellular dermal matrix in reconstruction of oral mucosal defects in 36 cases. *J Oral Maxillofac Surg* 2012;**70**:e586–91
 - 30 Ibrahim HZ, Kwiatkowski TJ, Montone KT, Evans SM, Rosenthal D, Chalian AA *et al.* Effects of external beam radiation on the allograft dermal implant. *Otolaryngol Head Neck Surg* 2000;**122**:189–94
 - 31 Dubin MG, Feldman M, Ibrahim HZ, Tufano R, Evans SM, Rosenthal D *et al.* Allograft dermal implant (AlloDerm) in a previously irradiated field. *Laryngoscope* 2000;**110**:934–7

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