

Peer review file

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Reviewer A

Comment 1: Why were 6 patients treated conservatively, how were they treated and what were their outcomes?

Reply 1: Thank you for your advices. We added some comments about conservative treatment (see Page 4, Line 81-86).

Changes in the text: These 6 patients were stable in respiratory and hemodynamic state, and were not in sepsis. 3 of 6 patients had limited contamination of mediastinum. Therefore, we had decided that conservative treatment was possible. We performed fasting, total parenteral nutrition, administration of antibiotics, nasogastric tube decompression, and chest tube drainage for these patients. All 6 patients improved and were discharged.

Comment 2: Operative duration. Duration of surgical procedures described as 359 minutes - 6 hours - this seems like a long time.

Reply 2: Actually, it takes long time. Because our method requires both laparotomy and VATS. It needs long time. This is the disadvantage of our method. We added some comments about operation time (see Page 9, Line 188-189).

Changes in the text: Since We perform VATS in addition to laparotomy, operation time becomes longer.

Comment 3: Mini thoracotomy. Performed because of severe contamination in 2 patients - how was that defined, was it early on in this VATS strategy and therefore? part of the learning curve and what were the outcomes.

Reply 3: We defined contamination by food residue as severe contamination. It was difficult to remove them only by VATS. So we need small thoracotomy. We added some comments about mini thoracotomy (see Page 6, Line 116-119).

Changes in the text: If the contamination of the mediastinum and thoracic cavity were severe by food residue, a small thoracotomy and lavage with a large amount of saline were performed. Because it was difficult to remove food residue only by VATS.

Comment 4: Closure of oesophagus. If there is oesophageal leakage after primary repair of the oesophagus in 50% of patients, why repair the oesophagus - all patients still survived ? Managing the perforation by means of lavage/drainage would avoid laparotomy and GI drainage/feeding tubes could be placed endoscopically.

Reply 4: As you pointed out, the percentages of anastomotic leakage was high. We

haven't found the cause of it. But we examined only 12 cases. It is necessary to increase number of cases and investigate the cause of it in the future. We added some comments about this (see Page 9, Line 198-201).

Changes in the text: In this study, the percentages of anastomotic leakage was high. At this point, we haven't found the cause of it. It is necessary to increase number of cases and investigate the cause of it in the future.

Reviewer B

Major Comment

Comment 1: I think that Boerhaave's syndrome is an acute disease.

It is described as "mediastinal abscess (p5L126)". Are there cases in which a long time has passed since the onset? It would be good if you could also describe the time since onset. Management will depend on the time since onset. If the time has passed, CT-guided drainage may be able to control the problem.

Reply 1: Thank you for your advices. As previously reported, the risk of operation increases more than 24 hours from onset. Then we examined time from onset to operation. We examined the proportion of cases with the time from onset to operation more than 24 hours. We added this data to Table 1.

Changes in the text: There were no significant differences in age, sex, the acute physiology and chronic health evaluation II (APACHE II) score, the sequential organ failure assessment (SOFA) score, and time from onset to operation (see Page 6, Line 129-132).

Comment 2: I think the preferred site is the left wall of the lower esophagus, but were there cases in which other sites were perforated?

Reply 2: In all cases, the perforation site was the left wall of the lower thoracic esophagus. We added this comment (see Page 5, Line 97-98).

Changes in the text: In all cases, the perforation site was the left wall of the lower thoracic esophagus.

Comment 3: If you are going to perform the Mann-Whitney U test, I think it is better to use the "MEDIAN".

Reply 3 : We changed the all data from means \pm SD to median (IQR) (see Page 6, Line 123, Table 1, Table 3).

Changes in the text: Data are reported as the medians (interquartile range (IQR)) or as proportions.

Minor Comment

Comment 1: It is described as "CT guided drainage group". I think it would be better to use a abbreviation such as "D group".

Reply 1: We abbreviated CT-guided drainage group to D group and Lavage and drainage

using VATS group to VATS group (see Page 4, Line 88-91, Table 1, Table 2, Table 3).

Changes in the text: From 2004 to 2011, CT-guided drainage was performed in 6 patients (D group). On the other hand, from 2011 to 2018, lavage and drainage were performed using VATS in 6 patients (VATS group).

Reviewer C

Comment 1: With regard to treatment selection, the authors had better explain the treatment indications for the lavage and drainage using VATS and CT-guided drainage in Material and methods section if the authors know. When they do not know, please describe that.

