

Peer Review File

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Reviewer A

This is a very interesting paper.

Comment 1. Stricture formation after ESD

Esophageal stricture occurs in 10-20% of patients undergoing ESD in the esophagus. Risk factors for stricture formation include a mucosal defect >75% of the luminal circumference of the esophagus, defect layer than 30mm and histologic depth extending to m2, stricture occurrence approaches 100% in patients who have had circumferential ESD performed.

The most common method to prevent stricture formation is local injection of steroids. Patients who had steroid injection had significantly lower rate of stricture formation compared to historical control (10% vs 66%). Therefore, comment to prevent stricture formation after ESD.

Reply: Thank you for this helpful addition. We have now included this in our text (lines 152-160).

Comment 2. Preoperative evaluation to predict the invasion depth of superficial squamous cell carcinoma.

NBI detected early SCC in the esophagus more frequently than white light endoscopy (WL) with higher sensitivity and accuracy using NBI compared to WL. Recently, NBI has been combined with magnification endoscopy to predict the invasion depth of superficial squamous cell cancer, Please comment the relationship between NBI and the invasion depth of esophageal cancer.

Reply: Thank you. Currently EMR is the only reliable method of determining depth of invasion in BE. We have mentioned this and added that NBI with magnification has been shown to be helpful in predicting depth of invasion in squamous cell cancer with more studies needed in BE. This has been added to the text (lines 54-63).

Comment 3. Cryoablation

Cryoablation has been explored as an alternative means of selective tissue ablation of IM with associated dysplasia. Cryoablation is a noncontact method that consist of directed spray of a cryogen,

like liquid nitrogen, which causes rapid freezing and thawing. This process causes vascular ischemia, and causes thrombosis, resulting in the necrosis of superficial esophageal mucosa layers. Several retrospective studies of cryotherapy have shown high rates of complete eradication of intestinal metaplasia and dysplasia, with minimal side effects.

Please comment about indication and side effect of cryoablation for superficial esophageal cancer.

Reply: We have discussed the use of cryoablation as a focal or circumferential treatment for BE dysplasia (lines 95-113, and 130-135)

Reviewer B

Comment 1. "For T1b cancers, surgery had traditionally been the preferred management given the risk of lymph node metastasis, however, currently endoscopic resection techniques can be considered as an alternative for patients with SM1 tumors(<500 micron submucosal invasion) and low risk features (well-differentiated, size<2cm, no lymphovascular invasion) especially if they are poor surgical candidates"

- I would be cautious for this as differentiating pT1a can be challenging, but pT1b from SM1 from SM2 is even more in community practice. I suggest to rewrite this in more cautious manner.

Reply: We have highlighted the challenging aspect of differentiating these lesions and urged caution (see lines 54-65)

Comment 2. I would voice more opinions for EMR vs. ESD - in respect to limits of ESD, as good intentions can turn into nightmares easily.

Reply: We have added a paragraph discussing stricture formation with ESD as an important adverse event and mentioned that referral to centers of excellence is advised when ESD is considered(lines 157-167).