

# Comparison of xenogeneic acellular dermal matrix and skin grafts in reconstruction of postoperative defects of hypopharyngeal cancer

## A retrospective cohort study

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### Abstract

Successful reconstruction after tumor resection facilitates rapid recovery and retention of good quality of life, and this is important for a successful operation. This study aimed to analyze and compare the application and efficacy of xenogeneic acellular dermal matrix (xeno-ADM) and abdominal skin graft in hypopharynx reconstruction.

This is a retrospective cohort study that included 25 patients with posterior hypopharyngeal wall cancer who underwent partial hypopharyngectomy with laryngeal preservation. The patients were divided into 2 groups according to the repair materials used. Eleven patients were treated with xeno-ADM, and 14 patients with abdominal skin grafts for repairing hypopharyngeal mucosal defects. The intraoperative data, postoperative recovery time of eating function, graft contraction, infection and pharyngeal fistula rate, and 1-year survival rate of the 2 groups were analyzed and compared.

Compared with skin grafts group ( $23.1 \pm 5.8$  days), the recovery time of eating function in xeno-ADM group was shorter ( $17.3 \pm 6.4$  days), ( $P = .026$ ). Also the number of postoperative hospitalization days were less in the xeno-ADM group ( $18.5 \pm 6.7$  days) than in the skin grafts group ( $24.1 \pm 5.6$  days) ( $P = .035$ ). Besides, no significant differences were observed in other comparisons between the 2 groups. Also no obvious rejection and severe graft contraction were observed in both the groups. All patients were successfully decannulated.

Both xeno-ADM and abdominal skin grafts demonstrated good effects in the reconstruction of hypopharynx, but the recovery time of eating function in patients with xeno-ADM was faster, which may be due to rapid epithelialization. In addition, it avoids trauma of donor sites.

**Abbreviations:** ADM = acellular dermal matrix, xeno-ADM = xenogeneic acellular dermal matrix.

**Keywords:** hypopharyngeal cancer, postoperative defects, reconstruction, skin grafts, xenogeneic ADM

## 1. Introduction

Hypopharyngeal cancer is one of the most frequent malignancies of head and neck,<sup>[1,2]</sup> accounting for an incidence of about 1 case per 100,000 persons per year in the United States.<sup>[3]</sup> The 5-year survival rate varied from 30% to 60% based on the clinical stage of the patients.<sup>[1,2,4]</sup> For posterior hypopharyngeal wall cancer

that does not involve the larynx and esophageal entrance, both complete resection of tumor and laryngeal preservation can be achieved. However, during postoperative reconstruction of partial hypopharyngeal resection, large mucosal defects are often formed after tumor resection. The primary reconstruction methods, such as the pectoralis major myocutaneous flap, fasciocutaneous free flap, and jejunal free flap, are clinically verified and considered reliable.<sup>[5-7]</sup> However, the use of pedicled myocutaneous flap reconstruction is bulky at times and affects the function recovery of feeding.<sup>[8]</sup> Free flap reconstruction requires vascular anastomosis, which subsequently increases the operation time. In addition, the postoperative complications such as infection, flap necrosis, pharyngeal fistula, deformities, and dysfunctions at the donor site affect the postoperative recovery. Therefore, it is necessary to find a simple, non-invasive and well-recovered reconstruction method for surgical treatment of posterior hypopharyngeal wall cancer.

The hypopharynx is a canal covered with mucous membrane, and the ideal repair material should be equivalent to the thickness of hypopharyngeal wall, easy to obtain, easy to survive, simple to repair, and finally achieve mucosalization. The abdominal free skin graft met the above conditions. Before 2015, abdominal skin grafting is used for repairing the defects in patients with posterior hypopharyngeal wall cancer in our department, and obtained satisfactory results. However, it is still necessary to harvest your own skin, which in turn increases the operation time as well as the

Editor: Wen-Jun Tu.

The authors have no funding and conflicts of interest to disclose.

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How to cite this article: Zang J, Feng S, Yang H, Guo X. Comparison of xenogeneic acellular dermal matrix and skin grafts in reconstruction of postoperative defects of hypopharyngeal cancer: A retrospective cohort study. *Medicine* 2020;99:9(e19361).

Received: 25 September 2019 / Received in final form: 24 December 2019 / Accepted: 31 January 2020

<http://dx.doi.org/10.1097/MD.00000000000019361>

risk of donor complications. With the development of repair materials, xenogeneic acellular dermal matrix (xeno-ADM) has gradually replaced the abdominal skin graft for repairing mucosal defects in recent years, and achieved good results.

Acellular dermal matrix (ADM) is a scaffold that consists of collagen and extracellular matrix, which is derived from human skin tissue.<sup>[9]</sup> After transplantation, it can be used as a good scaffold for cell migration and neovascularization, achieving rapid epithelialization. With the emergence of xeno-ADM from mammals,<sup>[10]</sup> the limitations of donor sources and the possible ethical problems have been resolved, making it more widely used.<sup>[11–15]</sup> At the same time, due to its biological characteristics, it has been gradually used in the field of otorhinolaryngology. At present, the reported repair applications included nasal septum repair, tympanic membrane repair, external auditory canal plasty, tracheal repair, vocal cord repair, pharynx and larynx tumor postoperative defect repairs, etc.<sup>[10,16–20]</sup> However, there is no study till date that compared abdominal free skin graft and xeno-ADM in the reconstruction of hypopharyngeal defects.

