**Name of Journal:** *World Journal of Gastrointestinal Endoscopy*

**Manuscript NO:** 87280

**Manuscript Type:** ORIGINAL ARTICLE

***Prospective Study***

**New hope for esophageal stricture prevention: A prospective single-center trial on acellular dermal matrix**

Fu XY *et al*. New hope for esophageal stricture prevention

Xin-Yu Fu, Zhen-Yu Jiang, Chen-Yang Zhang, Ling-Yan Shen, Xiao-Dan Yan, Xiao-Kang Li, Jia-Ying Lin, Yi Wang, Xin-Li Mao, Shao-Wei Li

**Xin-Yu Fu, Chen-Yang Zhang, Jia-Ying Lin,** Department of Gastroenterology, Taizhou Hospital of Zhejiang Province, Wenzhou Medical University, Linhai 317000, Zhejiang Province, China

**Zhen-Yu Jiang,** Department of Gastroenterology, The Second Affiliated Hospital of Baotou Medical College, Inner Mongolia University of Science and Technology, Baotou 014000, Inner Mongolia Autonomous Region, China

**Ling-Yan Shen, Xiao-Dan Yan, Yi Wang, Xin-Li Mao, Shao-Wei Li,** Department of Gastroenterology, Taizhou Hospital of Zhejiang Province Affiliated to Wenzhou Medical University, Linhai 317000, Zhejiang Province, China

**Xiao-Kang Li, Shao-Wei Li,** Key Laboratory of Minimally Invasive Techniques & Rapid Rehabilitation of Digestive System Tumor of Zhejiang Province, Taizhou Hospital of Zhejiang Province Affiliated to Wenzhou Medical University, Linhai 317000, Zhejiang Province, China

**Xiao-Kang Li,** Division of Transplantation Immunology, National Research Institute for Child Health and Development, Tokyo 1540001, Japan

**Shao-Wei Li,** Institute of Digestive Disease, Taizhou Hospital of Zhejiang Province Affiliated to Wenzhou Medical University, Linhai 317000, Zhejiang Province, China

**Co-first authors:** Xin-Yu Fu and Zhen-Yu Jiang.

**Co-corresponding authors:** Shao-Wei Li and Xin-Li Mao.

**Author contributions:** Fu XY, Zhang CY, Lin JY, Yan XD, Li XK, Wang Y, and Mao XL participated in the design of the study and performed the statistical analysis; Fu XY, Jiang ZY, Zhang CY, Lin JY, and Li SW drafted the manuscript. All authors read and approved the final manuscript.

**Supported by** Medical Health Science and Technology Project of Zhejiang Province, No. 2021PY083, 2019KY239; Program of Taizhou Science and Technology Grant, No. 23ywa33; Major Research Program of Taizhou Enze Medical Center Grant, No. 19EZZDA2; Open Fund of Key Laboratory of Key Laboratory of Minimally Invasive Techniques & Rapid Rehabilitation of Digestive System Tumor of Zhejiang Province, No. 21SZDSYS01 and No. 21SZDSYS09; Program of Taizhou Enze Medical Center Grant, No. 22EZD06.

**Corresponding author: Shao-Wei Li, PhD, Associate Professor,** Department of Gastroenterology, Taizhou Hospital of Zhejiang Province Affiliated to Wenzhou Medical University, No. 150 Xinmen Street, Linhai 317000, Zhejiang Province, China. li\_shaowei81@hotmail.com

**Received:** August 5, 2023

**Revised:** October 22, 2023

**Accepted:** November 3, 2023

**Published online:** December 16, 2023

**Abstract**

BACKGROUND

Given the high incidence of esophageal cancer in China, an increasing number of patients there are undergoing endoscopic mucosal dissection (ESD). Although the 5-year survival rate after ESD can exceed 95%, esophageal stricture, the most common and serious postoperative complication, affects the long-term prognosis of patients and the quality of life. Autologous mucosal grafts have proven to be successful in preventing stricture after ESD for early esophageal cancer.

AIM

To examine the viability of acellular dermal matrix (ADM) as an alternative to autologous mucosa for the prevention of stricture after ESD.

METHODS

This is a prospective, single-center, controlled study. Consecutive patients who underwent ESD surgery and were willing to undergo autologous mucosal transplantation were recruited between January 1 and December 31, 2017. Consecutive patients who underwent ESD surgery and were willing to undergo ADM transplantation were recruited between January 1 to December 31, 2019. A final three-year follow-up of patients who received transplants was conducted.

RESULTS

Based on the current incidence of esophageal stricture, the sample size required for both the autologous mucosal graft group and the ADM group was calculated to be 160 cases. Due to various factors, a total of 20 patients with autologous mucosal grafts and 25 with ADM grafts were recruited. Based on the inclusion exclusion and withdrawal criteria, 9 patients ultimately received autologous mucosal grafts and completed the follow-up, while 11 patients received ADM grafts and completed the follow-up. Finally, there were 2 cases of stenosis in the autologous mucosal transplantation group with a stenosis rate of 22.22% and 2 cases of stenosis in the ADM transplantation group with a stenosis rate of 18.18%, with no significant difference noted between the groups (*P* = 0.94).

CONCLUSION

In this prospective, single-center, controlled trial, we compared the effectiveness of autologous mucosa transplantation and ADM for the prevention of esophageal stricture. Due to certain condition limitations, we were unable to recruit sufficient subjects meeting our target requirements. However, we implemented strict inclusion, exclusion, and withdrawal criteria and successfully completed three years of follow-up, resulting in valuable clinical insights. Based on our findings, we hypothesize that ADM may be similarly effective to autologous mucosal transplantation in the prevention of esophageal stricture, offering a comparable and alternative approach. This study provides a new therapeutic idea and direction for the prevention of esophageal stricture.

