

Peer Review File

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Reviewer A

In this retrospective study the authors compared of safety with and without nasogastric tube decompression. It is a well-designed study in which heterogeneity is avoided by using propensity matched scores.

The message is clear: omitting nasogastric decompression is as safe as routine nasogastric decompression.

This confirms the already existing data from other series but the author's experience deals with a large number of patients treated within a short time period.

It is not clear whether omitting nasogastric decompression was introduced as a change of protocol at a given time point of left to the discretion of the surgeon. In the latter case being a possible source of bias. This should be clarified.

Reply: Thank you for your careful review and valuable suggestion. We apologize for not providing adequate information. Omitting nasogastric decompression is not a formal change of protocol, and the surgeons have the discretion depending on their own will, which is mainly judged by whether there is recurrent laryngeal nerve injury and whether the anastomosis went well. Bias indeed existed in the enrollment of patients, so we did this retrospective analysis for this change.

we have clarified this point in the method and discussion part.

Changes in the text: We have modified our text as advised (see Method-Surgical Procedure, Line 127-130; Discussion, line 280-282)

In the introduction authors refer to the high incidence of pulmonary and anastomotic complications as the source of morbidity and mortality according to the literature.

In reference three from their own experience with two and three field lymphadenectomy the anastomotic leak rate was 3.5%.

In this manuscript the leak rate is as high as 13% in the nasogastric tube group 10% in the non NG tub group.

And this is of great concern.

Indeed a three to four fold increase of anastomotic leaks has a far bigger impact on LOS or recurrence rate than the gain obtained from omitting a NG tube.

The first study was performed on patients treated between 2013-2016 and this study in 2019-2020 so not really a different time period.

So what is the author's explanation of this sudden 3-4 fold increase of leak rate.

Reply: Thank you for your careful review and valuable feedback. This increase of leak rate can due to the difference of inclusion criteria of patients. All patients underwent esophagogastric anastomosis in the thorax in the clinical trial of Dr.Li⁽¹⁾, while 35.54% of patients accepted cervical anastomosis in our research. In our previous reports, the incidence of cervical anastomotic fistula was significantly higher than that of intrathoracic anastomosis, with the former over 20% and the latter about 5%.⁽²⁻³⁾.

Reviewer B

This manuscript presents the largest number of cases of esophagectomy with no NGT, the outcomes are similar to previously reported studies. The authors reported incidence of pneumonia, anastomotic leak as well as morbidity and mortality. The results are very useful for they add evidence supporting not using routine NGT for esophagectomy patients.

Recommendations:

Details of the surgical procedure itself would be useful to better assess the results presented.

How many surgeons performed the procedures?

Was the abdominal part always done as open procedure?

Was pyloroplasty or other gastric drainage procedure performed?

The association of length of stay and no use of NGT needs more objective analysis and from the data would only be suggested

Also the incidence of anastomotic leak is recognized as multifactorial with NGT being one of them

It is not clear why NGT needs to be reinserted in the setting of anastomotic leak, the authors should elaborate what their management strategy is for leaks.

With 70% of procedures performed open, it is impressive the outcomes reported by the group, almost similar to reported for minimally invasive esophagectomy.

It would be helpful if the authors could elaborate based on their large experience if there was a subset of patients benefiting from NGT drainage

Reply: Thank you for your thoughtful suggestion and valuable questions. Eight surgeons in our center performed the procedures.

Abdominal part was done by VATS or open procedure. As you mentioned, we have calculated that the proportion of laparoscopic and open procedure of abdominal part is

15.2% and 84.8% respectively There were no pyloroplasty or other gastric drainage procedure performed.

Thanks for your kind suggestion. We revised the description of the effect of NG tube omission on hospital stay.

