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Manuscript NO: 87280

Title:

Responses for reviewer's comments

Reviewer's code: 06267313

Comment:

The article deals with a very interesting and new issue regarding the acellular dermal matrix transplantation as a prevention method for esophageal stenosis after ESD. The study is well set up. The number of patients is relatively low and the authors should describe more about the complications of the method. Also what about the cost? Also the possibility of stenosis after ESD is low especially if you use a stent. It is a new method with prosperous results but we need more studies to establish this method in common practice.

Author's response:

Thank you very much for the acknowledgement of our research. We deeply regret and feel sorry for not being able to recruit a sufficient number of participants. As for the cost issue mentioned by the reviewer, since our study is a prospective clinical trial, the use of ADMs is funded by research grants, and thus we did not meticulously calculate their costs. We apologize for this shortcoming. Additionally, we will make efforts to recruit more participants in order to continue our study and carefully evaluate the cost-effectiveness of this transplantation approach.

Reviewer's code: 00724887

Comment:

I am grateful for the opportunity to review this interesting manuscript entitled: "New hope for esophageal stricture prevention: a prospective single-center trial on acellular dermal matrix". This report is interesting because it focused on the utility of ADM to prevent esophageal stricture after ESD in a prospective manner. However, your manuscript has major problems as following. Comments 1. I think that the sample size in this study is so small as you mentioned in the limitation that the clinical utility of ADM for esophageal stricture cannot accurately evaluated. 2. I cannot understand the utility of ADM as prevention of esophageal stricture after ESD from your results. I think you had better compare between ADM and non-treatment as prevention of stricture after ESD. Minor comments 1. You mentioned in Discussion part that "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-value: 0.94)". These data should be shown in Result part and Table 2. 2. In Table 2, you should clear which group (group 1 or 2) is for ADM group. 3. You should show the definition of stricture more concretely (Line 210-213).

Author's response:

We sincerely appreciate the professional suggestions provided by the reviewer. We deeply regret and apologize for not being able to recruit an adequate number of participants to support our research conclusions. The reason we did not compare patients using ADM with those not using ADM in our study is that during the recruitment phase, we were able to enroll significantly fewer patients willing to undergo ADM treatment compared to those not receiving ADM transplantation. Therefore, we decided to compare ADM with autologous mucosal transplantation to demonstrate its efficacy, as there is existing literature suggesting that autologous mucosa effectively prevents esophageal stricture [1]. Thank you once again for pointing out the shortcomings of the article. We have now included a definition for esophageal stenosis,

corresponding to lines 218-219 of the original text. Furthermore, we have made aesthetic enhancements to both Table 1 and Table 2, while also providing explanations for group 1 and group 2 in Table 2, to enhance comprehension and readability.

1. 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 May;114(5):822-825. doi: 10.14309/ajg.000000000000169. PMID: 30882422.

Esophageal stenosis is defined as the inability of an Olympus GIF-Q260J gastroscope (with a diameter of 9.9mm) to pass through the narrow area.

Table 1. Basic information of 20 patients

Participants	Age (years)	Gender	Endoscopic morphology	Trauma length (cm)	Circumference of the wound	Infiltration depth	Postoperative stenosis	Occurrence of stenosis time (days)	Number of ADM used (slices)	Follow-up time (months)	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

Table 2. An analysis of lesions in the autologous mucosal transplantation group and ADM 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 years	3	4	
<60 years	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 (months)	39.67 (34.57-44.13)	43.16 (38.60-44.90)	0.52

Reviewer's code: 06267313

Comment:

This study has been done very meticulously with proper planning and execution. The concept of acellular dermal matrix use is innovative with excellent result. This will pave the way for its use in other conditions to prevent stricture formation like healing of anastomotic stricture. Although required sample size was not achieved, still the no. of subjects recruited is good enough to show the proof of concept. My suggestion to continue this study and enrol more patients and also use this in other areas where stricture formation can happen.

Author's response:

We greatly appreciate the recognition given by the reviewer to our research findings. Unfortunately, due to limitations, we were unable to recruit a sufficient number of participants within the designated timeframe, with a significant factor being the impact of COVID-19 pandemic. All aspects have been hampered by the restrictions imposed during this pandemic, impeding the progress of our study. However, based on the current outcomes of our research, we believe there is potential to continue with this study, and we will dedicate more effort to enhance it. Once again, I express my gratitude for the recognition bestowed upon our research by the reviewer, and we hope that our study can offer further options for the prevention of esophageal stenosis.