**Key Words:** Over-the-scope clip; Duodenal subepithelial lesion; Endoscopic resection; Perforation

**©The** **Author(s) 2023.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Citation:** Fu XY, Jiang ZY, Zhang CY, Shen LY, Yan XD, Li XK, Lin JY, Wang Y, Mao XL, Li SW. New hope for esophageal stricture prevention: A prospective single-center trial on acellular dermal matrix. *World J Gastrointest Endosc* 2023; 15(12): 725-734

**URL:** <https://www.wjgnet.com/1948-5190/full/v15/i12/725.htm>

**DOI:** https://dx.doi.org/10.4253/wjge.v15.i12.725

**Core Tip:** Preventing esophageal stricture after endoscopic submucosal dissection (ESD) is a critical challenge in the successful treatment of early esophageal cancer. Acellular dermal matrix (ADM) has recently emerged as a potential solution. This study showed that the preventive effect of ADM on esophageal stricture was comparable to that of autologous mucosa. Despite the study's limited sample size, it includes improved postoperative follow-up and holds clinical significance. The results validate ADM as a viable alternative for preventing esophageal stricture. These findings will potentially revolutionize ESD treatment for early esophageal cancer and provide safer and more accessible options for such patients.

**INTRODUCTION**

With the maturity of endoscopic technology, endoscopic submucosal dissection (ESD) can now be used to remove large lesions and ensure a negative margin to the greatest extent[1], making it the preferred treatment for early esophageal cancer. Esophageal stricture is one of the most common and serious complications after ESD, with an incidence of approximately 37%-92%[2]. Its incidence is affected by many factors, mainly including mucosal resection > 3/4 of the esophagus circumference[3], resection length > 30 mm, muscular propria injury, and deep resection depth[4].

Among these factors, the one most closely related to the incidence of stenosis was found to be the scope of resection. According to reports, the incidence of stenosis in mucosal resection > 3/4 cases is 60%-100%, while the stenosis rate in near-total resection can reach 88%-100%[5]. Patients with esophageal stenosis may have varying degrees of dysphagia in more stenotic cases. In severe cases, nausea and vomiting may occur after eating, resulting in long-term insufficiency in the nutritional intake, water and electrolyte imbalance, cachexia, and even fatal inhalation[6,7], seriously affecting the long-term quality of life of patients. Furthermore, in severe cases, repeated endoscopic esophageal dilation or even surgical intervention may be required[8]. This increases the financial, physical, and psychological burden on patients. How to prevent esophageal stricture safely and effectively is thus a key issue influencing the ESD-based treatment of early esophageal cancer.

At present, the commonly used measures to prevent stenosis are mainly local or systemic applications of glucocorticoids[9]. After the application of hormones, the overall incidence of esophageal stricture was 13.5%, thus effectively reducing the incidence of esophageal stricture[6,10]. However, there is a risk of local esophageal perforation or secondary fatal infection, and some patients are contraindicated for hormone application due to their condition, so hormone therapy cannot be used to prevent stricture in all cases.

With the advent of autologous mucosal transplantation technology, relevant studies have explored the effectiveness of mucosal transplantation in preventing esophageal stricture through animal and human experiments[11,12]. However, while the utility of autologous mucosa for preventing esophageal stricture is well-established, autologous mucosal grafts are still subject to many limitations, as the acquisition of autologous mucosa is dependent on the patient and the required slice of mucosal cells, depending on the extent of the lesion. For example, for large lesions, it is necessary to obtain and prepare the appropriate mucosal slices, which can cause secondary damage to the patient. In addition, not all patients are in a condition to accommodate the acquisition and preparation of autologous mucosa. Therefore, such patients may not be able to undergo transplantation and thereby reduce their risk of stenosis.

Several trials have confirmed that cell sheets prepared by culturing oral mucosal cells have the same characteristics as mucosa and can be applied to prevent stenosis. However, the preparation process is time-consuming, which may delay the patient's treatment window and affect the prognosis. Acellular dermal matrix (ADM) is a kind of dermal substitute obtained from the allogeneic dermis after special treatment to remove its cellular components[13]. It is usually made of pig or human skin inactivated by a virus and cobalt-60[14]. It is prepared by sterilization, decellularization, and other processes[14]. The allogeneic dermis that has cellular components removed and retains elastin, keratan sulfate, laminin, and collagen has very low immune activity and will not induce any rejection[15,16]. In addition, studies have shown that ADM can be beneficial for inducing tissue regeneration and promoting cell growth[17]. During this process, ADM is degraded and utilized by local tissues, which is accompanied by the degradation of ADM itself[18]. It is expected to replace autologous mucosa as a graft after ESD for esophageal cancer and thereby prevent the occurrence of esophageal stricture.

Overall, as a novel material, ADM has the potential to replace autologous mucosal grafts for the prevention of esophageal stenosis. This prospective, single-center controlled study investigated the role of ADM as a substitute for autologous mucosa in the prevention of post-cancer surgery stenosis, with an aim to provide a new perspective and approach for the treatment of esophageal stenosis.

**MATERIALS AND METHODS**

***Study design***

This prospective, single-center, controlled study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Taizhou Hospital, Zhejiang Province, under the Institutional Review Board of Wenzhou Medical University (autologous mucosa transplantation approval number: K20190123; ADM transplantation approval number: X20190603). It was registered with the Center for Clinical Trials under registration number ChiCTR200040119.

**Inclusion criteria:** A preoperative chromoendoscopy assessment meeting the surgical indications; lesion circumference > 1/2; endoscopic treatment under general anesthesia able to be tolerated; agreed to accept inclusion in the clinical trial and sign the informed consent form for the operation.

**Exclusion criteria:** Eating disorders and absorption disorders with other causes; complication with diabetes and autoimmune diseases or a recent history of taking hormones and immunosuppressants; a history of serious cardiovascular and cerebrovascular diseases, serious liver and kidney insufficiency, or serious chronic lung diseases; acute or chronic infection.