Hence, we retrospectively observed and compared the application of xeno-ADM and abdominal skin grafting in the reconstruction of hypopharyngeal mucosal defects after partial hypopharyngectomy with larynx preservation. This study aimed to investigate the feasibility of 2 kinds of transplantation materials, and to provide a more optimal choice for postoperative reconstruction methods.

## 2. Materials and methods

### 2.1. Patients

This is a retrospective cohort study conducted in patients diagnosed with hypopharyngeal cancer and who underwent partial hypopharyngectomy in the department of Otolaryngology, The First Affiliated Hospital of China Medical University between May 2010 and November 2017. Patients were selected based on the following inclusion criteria:

- (1) the main part of the tumor should be located in the posterior hypopharyngeal wall, which might involve the lateral hypopharyngeal wall and the posterior oropharyngeal wall;
- (2) patients pathologically diagnosed with squamous cell carcinoma;
- (3) the tumors should not involve larynx and the laryngeal function should appear normal;
- (4) all patients should have undergone partial hypopharyngectomy with laryngeal preservation; and
- (5) postoperative adjuvant irradiation was performed in all patients, while no chemotherapy should be involved.

Exclusion criteria were as follows:

- (1) patients with stage T4 tumors;
- (2) patients with tumors of size more than 5 cm;
- (3) patients with secondary operation;
- (4) patients who underwent chemotherapy or preoperative radiotherapy; and
- (5) patients with esophageal involvement or distant metastasis and multiple cancerous lesions were excluded.

Repair was performed with abdominal skin grafting before 2015 and later with xeno-ADM. All patients signed the informed consent forms for operation and the use of xeno-ADM, and the

study was reviewed by the Ethics Committee of the First Affiliated Hospital of China Medical University.

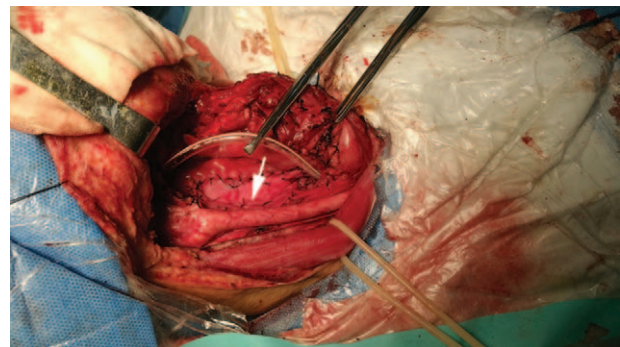
### 2.2. Repair material preparation

The xeno-ADM (bovine) was obtained from Zhenghai Biotechnology Co., Ltd. (Yantai, Shandong, China). The specifications of it were as follows: 4 cm × 6 cm, 6 cm × 8 cm, and thickness was 0.3 to 0.69 mm. It was divided into basement surface (UP surface) and dermal surface. Abdominal skin graft: the patient's abdominal full-thickness skin grafting was done based on the size of the intraoperative defect. For this, an appropriate skin graft was cut, and the abdominal donor site incision was sutured directly.

### 2.3. Surgical procedure and postoperative management

The patient was placed in supine position and given general anesthesia before undergoing surgery. The following surgical procedures were performed in patients:

- (1) the bilateral neck lymph node dissection was performed according to lymph node metastasis;
- (2) partial hypopharyngectomy: the tumor was fully exposed and completely resected under direct vision. The safety margin was set to 2 cm and was confirmed by intraoperative frozen pathology;
- (3) preparation of repair materials: the appropriate size of xeno-ADM graft was soaked in normal saline 3 times before use, with no less than 60 seconds each time. Both xeno-ADM and abdominal skin grafts are cut according to the size and shape of the defect and this requires punching of 2 to 3 small holes in the center and bottom to facilitate drainage to prevent hematoma or abscess;
- (4) repair methods: before repair, the wound surface was cleaned and disinfected repeatedly and bleeding was stopped completely. When repairing the posterior wall of the hypopharynx, the xeno-ADM graft was used to directly cover the prevertebral fascia of the posterior pharyngeal wall. The graft was intermittently sutured with the surrounding normal mucosa and fixed to the attached prevertebral fascia with the UP surface upward (Fig. 1). When the lateral wall of the hypopharynx was repaired, the posterior 1/3 of the lateral plate of the thyroid cartilage was removed together with the tumor, and the xeno-ADM graft was sutured to the residual



**Figure 1.** The hypopharyngeal defect has been covered and sutured by xeno-ADM graft (white arrow).

mucosa between the posterior hypopharyngeal wall and the piriform fossa. The inferior pharyngeal constrictor and the sternohyoid were sutured and fixed on the xeno-ADM graft for soft tissue support. The ipsilateral thyroid gland and superior thyroid vessels were then dissociated. Next, the gland was lifted up and fixed with pharyngeal inferior constrictor and sternohyoid to reinforce the lateral pharyngeal wall. The repair process of abdominal skin graft was similar to that of xeno-ADM;

- (5) postoperative treatment: negative pressure drainage was conducted and then covered with bandage under pressure for 7 days. The dressing was changed regularly and the postoperative wound recovery and the infection were observed, the drainage tube was removed when the daily drainage volume was less than 10ml, and antibiotics were used to prevent infection after operation (Ceftriaxone 1g each time, BID intravenous drip, 7–10 days).