The basic treatment strategies for anastomotic leak at our center were similar to those reported previously, and they included conservative management, surgical intervention, and endoscopic intervention depending on the presence of symptoms, course of the disease, and surgeon preference^(4,5). Most of our patients received conservative treatment, including fasting, drainage of the anastomosis area, decompressing the conduit, parenteral or enteral nutrition and broad-spectrum antibiotics. For asymptomatic patients with contained leaks, only fasting, nutritional support and antibiotics were required. If patients were suspicious for uncontained leaks and infection, they were required to get NG tube inserted in our center, as continuous decompression can empty the stomach and reduce the tension of anastomosis. Patients without NG tube need to reinserted under the guidance of radiography or gastroscopy.

Changes in the text: We have modified our text as advised (see Method- Patients and samples, line 107,126-127; Method-Surgical Procedure, line 138-148)

Reviewer C

This manuscript entitled "Safety of no nasogastric decompression after esophagectomy: a propensity score-matched study" assessed the effects of NG decompression on postoperative complications after esophagectomy.

I think that this is a valuable study, but the following queries are raised before it can be considered ready for a final acceptance decision.

1. Indication

In which cases do you insert the NG tube and in which cases do you omit it? Please indicate the criteria. Is that criterion included in the covariates for calculating PS?

Reply: Thank you for your careful review and valuable suggestion.

The criterion was not included in the covariates for calculating PS, because this change was mainly judged by the surgeons' own will, which was unable to be gathered in clinical data when we did retrospective analysis. So bias indeed existed in the enrollment of patients, and we hope to do prospective RCT in the future to avoid these.

Changes in the text: We have modified our text as advised (see Method-Surgical Procedure, line 127-130; Discussion, line 280-282)

2. Material and methods

A. The methods of PSM should be described in the Statistical Analysis section.

Reply: Thank you for your kind suggestion. We have changed the position of methods of PSM.

Changes in the text: We have modified our text as advised (see Method-Statistical Analysis. line 163-169)

B. Please describe the protocol for NG tube application. Size (Fr)? How many days are you typically planning to keep in? What criteria are required for removal?

Reply: Thank you very much for your careful review and valuable suggestion. In our research, a 14-Fr single-lumen nasogastric tube was placed in all patients in the NG tube group. The NG tubes were retained until the return of bowel function (passage of flatus or passage of stool).

Changes in the text: We have modified our text as advised (see Method-Surgical procedure, line 131-147)

3. Discussion

What are good candidates for insertion?

Reply: Thank you for your careful review. If the recurrent laryngeal nerve is probably injured or the operation of anastomosis does not go well, the NG tube will be inserted in the surgery. After surgery, only patients with anastomotic leak, high risk of aspiration or gastric dilation need to insert nasogastric tubes.

Changes in the text: We have modified our text as advised (see Result-reinsertion of NG tube, line 210-211)

References:

1. Li B, Zhang Y, Miao L, et al. Esophagectomy With Three-Field Versus Two-Field Lymphadenectomy for Middle and Lower Thoracic Esophageal Cancer: Long-Term Outcomes of a Randomized Clinical Trial. *J Thorac Oncol*. 2021;16(2):310-317. doi:10.1016/j.jtho.2020.10.157
2. Li, B., Xiang, J., Zhang, Y. et al. Factors Affecting Hospital Mortality in Patients with Esophagogastric Anastomotic Leak: A Retrospective Study [J]. *World J Surg* 40, 1152–1157 (2016).

3. Shao L, Ye T, Ma L, Lin D, et al. Three-field versus two-field lymph node dissection for thoracic esophageal squamous cell carcinoma: a propensity score-matched comparison. *J Thorac Dis.* 2018 May;10(5):2924-2932.
4. Turkyilmaz A, Eroglu A, Aydin Y, Tekinbas C, Muharrem Erol M, Karaoglanoglu N. The management of esophagogastric anastomotic leak after esophagectomy for esophageal carcinoma. *Dis Esophagus.* 2009;22(2):119-26. doi: 10.1111/j.1442-2050.2008.00866.x.
5. Schaheen L, Blackmon SH, Nason KS. Optimal approach to the management of intrathoracic esophageal leak following esophagectomy: a systematic review. *Am J Surg.* 2014 Oct;208(4):536-43. doi: 10.1016/j.amjsurg.2014.05.011.