**Exit criteria:** Postoperative pathological results indicating the need for further surgery, radiotherapy, chemotherapy, or other treatments; severe postoperative stenosis with a poor effect of repeated endoscopic catheter dilation, necessitating radial esophagotomy and surgery; withdrawing from the trial or being lost to follow-up for any reason; patient death.

At the follow-up evaluation, cases with difficulty swallowing and endoscopy showing that the gastroscope could not pass smoothly through the narrowest part, requiring intervention such as endoscopic dilation therapy, were defined as having postoperative stenosis.

***Operation details***

The surgery was performed using an Olympus GIF-Q260J gastroscope (Olympus Corporation, Japan), high-frequency electric generator, needle-type incision knife, terminal insulated scalpel (IT knife), triangular terminal scalpel (TT knife), trap, and thermal biopsy forceps.

Eligible patients underwent routine ESD and postoperative stenting. At the same time, autologous mucosal transplantation and ADM transplantation were performed for patients in need. Figure 1 illustrates the surgical procedure in brief. Postoperative fasting was performed for 1 to 2 d, and proton pump inhibitor injections were performed for 3 d. Cases with no gastrointestinal bleeding or esophageal perforation were discharged for follow-up. The stent was removed 1 wk after the operation, and gastroscopy was rechecked at 2 wk and 1 and 6 mo to judge whether or not the ESD wound was stenotic using a standard gastroscope entering the gastric cavity to check the survival of the grafted mucosa. Esophageal stenosis was defined as the inability of an Olympus GIF-Q260J gastroscope (with a diameter of 9.9 mm) to pass through the narrow area.

**RESULTS**

Based on the current incidence of esophageal stricture, a sample of 160 cases was calculated to be required for both the autologous mucosal graft group and the ADM group. A total of 20 patients were recruited in the autologous mucosal transplantation group during the recruitment period from January 1 to December 31, 2017, and a total of 13 patients met the inclusion criteria (excluding 1 with a lesion circumference < 1/2, 1 who refused to sign the informed consent form, 2 with reflux esophagitis, 2 with chronic hepatitis, and 1 with coronary artery disease); of these, 2 patients requested to withdraw from the trial after surgery, 2 were lost to follow-up, and 9 were ultimately included and completed the follow-up.

During the patient recruitment period for the ADM group from January 1 to December 31, 2019, 25 patients were recruited, of whom 14 met the inclusion criteria (excluding 2 with a lesion circumference < 1/2, 3 with reflux esophagitis, 1 with chronic hepatitis, 1 with coronary artery disease, 1 with reflux esophagitis, and 3 with recent aspirin or hormone use), and 3 were lost to follow-up; thus, a total of 11 patients were included and completed the follow-up.

The flow chart is shown in Figure 2. A total of 20 patients in the two groups included in the analysis had completed ESD surgery and follow-up, including 14 males and 6 females, with a mean age of 63.85 ± 7.66 years old and a median age of 64 years old. Four of the patients had hypertension, with the rest showing no other remarkable medical history, and 10 cases had a lesion circumference ≥ 3/4, while another 10 had a circumference of 1/2 to 3/4. There were 3 cases with a lesion length of 1 to 3 cm and 17 with a lesion length of > 3 cm. Six cases of stage IIa, three stage IIb, four stage IIc, and six stage IIa + IIc were analyzed endoscopically; seven cases showed an infiltration depth to the mucosal layer, three to the lamina propria, five to the myxomucosa, and four to the submucosa. Four patients had stenosis after surgery, with a stenosis rate of 20.00%, including 2 patients in the autologous mucosa group with a stenosis rate of 22.22% and a mean follow-up period of 39.67 ± 2.79 d and 2 patients in the ADM group with a stenosis rate of 18.18% and a mean follow-up period of 43.16 ± 1.77 d (*P* = 0.94).

Specific details concerning the enrolled patients are shown in Table 1. The comparison between the autologous mucosa group and the ADM group is shown in Table 2.

**DISCUSSION**

The main components of ADM are collagen and other extracellular matrices, and after modification, it has suitable pore size, porosity, and mechanical strength[19]. It is a scaffold-like repair material with a three-dimensional spatial structure[20]. A large number of studies have confirmed that ADM can induce vascularization and promote cell growth and proliferation when used in the repair of tissues and organs and has good histocompatibility and a low inflammatory response[17,21-23]. Because ADM retains its complete matrix structure and has a unique three-dimensional spatial structure[24], when transplanted into wound repair, it can achieve clinical effects equivalent to autologous full-thickness skin grafting, mainly because ADM plays the role of the dermis when repairing wounds[25]. As a template, ADM can function as a scaffold for cell growth. When ADM is used as an implant, a physical barrier layer can be formed locally to prevent tissue adhesion and pathological proliferation in the local wound so that different tissues can independently complete their healing processes[25].

Some studies have reported the use of ADM as an implant barrier to prevent Frey’s syndrome after parotidectomy[26,27], with none of the implants showing rejection reactions. The iodine G-starch test was used one year after surgery, and only two cases were positive, showing a significant difference from the control group[26]. ADM also covers wounds and fills tissue defects. The suitable structure, performance, and function of ADM are a strong guarantee of its utility as a bioremediation material.

ADM has received much attention and been widely used in clinical practice, such as in the repair of burn wounds[28], breast reconstruction[29], and oral mucosa repair[30]. In addition, as a new medical material, it can be degraded and absorbed by the human body. The process of degradation and absorption promotes the regeneration of the patient’s own tissues and reduces the occurrence of inflammation. In theory, it can also completely replace autogenous mucosa[18,31].

