Author’s response to reviews

Title: Endoscopic vacuum therapy for postoperative esophageal leak

Authors:

Yang Min (yangwonee@gmail.com)
Taewan Kim (attack836@naver.com)
Hyuk Lee (lhyuk.lee@samsung.com)
Byung-Hoon Min (jason.min@samsung.com)
Hong Kim (hkts.kim@samsung.com)
Yong Choi (ysooyah.choi@samsung.com)
Jun Lee (stomachlee@gmail.com)
Poong-Lyul Rhee (pl.rhee@samsung.com)
Jae Kim (jaej.kim@samsung.com)
Jae Zo (yangwonee@gmail.com)
Young Shim (youngmog.shim@samsung.com)

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Author’s response to reviews:

Dear Editor:

We would like to thank you and the reviewers of the BMC Surgery for taking the time to review our article. We have responded to each of the Reviewers’ comments and have incorporated all the modifications suggested into the revised manuscript. Our responses to the comments are as follows:
Reviewer reports:

Tim Bright (Reviewer 1): Thank you for allowing me to review this article detailing an experience with Endovac drainage of anastomotic leak post oesophagectomy. The paper describes the outcome for 20 patients managed this way. My comments as below.

ABSTRACT The abstract summarises the paper adequately. The introductory statement that EVAC works well in this situation suggests a bias that can only really be put in the conclusions if the results justify

Response: We have changed background in Abstract following your comments.

“Background: Anastomotic leak is the most common and serious complication following esophagectomy. Endoscopic vacuum-assisted closure (EVAC) is a promising method for treating anastomotic leak. We aimed to evaluate the efficacy of EVAC and to identify factors associated with longer treatment duration for esophageal anastomotic leak following esophagectomy for cancer.”

INTRODUCTION The authors rightly state that there are multiple methods for dealing with an anastomotic leak post oesophagectomy. However they only detail one alternative, the placement of a SEM. There is no consensus that this is best practice and there are many other options that should be mentioned. The penultimate sentence of paragraph 2 does not make sense.

Response: We have additionally described therapeutic options following your comments.

“The optimal treatment for anastomotic leak remains unclear. Conservative management with nil per oral, intravenous antibiotics, and drainage, surgical, and non-surgical therapies could be applied according to patient status and institutional preference [6-8]. Surgical intervention may be the treatment of choice for leaks with sepsis. In a study by Crestanello et al, survival was similar between the reoperative and nonoperative groups despite the fact that the reoperative group had more severe patients [9]. If leak is minimal and patient is stable, leak could be conservatively managed avoiding a repeated surgery. When between these extremes, endoscopic treatment could be applied. Among endoscopic treatments, the insertion of a fully covered self-
expanding metal stent (SEMS) has been most extensively studied and has proven to be effective [1, 10, 11].”

METHODS The paper does not explain patient recruitment. Was it all leaks? Consecutive patients? It is not clear what adjunct drains were allowed

Response: We have further described study population following your comments. We have also made figure 1 showing subjects flow.

“This retrospective study investigated 48 patients who had an esophageal anastomotic leak following esophagectomy for cancer in the Samsung Medical Center between October 2015 and December 2017. The diagnosis of postoperative anastomotic leak was made according to the associated clinical symptoms, signs, and abnormal findings on endoscopy and esophagography. The associated symptoms and signs were fever, cough, neck wound swelling, and drainage of food or purulent material. Abnormal findings on endoscopy and esophagography were visualization of a wall defect and contrast leakage. Excluding 28 patients who received only conservative management including intravenous antibiotics, nil per oral with jejunal tube feeding, and drainage (JP drain and/or chest tube) (n = 22) and surgical repair (n = 6), 20 consecutive patients who received EVAC were analyzed (Fig. 1). When leak did not improve after conservative management and/or resulted in septic condition, patients underwent EVAC or surgical repair. The study was approved by the institutional review board of Samsung Medical Center.”

RESULTS It is curious that clinical parameters such as inflammatory markers, organ failure etc were not included

Response: We have added more data including WBC count, CRP level, and presence of organ failure at the time of EVAC insertion following your comment (Table 1 and results section).

