New Approaches In Digestive Surgery

A REVIEW OF ESOPHAGEAL TISSUE ENGINEERING IN DOG

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INTRODUCTION

Oesophageal surgery has been associated with greater incisional dehiscence than surgery in other portions of the alimentary tract. Several factors may contribute to the high complication rate, including lack of serosa and omentum, the segmental nature of blood supply, the constant motion of swallowing and respiration and the tension at the surgical site.

Regenerative medicine approaches facilitate the use of biological constructs to replace or regenerate normal tissue function. The aim of this review is to collect the literature of oesophageal tissue engineering using two types of manufactured bioscaffolds for oesophageal tissue replacement: A double-layer of collagen sponge/silicone stent and decellularized matrices.

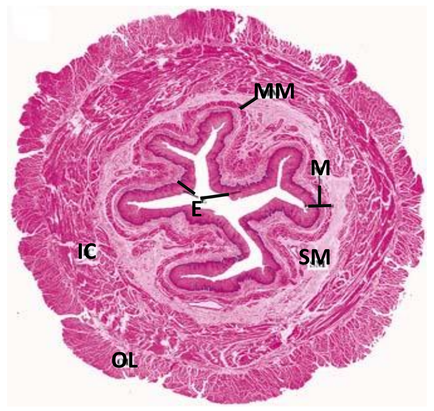

Figure 1. Cross-sectional histological organization of the esophagus: Mucosa (M) consisting of epithelium (E) and the *muscularis mucosa* (MM), the submucosa (SM) and muscularis externa showing the inner circular (IC) and outer longitudinal (OL) muscle layer. **Ref. [1]**

REVIEW

Table 1. Results and complications using a double-layer of collagen sponge/silicone stent

Cells	Defect	Regeneration	Complications
OMEC*	[a]	Complete epithelialization after **2wk.**	Low-mild stricture
Acell.*	[a]	Stenting time **< 3 wk:** Partial epithelialization and fibrous tissue Stenting time **3-4 wk:** complete epithelial regeneration Stenting time **4 wk:** complete epithelial and muscle regeneration	Fast stricture development Gradual stricture No stricture
Acell.	[b]	Stenting **47d:** Complete epithelial regeneration , immature muscle with non- synchronic peristalsis	† 2/7 anesthetic accident
Acell.	[c]	**1mo.:** granulation tissue and collagenus reabsorption **3mo.:** complete epithelial regeneration with smooth muscle bundles	†1/9 malnutrition 13-54% strictures

Table 2. Results and complications using a decellularized matrix

Scaffold	Defect	Regeneration	Complications
SIS & UBS	40-50% defect	**35d** complete epithelialization **50d** scaffold reabsorption **5m** muscular regeneration	-
	Complete defect	Fibrous tissue	100% stricture
UBM	Complete defects in different reconstruction: 1. ECM-UBS 2. Muscle tissue	1&2: Inflammatory cell infiltration No intact epithelium layer.	1&2: severe strictures
	3. ECM-UBS+30% muscle 4. ECM-UBS+ 100% muscle	3&4: Epithelial and muscle regeneration.	3&4 low stricture (<20%)
SIS OMEC	Partial defect	**4wk:** Complete epithelialization **8 wk:** Muscle regeneration	-
SIS BMSC*	Partial defect	**4 wk:** Partial epithelialization and mild inflammation **8 wk:** Complete mucosal and muscle regeneration	-

OMEC: Oral mucosal epithelial cells | Acell: Acellular| BMSC: bone marrow mesenchymal stem cell| [a]: 5 cm full-diameter defect in cervical portion | [b]: 10 cm full-diameter defect in cervical portion| [c]: 5 cm full-diameter defect in thoracic portion | † died.

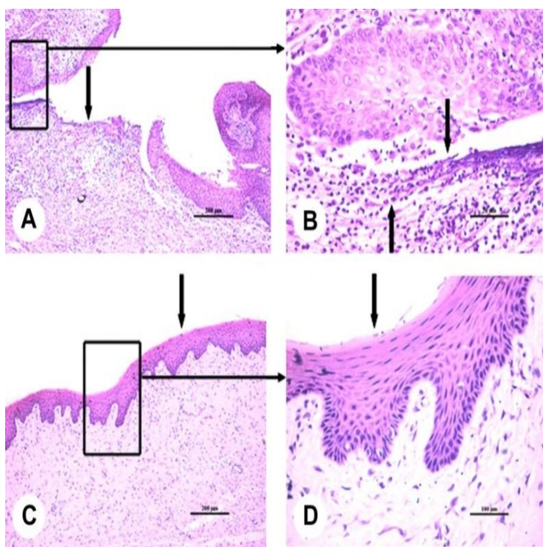

Figure 2. Epithelialization and postoperative inflammation in the two groups 4 wk after operation. Hematoxylin-eosin staining showed only immature squamous epithelium (downward arrows) at the center of graft in the SIS group, which was accompanied by a considerable accumulation of inflammatory cells (upward arrows) (A, B). By contrast, the BMSCs-SIS group showed an intact squamous epithelial coverage (downward arrows) with well-organized fibroblastic cells. There was almost no sign of inflammation (C, D). **Ref. [2]**

FUTURE PERSPECTIVES AND CONCLUSIONS

The recovery of a functional oesophagus requires an engineered tissue to closely resemble the anatomical and histological native structure and thus prevent the main complication derived of the poor integration of the oesophageal substitutes: the stricture.

Despite the promising results, the use of a double-layer collagen sponge/silicone stent was unsuitable for clinical setting due to the long periods of stenting time needed (up to 4 weeks), the requirement of two surgeries and a complicated postoperative period.

In the last decade, the research has been focused on a natural scaffold derived from decellularized tissues with biomechanical and bioinductive properties that allow the cellular migration, differentiation and organization, restoring the normal architecture of the oesophagus. In spite of the numerous efforts using different techniques of replacement and cell seeding, there is still not a suitable decellularized matrix scaffold than can be safely used in the clinical setting to replace full-diameter defects.

It is necessary to continue researching an optimal scaffold and a cell seeding source to succeed in the development of a functionally substitute that could mimic the normal oesophagus.

REFERENCES:

[1] Tan, J. Y., Chua, C. K., Leong, K. F., Chian, K. S., Leong, W. S., Tan, L. P. 2011. Esophageal tissue engineering: An in-depth review on scaffold design. Biotechnology and Bioengineering. Biotechnology and Bioengineering, 109 (1), 1-15.

[2] Tan, B., Wei, R. Q., Tan, M. Y., Luo, J. C., Deng, L., Chen, X. H., Hou, J.L., Li, X.Q., Yang, Z.M., Xie, H. Q. 2013. Tissue engineered esophagus by mesenchymal stem cell seeding for esophageal repair in a canine model. Journal of Surgical Research, 182(1), 40–48.