Compared to ADM, autologous mucosa requires a longer preparation time, which can delay treatment and result in a poor prognosis. In addition, the mucosa can be obtained and prepared in such a way that it can cause secondary damage to the patient, which can be aggravated if the lesion is large; at the same time, since the autologous mucosa is taken from the patient, the quality of the mucosa can be affected if the patient has more underlying diseases, thus affecting the outcome. In addition, if the patient is unable to donate mucosa for the preparation of a mucosal sheet for grafting, the mucosa cannot be grafted postoperatively to prevent stenosis. It has been reported that the same effect can be achieved by preparing mucosal slices from autologous oral mucosa culture. Although this approach reduces the damage and impact caused by the patient's own factors, it also requires a relatively long preparation time.

For early-stage esophageal cancer, early surgery is necessary to obtain a better prognosis. The use of ADM overcomes these issues. The preparation of ADM is not dependent on the patient, so it is not affected by the patient's own condition and does not delay treatment. Furthermore, since the components of the cells that cause the body's immune response are removed, there is basically no immune response.

Given the above, ADM seems to have the same potential as autologous mucosa to prevent esophageal stricture, but no reports or studies on the use of ADM to prevent stricture after human esophageal ESD have yet been published. The present study was conducted to verify the utility of ADM to prevent esophageal stricture in a prospective manner. A total of 9 patients with autologous mucosal grafts and 11 with ADM grafts were enrolled in the study and followed for approximately 3 years with a mean follow-up time of 41.59 mo. There were 2 cases of stenosis in the autologous mucosa, with a stenosis rate of 22.22%, and 2 cases of stenosis in the ADM graft group, with a stenosis rate of 18.18%, with no marked difference noted between the groups (*P* = 0.94). In this prospective study, strict inclusion and exclusion criteria were established during the experimental design phase, and by estimating the sample size, a sample of 160 cases per group was deemed to be required if the effects of autologous mucosal transplantation and ADM transplantation were to be compared. A total of 20 patients willing to receive autologous mucosal transplantation were recruited from January 1 to December 31, 2017, and 9 patients received autologous mucosal transplantation; a total of 25 patients willing to receive ADM transplantation were recruited from January 1 to December 31, 2019, and 11 patients received ADM transplantation. All of these patients completed a three-year follow-up.

During recruitment, the study failed to enroll sufficient patients who completed the three-year follow-up as required by the trial. Only 9 patients in the autologous mucosa group and 11 patients in the ADM group completed the 3-year follow-up, which is insufficient to draw definitive conclusions. While the stenosis rate did not differ significantly between the groups, it is less than the 37% stenosis rate noted in the relevant study[2]. While it has been shown to have some effect in preventing esophageal stricture, the effect of ADM remains unknown[12,32]. Based on the above results, we can speculate that ADM may exert some preventive effects against esophageal stricture, and its effects may be comparable to those of autologous mucosa. However, due to the many limitations of this trial, including the recruitment of an insufficient number of subjects, the results should be interpreted with caution.

**CONCLUSION**

Future studies using our established strict inclusion and exclusion criteria and improved follow-up may provide new insight into the prevention of esophageal stricture.

**ARTICLE HIGHLIGHTS**

***Research background***

Mucosal autograft transplantation has been reported to be effective in preventing esophageal stricture after endoscopic submucosal dissection (ESD) for esophageal cancer.

***Research motivation***

The preparation of autologous mucosa is an intricate process that demands a significant amount of time, potentially delaying the treatment of diseases. It is imperative to explore potential substitutes for autologous mucosa.

***Research objectives***

The efficacy of acellular dermal matrix (ADM) in preventing esophageal stricture is equivalent to that of autologous mucosal transplantation and has a substitutive effect.

***Research methods***

This is a prospective, single-center controlled study. Patients who underwent ESD surgery and were willing to undergo autologous mucosal transplantation and ADM transplantation were consecutively recruited for the study. A three-year follow-up was conducted for the transplanted patients.

***Research results***

Autologous mucosal grafts and ADM grafts demonstrated no significant differences in preventing esophageal stenosis, exhibiting similar preventive effects against esophageal narrowing.

***Research conclusions***

ADM possesses the potential to prevent esophageal stricture, exhibiting comparable preventative efficacy to autologous mucosal grafts while providing substitutive benefits.

***Research perspectives***

We shall persist in our research endeavors, enlisting additional participants to further validate the efficacy of ADM in preventing esophageal stricture. This shall furnish a multitude of options and avenues towards the treatment of esophageal stenosis.

**REFERENCES**

1 **Bourke MJ**, Neuhaus H, Bergman JJ. Endoscopic Submucosal Dissection: Indications and Application in Western Endoscopy Practice. *Gastroenterology* 2018; **154**: 1887-1900.e5 [PMID: 29486200 DOI: 10.1053/j.gastro.2018.01.068]

2 **Isomoto H**, Yamaguchi N, Nakayama T, Hayashi T, Nishiyama H, Ohnita K, Takeshima F, Shikuwa S, Kohno S, Nakao K. Management of esophageal stricture after complete circular endoscopic submucosal dissection for superficial esophageal squamous cell carcinoma. *BMC Gastroenterol* 2011; **11**: 46 [PMID: 21542926 DOI: 10.1186/1471-230X-11-46]

3 **Uno K**, Iijima K, Koike T, Shimosegawa T. Useful strategies to prevent severe stricture after endoscopic submucosal dissection for superficial esophageal neoplasm. *World J Gastroenterol* 2015; **21**: 7120-7133 [PMID: 26109798 DOI: 10.3748/wjg.v21.i23.7120]

4 **Miwata T**, Oka S, Tanaka S, Kagemoto K, Sanomura Y, Urabe Y, Hiyama T, Chayama K. Risk factors for esophageal stenosis after entire circumferential endoscopic submucosal dissection for superficial esophageal squamous cell carcinoma. *Surg Endosc* 2016; **30**: 4049-4056 [PMID: 26703127 DOI: 10.1007/s00464-015-4719-3]

5 **Oliveira JF**, Moura EG, Bernardo WM, Ide E, Cheng S, Sulbaran M, Santos CM, Sakai P. Prevention of esophageal stricture after endoscopic submucosal dissection: a systematic review and meta-analysis. *Surg Endosc* 2016; **30**: 2779-2791 [PMID: 26487197 DOI: 10.1007/s00464-015-4551-9]