After operation, intravenous nutrition was combined with gastrointestinal decompression and acid inhibitor for 5 to 7 days, which was then changed to nasogastric feeding. Oral food was given from 10 to 15 days after operation. Liquid diet with certain viscosity was given initially, followed by soft diet, and finally slowly transitioning to a normal diet. All patients were treated with conventional adjuvant irradiation at weeks 4 to 6 after operation, and the total dose was 60 to 66 Gy. All operations were performed by a doctor with senior professional post title and with more than 20 years of surgical experience.

#### 2.4. Postoperative observation and follow-up

The general data of patients, such as operation records, operative time, intraoperative blood loss, mucosal defect sizes, postoperative hospitalization time, drainage volume, infection, and pharyngeal fistula were obtained by reviewing the medical records during hospitalization. At 1 month, 2 months, 3 months, 6 months, and 1 year postoperatively, the outpatient records and electronic laryngoscope were used to observe and record the recovery time of eating function and grafting. When the graft is eventually replaced by a smoother mucosa-like tissue, then it is considered as successful epithelialization. The recovery of eating function is

defined as smooth oral feeding without any dysphagia or coughing and able to achieve all nutritional needs without a gastrogavage. Recurrence and metastasis were confirmed by electronic laryngoscope, CT scan, and pathological biopsy. Graft contraction was also confirmed by electronic laryngoscope. Mild-to-moderate contraction was defined as grafting that does not affect respiration and eating, and able to remove the tracheotomy cannula and nasogastric feeding tube in a short period of time or gradually over a period of time. In contrast, severe contraction or stenosis hinders respiration and oral feeding and cannot decannulate successfully. The assessment of preoperative and postoperative data of all patients was completed by the same observer.

#### 2.5. Statistical analysis

SPSS 22.0 (SPSS, Chicago, IL) was used to analyze the data. The quantitative variables were presented as ( $\bar{x} \pm SD$ ). *T* test and Mann–Whitney *U* test were used to compare these variables. The qualitative data were presented as n (%) and analyzed by Fisher's accurate test.  $P < .05$  two-tailed test was considered to be statistically significant.

### 3. Results

#### 3.1. Patient demographics

A total of 28 patients were eligible for inclusion in this study over a 7-year period, of which 25 well-documented patients were selected and divided into 2 groups according to the repair materials used. In the xeno-ADM group, 11 patients (including 10 males and 1 female, aged between 46 and 76 years, with an average age of  $60.2 \pm 8.6$  years) were treated with xeno-ADM for repairing the hypopharyngeal wall defects. In the skin graft group, 14 patients, all male, were treated with abdominal skin graft, and their age ranged from 41 to 71 years, with average age being  $58.0 \pm 8.4$  years. TNM staging was done according to the staging system of 2009 Union for International Cancer Control (UICC) criteria. Patients in xeno-ADM group included T2N0M0, 3; T2N1M0, 1; T2N2M0, 2; T3N0M0, 1; T3N1M0, 2; and T3N2M0, 2. Patients in skin graft group included T2N0M0, 4; T2N1M0, 2; T2N2M0, 2; T3N0M0, 2; T3N1M0, 3; and T3N2M0, 1. The specific clinical data regarding the subjects are shown in Table 1.

**Table 1**

**Comparative analysis of general data and postoperative data of patients in the 2 groups.**

Characteristics	Xeno-ADM group	Skin graft group	<i>P</i>
Patients, n	11	14	
Age (yr)	$60.2 \pm 8.6$ (46–76)	$58.0 \pm 8.4$ (41–71)	.529
Sex	Male 10/Female 1	Male 14	.440
Stage			
T2	6 (54.6%)	8 (57.1%)	1.000
T3	5 (45.5%)	6 (42.9%)	
Maximum diameter of defect size (cm)	$7.1 \pm 1.0$ (5.2–8.6)	$6.9 \pm 0.9$ (5.4–8.5)	.662
Operative time (h)	$6.5 \pm 1.3$	$7.4 \pm 1.4$	.108
Intraoperative blood loss (ml)	$389.1 \pm 83.6$	$432.9 \pm 96.0$	.244
Infection with pharyngeal fistula	1 (9.1%)	1 (7.1%)	1.000
Postoperative drainage volume (ml)	$409.3 \pm 147.5$ (200–720)	$353.6 \pm 130.4$ (185–608)	.327
Recovery time of eating (d)	$17.3 \pm 6.4$ (13–36)	$23.1 \pm 5.8$ (18–41)	.026
Postoperative hospitalization days	$18.5 \pm 6.7$ (15–38)	$24.1 \pm 5.6$ (20–42)	.035
Mild-to-moderate contraction	4 (36.4%)	3 (21.4%)	.656
1-yr survival rate	90.9%	85.7%	1.000

The quantitative variables were expressed as ( $\bar{x} \pm SD$ ), and comparison between them was carried out by *t* test and Mann–Whitney *U* test according to whether the normal distribution was satisfied or not, and the qualitative data were analyzed by Fisher's accurate test.  $P < .05$  was considered to be statistically significant. Recovery time of eating means the time for removing nasal feeding tube. This study focused on defects repair, and so only T-stages that are related to tumor size were compared between the 2 groups.