Reply 1: Thank you for your advices. As mentioned in Introduction section, we performed laparotomy with CT-guided drainage from 2004 to 2011. All patients survived. However mechanical ventilator days and the length of ICU stay prolonged compared to thoracotomy. Then we added lavage and drainage using VATS to primary repair with laparotomy from 2011 to 2018. We have modified our text as follows in Patient and Methods section (see Page 4, Line 88-91)

Changes in the text: From 2004 to 2011, CT-guided drainage was performed in 6 patients (D group). On the other hand, from 2011 to 2018, lavage and drainage were performed using VATS in 6 patients (VATS group).

Reviewer D

Comment 1: How was the time from onset of perforation to start the operation.

Because it will make respiratory dysfunction. You had better describe these results.

Reply 1: Thank you for your advices. As previously reported, the risk of operation increases more than 24 hours from onset. Then we examined time from onset to operation. We examined the proportion of cases with the time from onset to operation more than 24 hours. We added this data to Table 1.

Changes in the text: There were no significant differences in age, sex, the acute physiology and chronic health evaluation II (APACHE II) score, the sequential organ failure assessment (SOFA) score, and time from onset to operation (see Page 6, Line 129-132).

Comment 2: Although you wrote conservative treatment a little we know the conservative treatments are useful without respiratory dysfunction (Stent, Endoscopic clipping, Naso-esophageal extra drainage, etc.) Boerhaave syndrome has a severe respiratory disfunction and it is difficult to operate safely. You should describe why you choose such an operative treatment. In the case of Boerhaave syndrome, such a strategy is very important.

Reply 2: You have a point. Endoscopic treatment for Boerhaave's syndrome has been reported in recent years. So we added some comments about it (see Page 9, Line 190-

196).

Changes in the text: Recently, some successful endoscopic treatments for Boerhaave's syndrome have been reported. Endoscopic clipping, stent may be useful. For particularly elderly individuals with hemodynamic and / or respiratory instability, less invasive endoscopic treatment may be preferred to more invasive surgical treatment. However, randomized trials haven't been conducted to compare endoscopic treatment with surgical treatment. Even now, the gold standard treatment for Boerhaave's syndrome is surgical repair. Therefore, we choose it for operable patients.

Comment 3: Although you do not have significant differences, you have anastomotic leakage after thoracoscopic treatment in 67% of these cases. I understand that you only performed lavage and drainage using VATS. Does anastomotic leakage mean it remains the esophageal perforation? If so, why you did not suture this perforation point?

Reply 3: I'm sorry that it is difficult for you to understand it. We don't repair with VATS, but we do repair with laparotomy. We also wrote the reason in the text as follows. Primary repair with thoracoscopic surgery requires a high level of surgical technique, whereas lavage and drainage using VATS can be performed relatively easily (see Page 8-9, Line 184-186). As you pointed out, the percentages of anastomotic leakage was high. We haven't found the cause of it. But we examined only 12 cases. It is necessary to increase number of cases and investigate the cause of it in the future. We added some comments about this (see Page 9, Line 198-201).

Changes in the text: In this study, the percentages of anastomotic leakage was high. At this point, we haven't found the cause of it. It is necessary to increase number of cases and investigate the cause of it in the future.

Comment 4: If you do not suture this perforation point, we do not need the operation under anesthesia with risk. You should choose only conservative treatment with drainage and lavage. You should describe more these opinions.

Reply 4: I'm sorry that it is difficult for you to understand it. Primary suture is performed with laparotomy, not with VATS.

Changes in the text: Please refer to Reply 2 and 3.

Reviewer E

Comment 1: This is a retrospective review of small number of cases, prompted by bad outcome of single patients in their past experience. Primary repair and debridement and drainage would be the treatment of choice and possibility of endoscopic intervention and limited drainage could be an option in less contaminated cases. Not one size fit all. Following the surgical principles are important and individualizing therapy is important. In a widely contaminated lower esophageal (GE Junction) tear can be well treated by laparotomy and repair and thoracic debridement and drainage, where as repair and catheter drainage would be enough in a patient with limited contamination of

mediastinum, however generalizing treatment on a small number of unselected patients is troublesome.

Reply 1: Thank you for your advices. You have a point. Boerhaave's syndrome is a rare disease. Therefore, it is difficult to establish only one surgical method. From past experiences, we perform the current surgical method. On the other hand, we performed conservative treatment for 6 patients. These 6 patients were stable in respiratory and hemodynamic state, and were not in sepsis. 3 of 6 patients had limited contamination of mediastinum. Therefore we had decided that conservative treatment was possible (see Page 4, Line 81-86).

Changes in the text: These 6 patients were stable in respiratory and hemodynamic state, and were not in sepsis. 3 of 6 patients had limited contamination of mediastinum. Therefore, we had decided that conservative treatment was possible. We performed fasting, total parenteral nutrition, administration of antibiotics, nasogastric tube decompression, and chest tube drainage for these patients. All 6 patients improved and were discharged.