6 **Chian KS**, Leong MF, Kono K. Regenerative medicine for oesophageal reconstruction after cancer treatment. *Lancet Oncol* 2015; **16**: e84-e92 [PMID: 25638684 DOI: 10.1016/S1470-2045(14)70410-3]

7 **Ohki T**, Yamato M, Ota M, Takagi R, Murakami D, Kondo M, Sasaki R, Namiki H, Okano T, Yamamoto M. Prevention of esophageal stricture after endoscopic submucosal dissection using tissue-engineered cell sheets. *Gastroenterology* 2012; **143**: 582-588.e2 [PMID: 22561054 DOI: 10.1053/j.gastro.2012.04.050]

8 **Bhatt A**, Mehta NA. Stricture prevention after esophageal endoscopic submucosal dissection. *Gastrointest Endosc* 2020; **92**: 1187-1189 [PMID: 33236991 DOI: 10.1016/j.gie.2020.07.005]

9 **Bartel MJ**, Mousa OY, Brahmbhatt B, Coffman DL, Patel K, Repici A, Tokar JL, Wolfsen HC, Wallace MB. Impact of topical budesonide on prevention of esophageal stricture after mucosal resection. *Gastrointest Endosc* 2021; **93**: 1276-1282 [PMID: 33309653 DOI: 10.1016/j.gie.2020.11.026]

10 **Yang J**, Wang X, Li Y, Lu G, Lu X, Guo D, Wang W, Liu C, Xiao Y, Han N, He S. Efficacy and safety of steroid in the prevention of esophageal stricture after endoscopic submucosal dissection: A network meta-analysis. *J Gastroenterol Hepatol* 2019; **34**: 985-995 [PMID: 30566746 DOI: 10.1111/jgh.14580]

11 **Hochberger J**, Koehler P, Wedi E, Gluer S, Rothstein RI, Niemann H, Hilfiker A, Gonzalez S, Kruse E. Transplantation of mucosa from stomach to esophagus to prevent stricture after circumferential endoscopic submucosal dissection of early squamous cell. *Gastroenterology* 2014; **146**: 906-909 [PMID: 24512802 DOI: 10.1053/j.gastro.2014.01.063]

12 **Liao Z**, Liao G, Yang X, Peng X, Zhang X, Xie X, Zhao X, Yang S, Fan C, Bai J. Transplantation of autologous esophageal mucosa to prevent stricture after circumferential endoscopic submucosal dissection of early esophageal cancer (with video). *Gastrointest Endosc* 2018; **88**: 543-546 [PMID: 29704471 DOI: 10.1016/j.gie.2018.04.2349]

13 **Ohki T**, Yamato M, Ota M, Takagi R, Kondo M, Kanai N, Okano T, Yamamoto M. Application of regenerative medical technology using tissue-engineered cell sheets for endoscopic submucosal dissection of esophageal neoplasms. *Dig Endosc* 2015; **27**: 182-188 [PMID: 25181559 DOI: 10.1111/den.12354]

14 **Liu X**, Dan N, Dan W. Preparation and characterization of an advanced collagen aggregate from porcine acellular dermal matrix. *Int J Biol Macromol* 2016; **88**: 179-188 [PMID: 27039117 DOI: 10.1016/j.ijbiomac.2016.03.066]

15 **Holl J**, Pawlukianiec C, Corton Ruiz J, Groth D, Grubczak K, Hady HR, Dadan J, Reszec J, Czaban S, Kowalewski C, Moniuszko M, Eljaszewicz A. Skin Substitute Preparation Method Induces Immunomodulatory Changes in Co-Incubated Cells through Collagen Modification. *Pharmaceutics* 2021; **13** [PMID: 34959443 DOI: 10.3390/pharmaceutics13122164]

16 **Takami Y**, Matsuda T, Yoshitake M, Hanumadass M, Walter RJ. Dispase/detergent treated dermal matrix as a dermal substitute. *Burns* 1996; **22**: 182-190 [PMID: 8726254 DOI: 10.1016/0305-4179(95)00123-9]

17 **Chen X**, Yang R, Wang J, Ruan S, Lin Z, Xin Q, Yang R, Xie J. Porcine acellular dermal matrix accelerates wound healing through miR-124-3p.1 and miR-139-5p. *Cytotherapy* 2020; **22**: 494-502 [PMID: 32571650 DOI: 10.1016/j.jcyt.2020.04.042]

18 **Wang Y**, Lu F, Hu E, Yu K, Li J, Bao R, Dai F, Lan G, Xie R. Biogenetic Acellular Dermal Matrix Maintaining Rich Interconnected Microchannels for Accelerated Tissue Amendment. *ACS Appl Mater Interfaces* 2021; **13**: 16048-16061 [PMID: 33813831 DOI: 10.1021/acsami.1c00420]

19 **Xing H**, Lee H, Luo L, Kyriakides TR. Extracellular matrix-derived biomaterials in engineering cell function. *Biotechnol Adv* 2020; **42**: 107421 [PMID: 31381963 DOI: 10.1016/j.biotechadv.2019.107421]

20 **Kirsner RS**, Bohn G, Driver VR, Mills JL Sr, Nanney LB, Williams ML, Wu SC. Human acellular dermal wound matrix: evidence and experience. *Int Wound J* 2015; **12**: 646-654 [PMID: 24283346 DOI: 10.1111/iwj.12185]

21 **Wang X**, Liu Y, Deng Z, Dong R, Liu Y, Hu S, Li Y, Jin Y. Inhibition of dermal fibrosis in self-assembled skin equivalents by undifferentiated keratinocytes. *J Dermatol Sci* 2009; **53**: 103-111 [PMID: 18990546 DOI: 10.1016/j.jdermsci.2008.08.010]

