Heterogeneous Bovine Acellular Dermal Matrix for Mucosal Repair in Reconstructive Surgery for Laryngeal and Hypopharyngeal Carcinoma

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Introduction

The repair of mucosal defects following laryngeal and hypopharyngeal surgery is critical to the success of the surgery. The reconstruction of laryngeal and hypopharyngeal mucosa by pedicle, myocutaneous, free, and perforator flaps is a common procedure. In recent years, the homogeneous bovine acellular dermal matrix (ADM) has been used for repairing mucosal defects [1]. We used a heterogeneous bovine ADM to repair mucosal defects in 93 patients who had undergone resection for laryngeal and hypopharyngeal carcinoma from May 2010 to March 2013, and achieved satisfactory results.

Clinical Data

General Data

There were 87 male and 6 female patients; the age range was 31–84 years and the average age was 57.95 years. Table 1 lists the patient details. All patients were pathologically diagnosed with squamous cell carcinoma. Patients with T3N1M0 and T3N2M0 disease and all patients with hypopharyngeal carcinoma received radiotherapy of 60–75 Gy.

The hospital ethics committee approved the study protocol, and we obtained informed consent from the patients. This study was carried out in accordance with the standards of the Declaration of Helsinki.

ADM Source and Preparation

We used the heterogeneous bovine ADM provided by Yantai Zhenghai Biotechnology, Ltd. The heterogeneous bovine ADM is a disposable sterile product measuring 2 cm × 2.5 cm or 4 cm × 3 cm; it is white, semi-translucent, shaped in cellular pieces and has rough and smooth sides. Before use, it is 3 times soaked and flushed with sterile saline.

Procedures

Maintaining a safety margin, patients with laryngeal and hypopharyngeal carcinoma underwent tumor resection; some patients underwent cervical lymph node dissection. We repaired laryngeal mucosal defects following verti...
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We repaired mucosal defects following anterior vertical partial laryngectomy using partial epiglottis + the heterogeneous bovine ADM. Mucosal defects following expanding vertical partial laryngectomy were repaired using piriform sinus mucosa + a platysma flap + the heterogeneous bovine ADM (fig. 1). We repaired mucosal defects following hypopharyngeal cancer resection along the lateral neck pathway or the lateral neck pathway and a tongue membrane pathway using (a) the heterogeneous bovine ADM or (b) pharyngeal mucosa + strap muscles + the heterogeneous bovine ADM. All patients underwent local compression of the laryngeal cavity with finger expansion for 7–10 days, followed by closure of the laryngeal cavity, suturing of the incision, and local pressure bandaging.

### Postoperative Treatment

All patients received second-generation (or above) cephalosporin antibiotics and received symptomatic and supportive treatment. Conventional nursing following throat surgery was also administered. 7 days post-surgery, the skin sutures were removed; the larynx expansion finger was removed at 7–10 days post-surgery, and the patients were required to eat soft food. All patients underwent electronic laryngoscopy review before discharge to observe the throat width of the larynx and the condition of the repairing mucosa. Patients with T3N1M0 and T3N2M0 disease and all patients with hypopharyngeal carcinoma received 60–75 Gy of radiotherapy.

### Results

The electronic laryngoscope review of 88 patients who had undergone stage I reconstruction revealed that, after 3–6 months, repaired mucosa had replaced the mucosal defects, subsequently recovering local function (fig. 2). Infection caused a laryngeal fistula in 3 cases and a pharyngeal fistula in 2 cases; the incidence rate was 5.4%. Successful tracheal extubation was performed for 86 patients; the extubation rate was 92.5%. The period from tracheotomy to extubation spanned 8–31 days (average, 10.4 days). The 1- and 2-year survival rates for patients with laryngeal carcinoma were 96.4% (54/56) and 80.0% (16/20), respectively. For patients with hypopharyngeal carcinoma, the 1- and 2-year survival rates were 88.2% (15/17) and 71.4% (5/7), respectively.

### Discussion

The ADM is essentially a natural extracellular matrix (ECM). The basic skeletal structure of the ADM is a collagen scaffold with a highly stable triple-helical structure, which, other than proteases, is generally decomposed by collagenases. Heterogeneous ADMs for clinical application are mainly obtained from mammalian dermis, such as cowhide, pigskin, etc. The immune responses induced by heterogeneous and allogeneic dermis mainly target epidermal cells, dermal fibroblasts, and endothelial cells. Therefore, the most important step in ADM preparation is to remove the cellular components, sweat glands, sebaceous glands, and type I and II histocompatibility antigens; the ECM of the dermis should be retained to maintain collagen morphology integrity and the basement membrane structure. As the antigen component has been removed completely, the ADM does not induce the rejection reactions induced by heterogeneous or allogeneic grafts [2].