### 3.2. Postoperative datas of the 2 groups

Postoperative follow-up time was 8 to 12 months in the skin graft group and 10 to 12 months in the xeno-ADM group. All repair materials survived in both groups, and no adverse reactions such as rejection were found. In the abdominal skin graft group, the donor site was well healed and no infections occurred. From Table 1, it can be deduced that there were no significant differences in age, sex, tumor stage, and maximum diameter of defects between the 2 groups. Also no significant differences were observed in the operative time, intraoperative blood loss, and total postoperative drainage between the 2 groups. However, the recovery time of postoperative eating function and postoperative hospitalization days in the xeno-ADM group were shorter than that in the skin graft group, and showed statistically significant differences (Table 1). One patient in each group had infection with pharyngeal fistula, which was cured after long-term dressing change, and the recovery time of eating function was 36 days (the xeno-ADM group) and 41 days (the skin graft group), respectively. After excluding the infected cases, the recovery time of eating function in both groups was  $15.4 \pm 1.4$  days (the xeno-ADM group) and  $21.7 \pm 2.7$  days (the skin graft group), respectively. Statistically significant differences were still observed between the 2 groups ( $P = .000$ ). There was no local recurrence in both groups within 1 year after operation. In xeno-ADM group, 1 patient had cervical lymph node metastasis and 1 patient had distant lung metastasis within 1 year after operation, and 1 patient died due to distant lung metastasis within 1 year. In the skin graft group, 2 patients had cervical lymph node metastasis within 1 year after operation, and 1 of them died within a year. In addition, 1 patient died due to myocardial infarction within 1 year in the skin graft group.

### 3.3. Laryngoscopy findings

Laryngoscope examination 1 month after operation revealed that the xeno-ADM graft was fused well with the repair area, which was similar to the reddish appearance of the surrounding mucosa, and with a thin layer of white pseudomembrane was attached to the repair area surface. Only local sutures and granulation were seen. Most of the xeno-ADM graft was close to epithelialization. At 2 months after operation, the xeno-ADM graft was basically replaced by a smooth mucosa-like tissue, considering it as epithelialized xeno-ADM membrane, and a small amount of granulation residue was seen locally. At 3 months, the appearance of the repair area showed no significant differences with that of the surrounding mucosa, and no traces of repair could be seen (Fig. 2). At 1 month postoperatively, laryngoscope showed that the skin graft was not completely fused with the covered repair area, and a thick white pseudomembrane was attached to the surface, showing granulation at the edge. The epithelialization was basically completed at 2 months, but the surface was not smooth, and was similar to that of white keratosis layer. At 3 months after operation, the surface of the repair area was smooth and showed complete epithelialization, but the repair surface was still different from the surrounding mucosa. The repair marks were still visible (Fig. 3). The whole laryngeal and hypopharyngeal mucosa showed swelling at varying degrees during postoperative adjuvant irradiation, but the swelling was gradually subsided and the mucosa returned to normal after radiotherapy. There was a mild-to-moderate contraction at the repair area in some patients of both groups, with 4 patients in the xeno-ADM group and 3 patients in the skin

graft group at 6 months postoperatively, but showed no significant differences between them. All patients were successfully decannulated finally.

### 3.4. Cost comparison

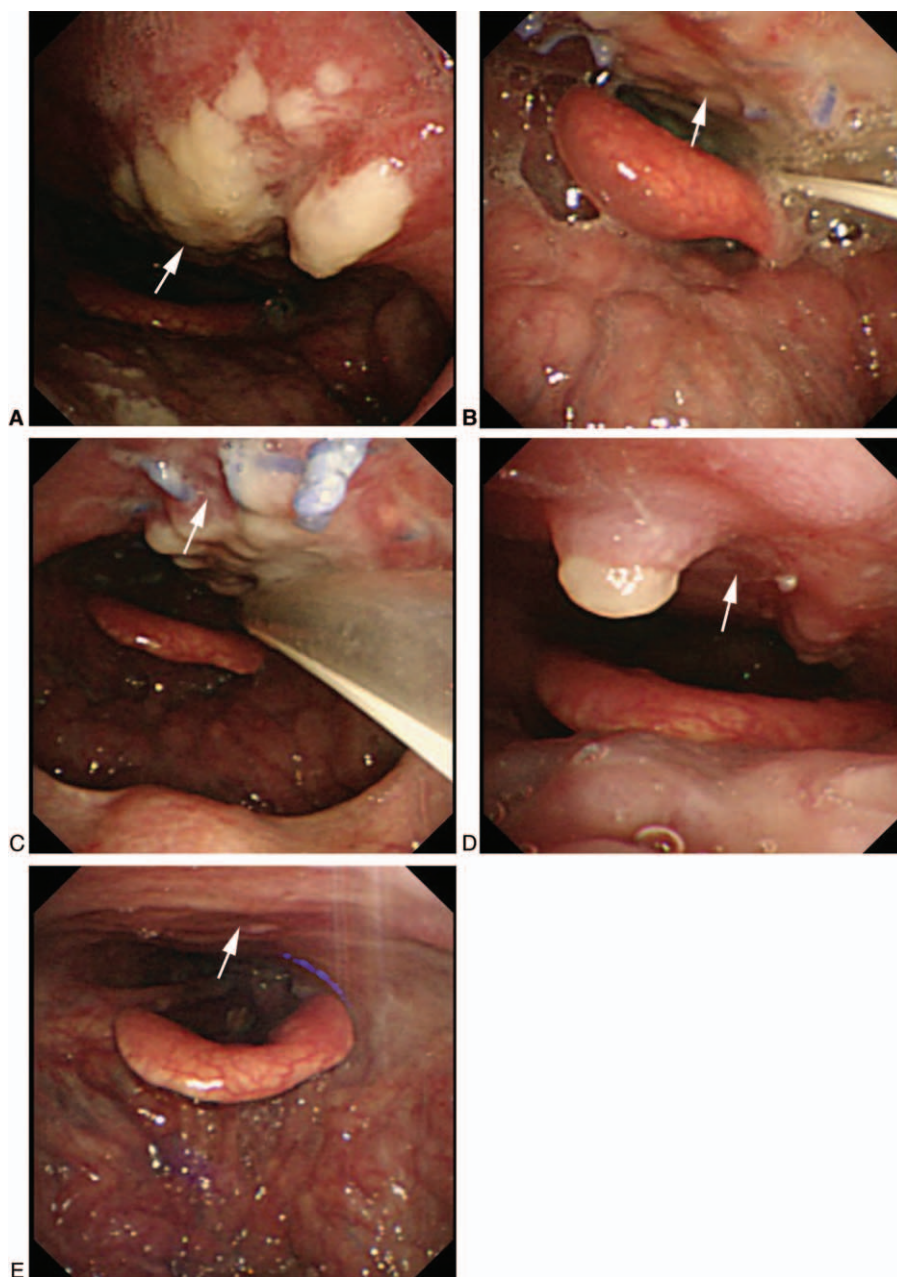
We compared the costs of the 2 groups. Although the xeno-ADM group has to pay for the product cost, the skin grafts group needs to pay for the additional surgical fee for skin graft harvest, as well as the costs of donor site dressing changes and additional hospitalization days. Overall, the average cost of the xeno-ADM group was 3.6% more than that of the skin grafts group. But the intangible costs, such as pain and scarring of donor site, were not included.