22 **Lin W**, Qi X, Guo W, Liang D, Chen H, Lin B, Deng X. A barrier against reactive oxygen species: chitosan/acellular dermal matrix scaffold enhances stem cell retention and improves cutaneous wound healing. *Stem Cell Res Ther* 2020; **11**: 383 [PMID: 32894204 DOI: 10.1186/s13287-020-01901-6]

23 **Henn D**, Chen K, Fehlmann T, Trotsyuk AA, Sivaraj D, Maan ZN, Bonham CA Jr, Barrera JA, Mays CJ, Greco AH, Moortgat Illouz SE, Lin JQ, Steele SR, Foster DS, Padmanabhan J, Momeni A, Nguyen D, Wan DC, Kneser U, Januszyk M, Keller A, Longaker MT, Gurtner GC. Xenogeneic skin transplantation promotes angiogenesis and tissue regeneration through activated Trem2(+) macrophages. *Sci Adv* 2021; **7**: eabi4528 [PMID: 34851663 DOI: 10.1126/sciadv.abi4528]

24 **Chocarro-Wrona C**, López-Ruiz E, Perán M, Gálvez-Martín P, Marchal JA. Therapeutic strategies for skin regeneration based on biomedical substitutes. *J Eur Acad Dermatol Venereol* 2019; **33**: 484-496 [PMID: 30520159 DOI: 10.1111/jdv.15391]

25 **Xue M**, Jackson CJ. Extracellular Matrix Reorganization During Wound Healing and Its Impact on Abnormal Scarring. *Adv Wound Care (New Rochelle)* 2015; **4**: 119-136 [PMID: 25785236 DOI: 10.1089/wound.2013.0485]

26 **Clayman MA**, Clayman LZ. Use of AlloDerm as a barrier to treat chronic Frey's syndrome. *Otolaryngol Head Neck Surg* 2001; **124**: 687 [PMID: 11391262 DOI: 10.1177/019459980112400617]

27 **Ye L**, Cao Y, Yang W, Wu F, Lin J, Li L, Li C. Graft interposition for preventing Frey's syndrome in patients undergoing parotidectomy. *Cochrane Database Syst Rev* 2019; **10**: CD012323 [PMID: 31578708 DOI: 10.1002/14651858.CD012323.pub2]

28 **Almeida IR,** Gonçalves AC, Corrêa FB, Castro JCD, Guirro ECO, Junior JAF, Coltro PS. Evaluation of Clinical and Biomechanical Features of Scars Resulting from the Treatment of Burn Contractures Comparing Acellular Dermal Matrices: A Randomized Clinical Trial. *Ann Surg* 2022 [DOI: 10.1097/sla.0000000000005371]

29 **Abd Elwahab SM**, Lowery AJ, Kerin MJ. Comment on "Implant-Based Breast Reconstruction With Acellular Dermal Matrix. Safety Data From an Open-Label, Multicenter, Randomized, Controlled Trial in the Setting of Breast Cancer Treatment". *Ann Surg* 2020; **271**: e106 [PMID: 32197006 DOI: 10.1097/SLA.0000000000003609]

30 **Lissek M**, Boeker M, Happe A. How Thick Is the Oral Mucosa around Implants after Augmentation with Different Materials: A Systematic Review of the Effectiveness of Substitute Matrices in Comparison to Connective Tissue Grafts. *Int J Mol Sci* 2020; **21** [PMID: 32708901 DOI: 10.3390/ijms21145043]

31 **Lohmander F**, Lagergren J, Johansson H, Roy PG, Brandberg Y, Frisell J. Effect of Immediate Implant-Based Breast Reconstruction After Mastectomy With and Without Acellular Dermal Matrix Among Women With Breast Cancer: A Randomized Clinical Trial. *JAMA Netw Open* 2021; **4**: e2127806 [PMID: 34596671 DOI: 10.1001/jamanetworkopen.2021.27806]

32 **Chai N**, Zou J, Linghu E, Chai M, Li L, Wang X, Zhang W, Xiang J, Li Z. Autologous Skin-Grafting Surgery to Prevent Esophageal Stenosis After Complete Circular Endoscopic Submucosal Tunnel Dissection for Superficial Esophageal Neoplasms. *Am J Gastroenterol* 2019; **114**: 822-825 [PMID: 30882422 DOI: 10.14309/ajg.0000000000000169]

**Footnotes**

**Institutional review board statement:** This prospective, single-center, controlled study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Taizhou Hospital, Zhejiang Province, under the Institutional Review Board of Wenzhou Medical University (autologous mucosa transplantation approval number: K20190123; ADM transplantation approval number: X20190603).

**Clinical trial registration statement:** The study was registered with the Center for Clinical Trials under registration number ChiCTR200040119.

**Informed consent statement:** All study participants, or their legal guardian, provided written consent prior to study enrollment.

**Conflict-of-interest statement:** All the authors declare that they have no conflict interests to disclose.

**Data sharing statement:** No additional data are available.

**CONSORT 2010 statement:** The authors have read the CONSORT Statement—checklist of items, and the manuscript was prepared and revised according to the CONSORT Statement—checklist of items.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review started:** August 5, 2023

