

Peer Review File

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Reviewer A

This experienced group from Pittsburgh present a review on endoluminal palliation for advanced esophageal cancer.

The review shows very well the alternatives for palliation. I have a few minor suggestions:

- 1) The title should reflect the aims (endoluminal endoscopic palliation apart from stenting).
- 2) et al. NOT et al

Thank you for your comments. We took your recommendation and changed the title. The reference format has been revised as well.

Reviewer B

General comment:

The article is well written and rather comprehensive in the discussion on PDT, Cryotherapy and YAG Laser. The article can be improved if the authors have done some research on and able to provide data on how widespread these therapies are performed globally or whether they are only performed in highly selected tertiary centres in very few countries.

Line 88:

Suggest using “viable tumor” instead of “viable cancer”.

Lines 142-143, 287-291:

Reference 11 is wrong and it is also a duplicate of reference 17. Reference 11 in the manuscript has nothing to do with cryotherapy.

Lines 143-145:

Please provide some references for some of the retrospective studies to support the safety and efficacy of cryotherapy for palliation of esophageal cancer. Suggest to include Greenwald et al’s paper [Gastrointest Endosc 2010 Apr; 71(4): 686-693].

Line 188-189:

Complete eradication of luminal tumors was achieved in 55.8% of patients, but 44.2% of patients had no response to therapy. This statement seems to imply that cryotherapy either is extremely effective or simply not effective at all. Suggest using “incomplete response” instead of “no response”. If 44.2% or nearly half of patients had no response to a certain therapy, then it could not have been considered an effective .

References:

The format in which the references are cited is not consistent. For example, in references 1, 10 and 18, the year of publication is in (parenthesis) and placed either after the title or at the very end. The volume number for each citation is also randomly present or absent. Where there are more than 3 authors in the citation, the use of “et al” is also randomly present or absent.

Thank you for your comments. We have made wording and the reference changes.

In regards to if these therapies are performed globally or only available in selected centers, we could not find definitive answers through literature. Seeing some of the literature comes from Japan and Europe, I can only assume that they are performed globally but likely in selected centers.

Reviewer C

The review is very well written and very informative providing a good summary of available modalities.

Some comments to the authors to consider:

Thank you for your comments. The following changes have been made following your recommendations:

1. In a study published in *Gastrointest Endosc.* 1995 Dec;42(6):507-12. Photodynamic therapy with porfimer sodium versus thermal ablation therapy with Nd:YAG laser for palliation of esophageal cancer: a multicenter randomized trial. By C J Lightdale et al. A prospective study with careful attention to adverse events, the rate of adverse events from PDT was significantly higher than stated in this review. The authors mention this study later in complaint PDT to laser where PDT was found to be more superior to laser.

The 1-4% complication rate stated in the review was in reference to serious adverse effects (ie perforation, death) not including photosensitivity. The adverse events quoted in the study in *Gastrointest Endosc.* 1995 Dec;42(6):507-12. Photodynamic therapy with porfimer sodium versus thermal ablation therapy with Nd:YAG laser for palliation of esophageal cancer: a multicenter randomized trial. By C J Lightdale et al. included photosensitivity. We have changed the wording of our review to clarify.

2. A stronger conclusion regarding laser is suggested. Given laser was found to be inferior to PDT and comparison to plastic stents were mixed. The data clearly show plastic stents are inferior to self expanding metal stents, I recommend the author has a conclusion stating the likely inferiority of laser compared to other modern modalities in terms of efficacy and adverse events.

We have revised concluding statement regrading laser treatment.

3. The author describes cryotherapy well. Consider however stating that cryotherapy is done every

2 to 6 weeks (instead of 4) but the administration can also be varied based on response.

We have changed the statement to cryotherapy can be done very 2-6 weeks

4. Regarding APC, APC addition to other modalities did not appear to improve outcomes and APC alone seemed ineffective. I recommend the author mentions this. (Am J Gastroenterol. 2011 Sep;106(9):1612-20. Randomized comparison of three palliative regimens including brachytherapy, photodynamic therapy, and APC in patients with malignant dysphagia (CONSORT 1a) (Revised II). Maciej Rupinski et al.)

We have revised and included this reference in the article

5. Finally a statement regarding the fact true palliation in esophageal cancer has to consider quality of life in addition to dysphagia as while some modalities like stenting clearly improve dysphagia their effect on quality of life can be mixed.

We had added a paragraph in the summary to comment on quality of life with stenting and endoluminal therapy

Reviewer D

The title correctly reflects the subject and content of the study, but the use of this title should include in my opinion the most widely used method of endoscopic palliation of dysphagia - esophageal stenting.

In Fig. 2 you show the scheme of a dysphagia palliation algorithm in which you recommend the use of esophageal stenting, but this method is not described in the article?

The summary provides a clear summary of information on the topic.

The references listed are modest, only 5/18 are from the last 5 years.

The endoluminal brachytherapy method used to palliate dysphagia should be included along with the other methods described.

The use of Argon Plasma Coagulation is insufficiently described as a palliative method.

I consider that the use of a paragraph on endoscopic stenting does not find its place in the Summary chapter, this chapter must conclude the aspects discussed in this article.

In my opinion, the article requires major additions with other methods of endoscopic palliation of dysphagia - endoluminal brachytherapy, esophageal stenting, injection of concentrated alcohol intratumorally, etc.

Thank you for your comments. Esophageal stenting will be described in a separate article as part of the same special series, which is why we did not go in details regarding stenting technique in this article. However, stenting remains a valuable endoscopic intervention for esophageal cancer

and we thought it should not be neglected as part of decision making just because we did not describe it in depth. We have added a paragraph in the summary briefly mentioning stenting and its role in esophageal cancer palliation.