## 4. Discussion

The survival rate of patients with hypopharyngeal cancer is not ideal, and so it is very important to avoid or reduce the impact of it on the quality of life regardless of treatment plan.<sup>[21]</sup> For hypopharyngeal posterior wall cancer, the thickness of the defect area is often not thick. However, if traditional reconstruction methods like pedicled flap or free flap are used, in addition to the injury of donor sites and possible risks of infection and pharyngeal fistula, it sometimes appears bulky, affecting the eating and increasing the recovery time after surgery. In this study, abdominal skin graft and xeno-ADM graft were used for the repair of mucosal defects of partial hypopharyngectomy, making up for the above shortcomings and simplifying the operation process. The 2 repair materials had good histocompatibility with the tissue at the repair area, and covered the wound area to effectively protect it and help it to epithelialize.

Joo et al have reported reconstruction of hypopharynx by fasciocutaneous free flap in 48 consecutive patients. The results revealed that the average time to achieve oral re-alimentation was 23.0 days postoperatively.<sup>[22]</sup> In this study, the average recovery time of eating function in the 2 groups was 17.3 days and 23.1 days, respectively. This meant that the xeno-ADM graft was conducive in restoring eating function, and assists in quickly restoring the postoperative quality of life. The recovery time of eating function in xeno-ADM group was faster than that in skin graft group. This was similar to the results of the study by Girod et al, in which he demonstrated better recovery of social eating function of ADM when compared to the efficacy of split skin graft during oral mucosal repair.<sup>[23]</sup> The reason for this might be that the postoperative epithelialization time of xeno-ADM was shorter, and its unique three-dimensional network structure of collagen can be used as a scaffold to guide the migration and growth of host cells in an orderly manner and for rapid vascularization. The graft can be fused with the surrounding tissue in the early stage, and the defect can be repaired quickly and effectively.<sup>[24,25]</sup> This is also confirmed by laryngoscope examination at different time points postoperatively in this study. At 1 month after operation, a large part of the repair area in xeno-ADM group was nearly epithelialized, but it was still covered with a thick white pseudomembrane in the skin graft group.

One patient had infection of pharyngeal fistula in both the groups in this study. Their hospitalization days, drainage volume, and recovery time of eating function were significantly higher than other patients, and so the effective control of infection after operation has great impact on the success rate of reconstruction. The incidence of pharyngeal fistula ranged from 7% to 26% in