### Table 1. Patient details (N = 93)

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Cases, n (%)</th>
<th>Tumor classification</th>
<th>Cases, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glottic</td>
<td>49 (52.7)</td>
<td>T1N0M0</td>
<td>5 (5.3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2N0M0</td>
<td>8 (8.6)</td>
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<tr>
<td></td>
<td></td>
<td>T3N0M0</td>
<td>25 (26.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T3N1M0</td>
<td>5 (5.3)</td>
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<tr>
<td></td>
<td></td>
<td>T3N2M0</td>
<td>6 (6.4)</td>
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<tr>
<td>Supraglottic</td>
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<td>T1N0M0</td>
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<td></td>
<td></td>
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<td>7 (7.5)</td>
</tr>
<tr>
<td>Hypopharyngeal</td>
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<td>T2N0M0</td>
<td>5 (5.3)</td>
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<tr>
<td></td>
<td></td>
<td>T3N0M0</td>
<td>4 (4.3)</td>
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<td></td>
<td>T3N1M0</td>
<td>9 (9.6)</td>
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<tr>
<td></td>
<td></td>
<td>T3N2M0</td>
<td>5 (5.3)</td>
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</tbody>
</table>

ADM for Repairing Mucosa in Reconstructive Surgery

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Fig. 1. Repair of mucosal defects following vertical partial laryngectomy. The mucosal defect and the ADM used in the reconstructive surgery are indicated.

Fig. 2. Electronic laryngoscope review 6 months post-surgery. The pharynx posterior wall, the ADM (‘repairing mucosa’), the left vocal cord, and the epiglottis are indicated.
In clinical applications, Heck et al. [3] in 1985 first carried out a burn treatment using an allogeneic dermis, and were successful. In 1993, Compton et al. [4] successfully produced an allogeneic ADM, greatly improving the success rate of allogeneic skin grafts. The allogeneic ADM provides a good scaffold for autologous endothelial cell and mesenchymal cell ingrowth and rapid vascularization. This scaffold forms a 3-dimensional framework and can be transplanted into the recipient site in the form of a cell scaffold, thereby guiding cell growth and angiogenesis and promoting tissue regeneration.

A large number of studies outside China found that the heterogeneous ADM causes no obvious irritation to the oral mucosa, submucosal tissue, fat, or muscle. There are also no dysplasia, hyperkeratosis or ulcers in the adjacent mucosa and no abnormal changes in the basal cells. However, connective tissue congestion, inflammatory cell infiltration, hemorrhage, and vascular dilation have been reported [5–8]. Nevertheless, other animal experiments have shown that a heterogeneous ADM repairing mucosa can be completely degraded within 6 months after implantation in the body, leaving no residue, and it does not affect the observation of postoperative recurrence [9, 10]. Accordingly, the important role of mucosa implantation in early tissue healing is confirmed, where it prevents the ingrowth of fibrous connective tissue, guides the structural arrangement of fibroblasts and new collagen, reduces scar formation and provides a protective barrier for epithelial cell migration and colonization, thereby enabling epithelial cell repair without inflammatory cell interference [7, 11].

Due to limitations of the material, the degree of contraction in the repairing mucosa should be noted during the surgery. The area of repair must be slightly larger than the area of mucosal defect. The mucosal edge of the wound should not be exposed and it should remain smooth. The ADM should be in proximity to the basal surface of the defect to reduce the formation of dead space, which is conductive to epithelial growth. The surface of the repairing mucosa is perforated using a scalpel to allow discharge of wound secretions. The finger expansion compresses the surface of the ADM, but we avoided too tight compression in fixation of the ADM to avoid affecting the blood supply to the repairing mucosa, which would have inhibited wound healing.

In conclusion, the heterogeneous bovine ADM has good biocompatibility and does not cause rejection reactions. When used in reconstructive surgery following resection for laryngeal and hypopharyngeal carcinoma, it acts as an early wound cover, promoting wound healing and reducing scar formation. In addition, the ADM is easy to maintain and is widely sourced and simple to use; therefore, it is recommended for widespread clinical application. As a retrospective analysis, our report has some limitations; nevertheless, our use of the ADM in reconstructive surgery following resection for laryngeal and hypopharyngeal carcinoma provides valuable information with regard to reconstructive surgery performed under similar conditions.

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Disclosure Statement

The authors declare that they have no conflicts of interest.