**First decision:** October 9, 2023

**Article in press:** November 3, 2023

**Specialty type:** Gastroenterology and hepatology

**Country/Territory of origin:** China

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): B

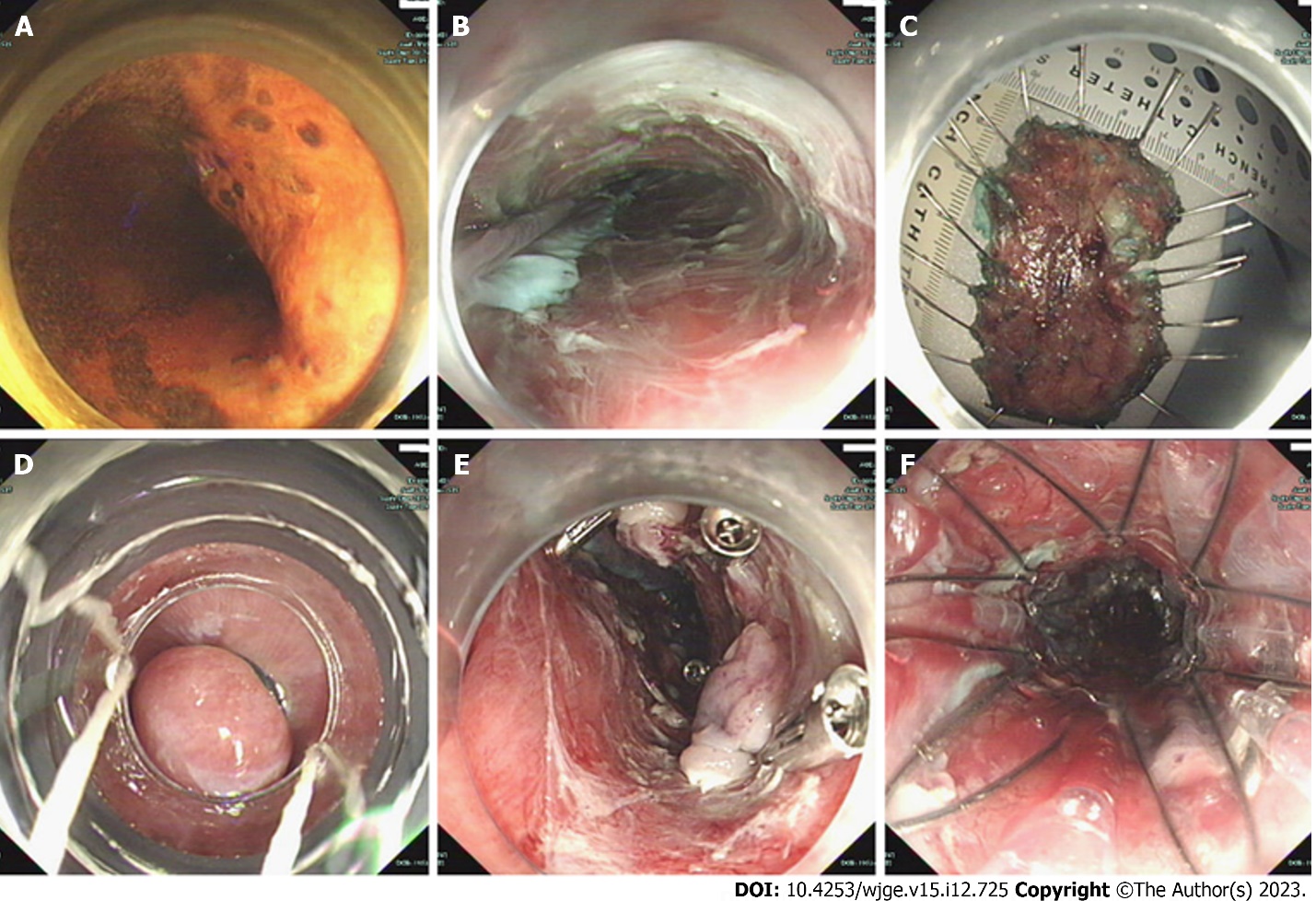
Grade C (Good): C

Grade D (Fair): 0

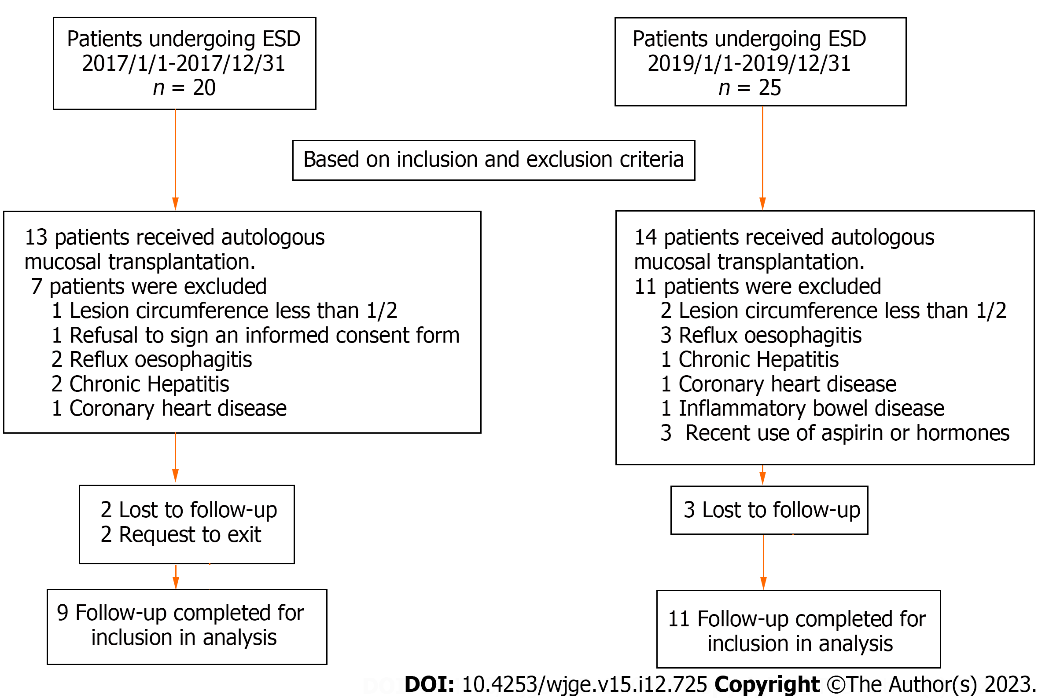
Grade E (Poor): E

**P-Reviewer:** Christodoulidis G, Greece; Oguma J, Japan; Rai VK, India **S-Editor:** Liu JH **L-Editor:** Wang TQ **P-Editor:** Cai YX

**Figure Legends**



**Figure 1 Operation process of 5/6 periesophageal endoscopic mucosal dissection resection combined with autologous esophageal mucosal transplantation and esophageal covered stent implantation.** A: Lugol fluid was sprayed on the whole esophageal mucosa; B: Endoscopic mucosal dissection was performed, and the wound after resection showed an annular mucosal defect; C: The cancerous tissue was removed; D: At the selected normal esophageal mucosa, the mucosa to be transplanted was removed by endoscopic mucosal resection using a polycyclic mucosal resection device; E: A titanium clip was used to secure the excised normal mucosa to the endoscopically peeled mucosal wound; F: The esophageal covered stent was implanted into the compressed transplanted mucosa.