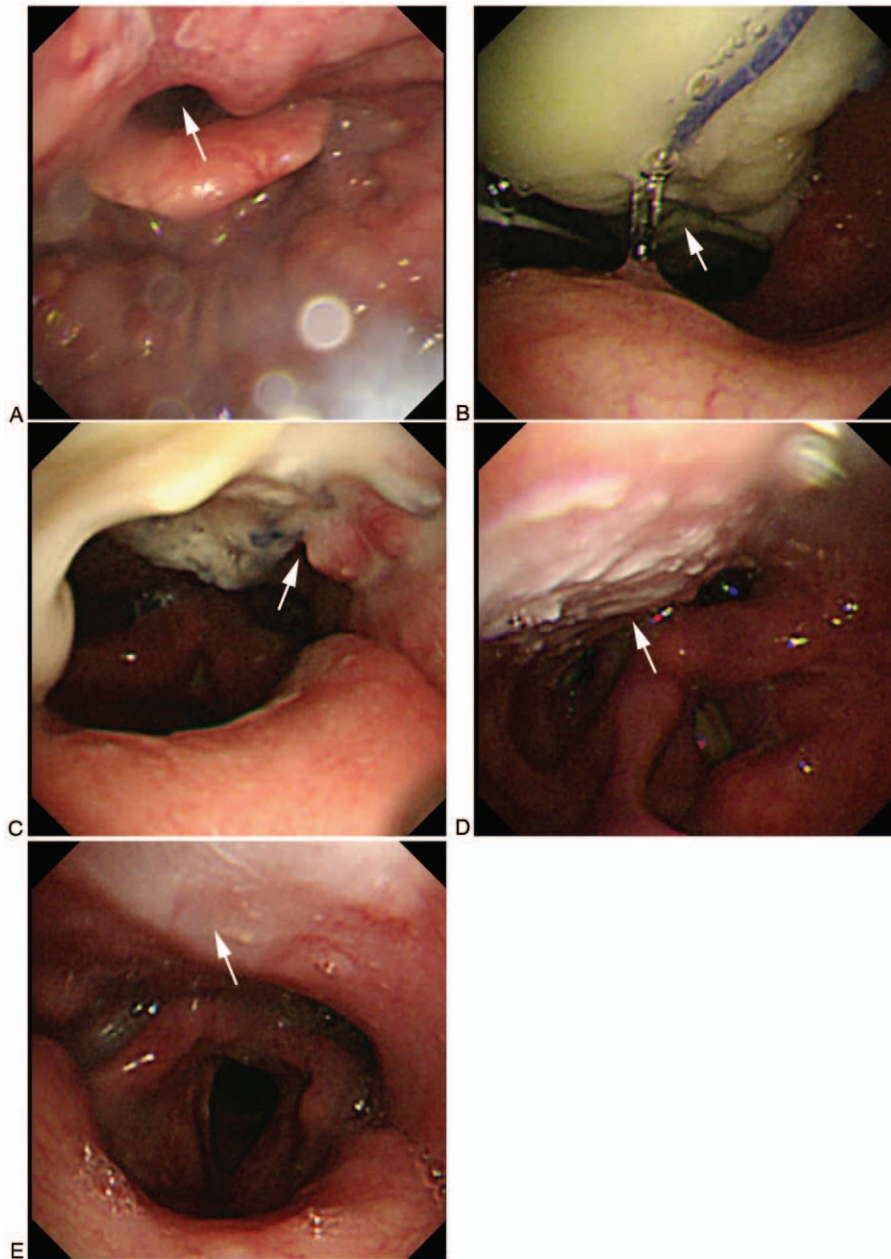


**Figure 2.** A case of a hypopharyngeal defect repaired with xenogeneic ADM graft was examined by electronic laryngoscope at different time points before and after operation. The hypopharyngeal cancer (*white arrow*) is located in the posterior hypopharyngeal wall, spreading upwards to the posterior oropharyngeal wall (A). At 1 mo after surgery, xeno-ADM graft (*white arrow*) showed well fusion with the repair area, and appeared red as the surrounding mucosa. A thin white pseudomembrane was attached to the surface (B), and then the sutures and spot granulation (*white arrow*) were seen locally (C). At 2 mo postoperatively, the xeno-ADM graft (*white arrow*) was basically replaced by smooth mucosa-like tissue, but a small amount of granulation has remained locally (D). At 3 mo, there was no significant difference between the appearance of the repair area (*white arrow*) and the surrounding mucosa, and no traces of repair were observed (E).

flap based reconstruction methods.<sup>[5-7]</sup> The incidence of pharyngeal fistula in both the groups was 7.1% and 9.1%, respectively, which was at a low level in this study. This indicated that the use of the 2 grafts did not increase the adverse conditions and risks of postoperative infection as well as pharyngeal fistula. Of course, prevention of infection and pharyngeal fistula involves multiple factors. Active adjustment of nutritional status, control of blood glucose levels, targeted use of antibiotics, strengthening of oral care, adherence to nasal feeding diet without premature oral intake are all considered to be very important during the

perioperative period. In addition, gastrointestinal decompression and intravenous nutrition for a period of time after operation could effectively reduce the irritation of gastric juice reflux to wound transplantation materials, and strengthen the whole body nutrition support at the same time. In addition, ADM graft also plays a role in resisting bacterial invasion.<sup>[26]</sup>

There is no severe contraction and stenosis. Some patients in both the groups had mild-to-moderate contraction at the repair area at 6 months after operation, but did not affect the normal function, eventually removing the tracheotomy cannula and



**Figure 3.** An individual with hypopharyngeal defect who underwent repair with abdominal skin graft was examined by electronic laryngoscope at different time points before and after operation. The hypopharyngeal cancer (*white arrow*) is mainly located in the posterior wall of the hypopharynx and has spread upwards till the posterior wall of the oropharynx (A). At 1 mo after operation, the abdominal skin graft (*white arrow*) still showed an incomplete fusion with the repair area, and a thick white pseudomembrane was attached to the surface (B), granulation and sutures (*white arrow*) could be seen at the edge (C). Epithelialization was basically completed at 2 mo, but the surface (*white arrow*) was not smooth and visible like a white keratinized layer (D). At 3 mo after operation, the surface of the repair area (*white arrow*) was smooth and showed complete epithelialization, but the color of the repair surface remained white, which was still different from that of the surrounding mucosa (E).

