

Dear Editors and Reviewers:

I am pleased to submit a revised version of our manuscript entitled “Clinical impact of gastrointestinal endoscopy on the early detection of pharyngeal squamous cell carcinoma: A retrospective cohort study” (Manuscript ID 65143). We would like to thank you and the reviewers for your insightful comments. In line with your suggestions, we have revised the manuscript to address the concerns raised by the reviewer. All of the comments have been addressed on a point-by-point basis and are listed below.

Reviewer #1: The study is aimed to clarify the clinical characteristics of pharyngeal squamous cell carcinomas detected by gastrointestinal endoscopy. The title is “Clinical impact of gastrointestinal endoscopy on the early detection of pharyngeal squamous cell carcinoma: A retrospective cohort study”.

1. This is a retrospective cohort study.

2. Who were the endoscopists? Experienced or Trainee

In this study, we assessed the clinical records of pharyngeal SCC patients retrospectively, and investigated the physician who detected the primary lesion (gastroenterologist, otolaryngologist, dentist, general physician). However, we could not survey each Physicians' experience. We added the related sentences discussing this point in our revised limitation section (page 12, line 4 to 5 in the revised manuscript).

3. Please review the literature add more details in the discussion section.

Thank you for your advice. We review the previous literature referring to utility of gastrointestinal endoscopy on detecting pharyngeal cancer in our revised discussion section (page 9, line 26 to page 10, line 17 in the revised manuscript).

4. What is the new knowledge from this study?

We appreciate your critical advice. The utility of gastrointestinal endoscopy for detection of pharyngeal cancer have been reported in several report on the setting of esophageal cancer patients. Indeed, the percentage of concurrent ESCC or with a history of ESCC was 27.8% in this study. To the best of our knowledge, this is the first study to explore the detection modality of oropharyngeal and

hypopharyngeal SCC, and revealed great contribution of gastroenterologists to detection and treatment for pharyngeal SCC regardless concurrent ESCC or with a history of ESCC. We added the related sentences discussing this point in our revised discussion section (page 10, line 14 to 17 in the revised manuscript).

5. Finally, please recommend to the readers “How to apply this knowledge for routine clinical practice?”.

Thank you for your thoughtful advice. We suggested that careful observation of pharynx in routine clinical practice will result in a better prognosis of pharyngeal cancer patients. We recommend to the readers active endoscopic participation for detection of pharyngeal cancer for symptomatic, alcohol-consuming patients as well as those with concomitant or previous ESCC, if not all cases (page 11, line 2 to 12 in the revised manuscript).

Reviewer #2: Authors highlighted the scope of detection of asymptomatic pharyngeal cancers using gastrointestinal endoscopy. Preservation of pharyngeal function with minimal morbidity using ELPS/ESD is well narrated. Koritala T, Zolotarevsky E, Bartley AN, Ellis CD, Krolikowski JA, Burton J, Gunaratnam NT. Efficacy and safety of the band and slough technique for endoscopic therapy of nonampullary duodenal adenomas: a case series. *Gastrointest Endosc.* 2015 Apr;81(4):985-8. doi: 10.1016/j.gie.2014.09.043. Epub 2014 Nov 22. PMID: 25440288. In this article we have noted no adverse effects with band and slough technique, unlike conventional treatment modalities, thereby preserving the function and promoting quick recovery. Please feel free to use this article to emphasize the endoscopic therapy.

Thank you for the recommendation to cite your manuscript. We added the related phrase in our revised Introduction section (page 5, line 7, references 6 in the revised manuscript).

In the results section, total number of patients enrolled should be 524 instead of 522. Please verify.

Thank you for your advice. If multiple lesions were detected at the same time, the largest lesion was included. Among study period, 563 lesions in 535 patients

were examined in our hospital. Of these, 41 lesions and 13 patients were excluded (28 lesions in 26 patients were excluded for the reason of multiple primary lesions, 7 lesions in 7 patients had undergone prior treatment for cancer in another hospital and 6 lesions in 6 patients had unspecified details of the detection process). Hence, a total of 522 lesions in 522 patients were enrolled in this study. We verified the related sentence in our revised Result section (page 7, line 23 to 27 in the revised manuscript).

In the discussion section, based on table 1, percentage of concurrent ESCC or with a history of ESCC is 27.8% unlike 29.3% listed. Please check again.

Thank you for the correction. We changed the percentage 29.3% to 27.8% (page 3, line 27 and page 10, line 22 in the revised manuscript).

In the discussion section, based on table 2, in group GE, only 38.4% (not 36.2%) of cases were symptomatic. Please change accordingly.

Thank you for your detailed review. We changed the percentage 36.2% to 38.4% (page 10, line 28 in the revised manuscript).

Conducting the study in a set up where there is an equal availability of endoscopists, nonendoscopists will help the readers compare and contrast the preference of patients in choosing the provider for diagnosis and management, provider preference for sending the referrals, and patient preference in opting endoscopic or non endoscopic modalities. If a pattern has been identified among patients and providers that is not favoring endoscopic evaluation; studies with larger sample size validating the improved prognosis with minimally invasive techniques should be done.

I completely agree with your comments. However, we could not get any information of availability of endoscopists and otolaryngologists in individual residential area. We added the related sentences discussing this point in our revised limitation section (page 12, line 4 to 7 in the revised manuscript).

The article has been carefully reviewed by an experienced medical editor whose first language is English and who specializes in editing papers written by

scientists whose native language is not English. We changed some phrase and sentence according to their advice. All authors have made major contributions to the manuscript and agree with its content. We declare that this article is original, has not been published before, and is not currently being considered for publication elsewhere.

We have two problems concerned with an automated manuscript editor.

- 1) I checked the automatically generated manuscript and found that “lesion” had been misconverted to “Lesion”, and we could not correct them.
- 2) We indicated the revision in red letters in the revised manuscript to make it easier for the reviewers to check, however, red letters were automatically converted to black letters.

We hope that our revised manuscript has satisfactorily addressed all of the reviewers’ comments, and that it will now be suitable for publication in JGH Open.

We look forward to hearing from you soon.

Sincerely,

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