**Figure 2 Flow chart of patient inclusion.**

**Table 1 Basic information of 20 patients**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Participant** | **Age (yr)** | **Gender** | **Endoscopic morphology** | **Trauma length (cm)** | **Circumference of the wound** | **Infiltration depth** | **Postoperative stenosis** | **Occurrence of stenosis time (d)** | **Number of ADM used (slices)** | **Follow-up time (mo)** | **Graft mucosa survival** |
| 1 | 63 | Male | IIa + IIc | 6 | 2/3 | Mucosal muscle layer | No | No | 0 | 44.13 | Yes |
| 2 | 63 | Male | IIb | 5 | 3/4 | Submucosa | No | No | 0 | 42.73 | Yes |
| 3 | 58 | Male | IIb | 2 | 1/2 | Mucosal muscle layer | No | No | 0 | 40.87 | Yes |
| 4 | 67 | Male | IIa | 4 | 1/2 | Mucosa layer | No | No | 0 | 39.93 | Yes |
| 5 | 73 | Female | IIb | 4 | 4/5 | Mucosal muscle layer | No | No | 0 | 39.70 | Yes |
| 6 | 58 | Male | IIa + IIc | 5 | 1 | Superficial submucosa | No | No | 0 | 38.77 | Yes |
| 7 | 69 | Female | IIa | 6 | 4/5 | Mucosal layer | No | No | 0 | 38.53 | Yes |
| 8 | 69 | Female | IIa | 5 | 3/4 | Mucosal layer | Yes | 98 | 0 | 37.83 | Yes |
| 9 | 56 | Male | IIa + IIc | 8 | 1 | Submucosa | Yes | 44 | 0 | 34.57 | Yes |
| 10 | 56 | Male | IIa | 2 | 2/3 | Mucosal layer | No | No | 1 | 44.90 | Yes |
| 11 | 65 | Male | IIa + IIc | 3 | 2/3 | Mucosal muscle superficial layer | No | No | 1 | 44.90 | Yes |
| 12 | 60 | Male | IIc | 3 | 2/3 | Mucosal lamina propria | No | No | 1 | 44.43 | Yes |
| 13 | 73 | Male | IIc | 5 | 3/5 | Mucosal lamina propria | No | No | 1 | 43.97 | Yes |
| 14 | 49 | Male | IIc | 3 | 1/2 | Mucosal layer | No | No | 1 | 43.97 | Yes |
| 15 | 73 | Female | IIa | 5 | 3/5 | Mucosal muscle layer | Yes | 41 | 4 | 43.50 | Yes |
| 16 | 66 | Male | IIc | 2 | 4/5 | Mucosal layer | No | No | 1 | 43.03 | Yes |
| 17 | 78 | Male | IIa + IIc | 5 | 3/4 | Mucosal layer | No | No | 3 | 42.57 | Yes |
| 18 | 61 | Female | IIa | 3 | 1/2 | Mucosal layer | No | No | 1 | 42.57 | Yes |
| 19 | 52 | Female | IIa | 10 | 1 | Submucosa | Yes | 62 | 4 | 42.33 | Yes |
| 20 | 68 | Male | IIa + IIc | 6 | 1 | Mucosal lamina propria | No | No | 1 | 38.60 | Yes |

ADM: Acellular dermal matrix.

**Table 2 Analysis of lesions in the autologous mucosal transplantation group and acellular dermal matrix transplantation group**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Group 1 (*n* = 9)** | **Group 2 (*n* = 11)** | ***P* value** |
| Gender |  |  | 0.77 |
| Male | 6 | 8 |  |
| Female | 3 | 3 |  |
| Age |  |  | 0.94 |
| ≥ 60 yr | 3 | 4 |  |
| < 60 yr | 6 | 7 |  |
| Wound circumference |  |  | 0.23 |
| 1/2-3/4 circumference | 3 | 7 |  |
| 3/4-full circumference | 6 | 4 |  |
| Wound length |  |  | 0.22 |
| < 10 mm | 0 | 0 |  |
| 10-30 mm | 1 | 2 |  |
| > 30 mm | 8 | 9 |  |
| Endoscopic morphology |  |  | 0.81 |
| IIa | 3 | 3 |  |
| IIb | 3 | 0 |  |
| IIc | 0 | 4 |  |
| IIa + IIc | 3 | 3 |  |
| Invasion depth |  |  | 0.19 |
| Mucosal layer | 3 | 4 |  |
| Lamina propria | 0 | 3 |  |
| Muscularis mucosa | 3 | 2 |  |
| Submucosa | 3 | 1 |  |
| Follow-up time (mo) | 39.67 (34.57-44.13) | 43.16 (38.60-44.90) | 0.52 |

Group 1: Autologous mucous membrane transplantation group; Group 2: Acellular dermal matrix transplantation group.



Published by **Baishideng Publishing Group Inc**

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

**Telephone:** +1-925-3991568

**E-mail:** bpgoffice@wjgnet.com

**Help Desk:** https://www.f6publishing.com/helpdesk

https://www.wjgnet.com



**© 2023 Baishideng Publishing Group Inc. All rights reserved.**