nasogastric feeding tube. This was also consistent with the results of other previous studies on ADM repair.<sup>[27,28]</sup> The reason for this might be that the ADM retains collagen fibers, elastic fibers, and reticular fibers in the original dermis, forming the material basis for soft texture, lighter contraction, and lighter color change after the survival of ADM graft.<sup>[29]</sup>

It is important to choose appropriate indication and the correct reconstruction method for application of xeno-ADM graft. Xeno-ADM is a membranous structure that lacked tissue support and filling, and its survival requires a good blood supply of

transplanted bed. Therefore, for massive resection of tumor with cervical fusion, the use of xeno-ADM repair was not recommended. In addition, when the tumor involves esophageal entrance or post-cricoid area, then pedicled myocutaneous flap, free flap or jejunal free flap was used to avoid the risk of reconstructed cervical esophageal stenosis caused by necrosis of xeno-ADM graft due to lack of blood supply. However, some scholars have reported that xeno-ADM graft can be used in combination with pectoralis major myocutaneous flap for reconstruction in the above situation.<sup>[30,31]</sup>



In this study, there was no statistical significance with regard to operative time and intraoperative bleeding volume in both the groups. The main reason for this is that each case involves different cervical lymph node metastasis and differences in surgical difficulties due to individual differences, resulting in a lot of interferential factors for statistical comparison of operation time and bleeding volume. However, for the same patient, the reconstruction process using xeno-ADM and abdominal skin graft remained the same, but the abdominal skin graft required additional time to obtain and subsequent suturing of the donor area, increasing the operation time and bleeding volume. Obviously, the use of xeno-ADM saves time and reduces blood loss, which is also supported by the conclusions of other previous studies.<sup>[27,30]</sup> In this study, the survival and recurrence rates within 1 year after operation were evaluated, and the results revealed that no patients had local recurrence in both groups. We believed that a good and sufficient repair material was conducive for adequate resection of lesions and ensure adequate safety of margins during operation. This in turn reduces the recurrence of tumors after operation, and remains beneficial to the survival rate despite of the factors affecting the survival rate, including tumor size, pathological classification, clinical stage, lymph node metastasis and so on, is complicated.

Although the average cost of the xeno-ADM group is 3.6% higher than that of the skin grafts group, considering the influence of donor site pain and scarring on quality of life, we believe that the additional cost is worth it.

## 5. Conclusions

These findings demonstrated that xeno-ADM graft and abdominal skin graft have good effects in hypopharyngeal reconstruction after partial hypopharyngectomy with laryngeal preservation. Both these methods simplified the operation process and solved the problems of bulky tissue after reconstruction, which are conducive for the recovery of eating function and reduce postoperative infection as well as scar contraction. Compared with abdominal skin graft, xeno-ADM showed faster epithelization, shorter recovery time of eating function and shorter hospitalization days. This also saved the time of obtaining skin graft, avoided trauma of the donor site and alleviated the pain of the patients. In addition, xeno-ADM has sufficient sources and is easy to use. It reduces the concern of reconstruction problems in tumor resection, removing the tumor as fully as possible, and this in turn would be helpful in reducing local tumor recurrence. However, this was a retrospective small-sample size study. So, a large-sample, long-term follow-up period, prospective study is still needed in the future to confirm these findings.

## Author contributions

**Conceptualization:** Jian Zang, Xing Guo.

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**Supervision:** Xing Guo.