DISCUSSION The discussion suffers from not comparing endovac therapy with other methods more widely. In particular there is no comparison with conservative treatment with drains and an nasogastric tube which likely would have resolved many of the included patients. The discussion of the one mortality should be intin the result section
Response: It was not possible to compare the efficacy between conservative management and EVAC therapy because conservatively managed patients usually had mild leak, as compared to the EVAC. Regarding literatures are also lacking. Instead, we addressed the comparative data between EVAC and stent placement. We have also added a literature comparing EVAC with other treatments in Discussion.

We have moved the discussion of the mortality case into the results section following your comment.

“Previous studies also showed high success rates with EVAC treatment. Brangewitz et al. reported 27 of 32 (84.4%) successful cases of EVAC treatment for esophageal defects with various causes including postoperative anastomotic leak [14]. Schorsch et al. reported 32 of 35 (91.4%) successful cases for all-cause esophageal defects and 20 of 21 (95.2%) successful cases for postesophagectomy or gastrectomy anastomotic leak [16]. Laukoetter et al. reported 49 of 52 (94.2%) successful cases of EVAC treatment for all cause esophageal defects and 36 of 39 (92.3%) successful cases for post-esophagectomy or gastrectomy anastomotic leak [17]. The success rate with EVAC treatment compared to that of SEMS for postoperative anastomotic leak was significantly high in several previous studies [14, 15, 18]. In a comparative study involving 62 patients developed an anastomotic leak after esophagectomy, EVAC showed better outcomes than stent placement and surgery [19]. Thus, EVAC is very effective for postoperative anastomotic leak, which is consistent with our results.”

George Kiroff (Reviewer 2): Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.

Please overwrite this text when adding your comments to the authors.

Although this is a small series of patients it has been well documented and represents an increasingly important method of managing a difficult post-operative complication. In discussion the authors make much of the increased duration of treatment in patients who have undergone neo-adjuvant treatment and those with a larger anastomotic defect. Neither of these characteristics are discretionary and consequently it is meaningless to over emphasise their importance. Impaired wound healing following radiotherapy has been extensively reported previously. My preference would be a revision of the discussion to decrease reference to neo-
adjuvant therapy and size of defect and an expanded description of the technical aspects of delivery of endo-vac therapy.

Response: We have reduced the discussion of risk factors for prolonged treatment. We have described the process of EVAC treatment in the Methods section and discussed about interval of sponge change in the Discussion section.

“EVAC treatment was started with intracavitary placement of the tip of a size-adjusted polyurethane sponge sutured to a nasogastric tube under direct-vision endoscopy. Nasogastric tube is inserted via the nose and brought out through the mouth. After cutting distal part of tube leaving a few side holes, polyurethane sponge is sutured to the tip of the tube. Trimming of the sponge is also required according to the size of cavity. The sponge size needed to be smaller than the wound cavity to promote collapse and subsequent closure of the fistula. The sponge can be inserted into the wound cavity using a grasping forceps and snare. After placement of the tube, continuous negative pressure 100 mmHg generated by a vacuum pump was delivered to the cavity through the tube. The sponge was changed every 3-4 days according to the changes of size and shape of the lesion. EVAC treatment was finished when the opening was closed.”

“We changed sponge every 3-4 days according to the lesion (leak cavity) status. The drains should be changed regularly to assess the lesion status and adapt the size of the sponge. However, frequent changes would not be cost-effective. Thus, we modified the protocol to change sponge every 1 week in 2018. In a recent study showing good outcomes of EVAC, the authors also changed sponge every 1 or 2 weeks [24]. Sponge could adhere firmly to the wound bed after prolonged placement. Therefore, weekly change seems reasonable and shorter interval could be considered depending on the lesion status. Future studies are needed to establish the optimal interval of EVAC change.”

We hope the revised manuscript will better meet the requirements of your journal for publication. We thank the editors and reviewers of the BMC Surgery once again for the constructive review of our paper.

Sincerely Yours,

Corresponding author: Jae Ill Zo, M.D., Ph.D.