**Writing – original draft:** Jian Zang.

**Writing – review & editing:** Jian Zang, Xing Guo.

## References

- [1] Carvalho AL, Nishimoto IN, Califano JA, et al. Trends in incidence and prognosis for head and neck cancer in the United States: a site-specific analysis of the SEER database. *Int J Cancer* 2005;114:806–16.
- [2] Cooper JS, Porter K, Mallin K, et al. National Cancer Database report on cancer of the head and neck: 10-year update. *Head Neck* 2009;31:748–58.
- [3] Kuo P, Chen MM, Decker RH, et al. Hypopharyngeal cancer incidence, treatment, and survival: temporal trends in the United States. *Laryngoscope* 2014;124:2064–9.
- [4] Pracy P, Loughran S, Good J, et al. Hypopharyngeal cancer: United Kingdom National Multidisciplinary Guidelines. *J Laryngol Otol* 2016;130(S2):S104–10.
- [5] Piazza C, Bon FD, Paderno A, et al. Fasciocutaneous free flaps for reconstruction of hypopharyngeal defects. *Laryngoscope* 2017;127:2731–7.
- [6] Cristalli G, Pellini R, Roselli R, et al. Pectoralis major myocutaneous flap for hypopharyngeal reconstruction: long-term results. *J Craniofac Surg* 2011;22:581–4.
- [7] Miyamoto S, Sakuraba M, Asano T, et al. Free jejunal patch graft for reconstruction after partial hypopharyngectomy with laryngeal preservation. *Arch Otolaryngol – Head Neck Surg* 2011;137:181–6.
- [8] 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.
- [9] Takami Y, Yamaguchi R, Ono S, et al. Clinical application and histological properties of autologous tissue-engineered skin equivalents using an acellular dermal matrix. *J Nippon Med Sch = Nippon Ika Daigaku zasshi* 2014;81:356–63.
- [10] Hui A, Hong P, Bezuhly M. Use of acellular dermal matrices in laryngotracheal and pharyngeal reconstruction: systematic review. *J Laryngol Otol* 2017;131:585–92.
- [11] Shahrokhi S, Arno A, Jeschke MG. The use of dermal substitutes in burn surgery: acute phase. *Wound Repair Regen* 2014;22:14–22.
- [12] Sodha NR, Azoury SC, Sciortino C, et al. The use of acellular dermal matrices in chest wall reconstruction. *Plast Reconstr Surg* 2012;130(Suppl 2):175S–82S.
- [13] Levin F, Turbin RE, Langer PD. Acellular human dermal matrix as a skin substitute for reconstruction of large periocular cutaneous defects. *Ophthalmic Plast Reconstr Surg* 2011;27:44–7.
- [14] Zhang B, Li J, Sarma D, et al. The use of heterogeneous acellular dermal matrix in the closure of hard palatal fistula. *Int J Pediatr Otorhinolaryngol* 2014;78:75–8.
- [15] Jansen LA, De Caigny P, Guay NA, et al. The evidence base for the acellular dermal matrix AlloDerm: a systematic review. *Ann Plast Surg* 2013;70:587–94.
- [16] Chhabra N, Houser SM. Endonasal repair of septal perforations using a rotational mucosal flap and acellular dermal interposition graft. *Int Forum Allergy Rhinol* 2012;2:392–6.
- [17] Evans MA, Sugihara EM, Chan EY. Acquired external auditory canal atresia: a comparison of acellular dermal matrix and split-thickness skin grafting techniques. *Otol Neurotol* 2017;38:1149–52.
- [18] Min J, Kim SH. Comparison of transcanal endoscopic tympanoplasty with sterile acellular dermal allograft to conventional endaural microscopic tympanoplasty with tragal perichondrium. *Am J Otolaryngol* 2018;39:167–70.
- [19] Li P, Li S, Tang Q, et al. Reconstruction of human oncological tracheal defects with xenogenic acellular dermal matrix. *Auris Nasus Larynx* 2017;44:237–40.
- [20] Liang Q, Liu S, Han P, et al. Micronized acellular dermal matrix as an efficient expansion substrate and delivery vehicle of adipose-derived stem cells for vocal fold regeneration. *Laryngoscope* 2012;122:1815–25.
- [21] Newman JR, Connolly TM, Illing EA, et al. Survival trends in hypopharyngeal cancer: a population-based review. *Laryngoscope* 2015;125:624–9.
- [22] Joo YH, Sun DI, Cho KJ, et al. Fasciocutaneous free flap reconstruction for squamous cell carcinoma of the hypopharynx. *Eur Arch Oto-rhino-laryngol: Off J European Federation of Oto-Rhino-Laryngological Societies (EUFOS): affiliated with the German Society for Oto-Rhino-Laryngology – Head Neck Surg* 2011;268:289–94.

- [23] Girod DA, Sykes K, Jorgensen J, et al. Acellular dermis compared to skin grafts in oral cavity reconstruction. *Laryngoscope* 2009;119:2141–9.
- [24] Carruthers CA, Dearth CL, Reing JE, et al. Histologic characterization of acellular dermal matrices in a porcine model of tissue expander breast reconstruction. *Tissue Eng A* 2015;21:35–44.
- [25] Sahin I, Ozturk S, Deveci M, et al. Experimental assessment of the neovascularisation of acellular dermal matrix in the wound bed pretreated with mesenchymal stem cell under subatmospheric pressure. *J Plast Reconstr Aesthet Surg* 2014;67:107–14.
- [26] Fahrenbach EN, Qi C, Ibrahim O, et al. Resistance of acellular dermal matrix materials to microbial penetration. *JAMA Dermatol* 2013;149:571–5.
- [27] Li P, Li S, Yang X, et al. Application of xenogenic acellular dermal matrix in reconstruction of oncological hypopharyngeal defects. *Eur Arch Oto-rhino-laryngol: Off J European Federation of Oto-Rhino-Laryngological Societies (EUFOS): affiliated with the German Society for Oto-Rhino-Laryngology – Head Neck Surg* 2016;273:4391–6.
- [28] Shi LJ, Wang Y, Yang C, et al. Application of acellular dermal matrix in reconstruction of oral mucosal defects in 36 cases. *J Oral Maxillofac Surg* 2012;70:e586–91.
- [29] Askari M, Cohen MJ, Grossman PH, et al. The use of acellular dermal matrix in release of burn contracture scars in the hand. *Plast Reconstr Surg* 2011;127:1593–9.
- [30] Zhang L, Cheng JP, Zhang WC, et al. Reconstruction of defects following surgery for hypopharyngeal carcinoma using artificial biological material. *Acta Otolaryngol* 2010;130:1293–9.
- [31] Yin D, Tang Q, Wang S, et al. Xenogeneic acellular dermal matrix in combination with pectoralis major myocutaneous flap reconstructs hypopharynx and cervical esophagus. *Eur Arch Oto-rhino-laryngol: Off J European Federation of Oto-Rhino-Laryngological Societies (EUFOS): affiliated with the German Society for Oto-Rhino-Laryngology – Head Neck Surg* 2015;272:3457–61.