

# Application of Mediastinal Drainage Tube in Intrathoracic Esophageal Anastomotic Leakage for Early Diagnosis and Effective Treatment: A Retrospective Study

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## Research article

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# Abstract

**Background:** Intrathoracic esophageal anastomotic leakage (AL) is one of the most fatal complications after esophagectomy. In this study, we tried to place an additional drainage tube in esophagus bed and evaluate its effect in early diagnosis and treatment of AL.

**Methods:** From January 2010 to August 2020, a total of 312 patients, who suffered from esophageal or cardia carcinoma, underwent esophageal resection with intrathoracic esophagogastric anastomosis. Among them, we identified 138 patients with only one pleural drainage tube as “Control Group” and 174 patients with a pleural drainage tube and an additional mediastinal drainage tube (MDT) as “Tube Group”. The incidence of postoperative AL, time to diagnosis, time to recovery, and patient outcome were analyzed.

**Results:** There were no significant differences in the AL rate ( $P = 0.837$ ) and postoperative pain between two groups. However, in the Tube Group, almost all the patients were definitely diagnosed prior to the appearance of hyperpyrexia, which was regarded as the earliest and most common symptom after AL. Moreover, in the Tube Group, there was significant decrease in the incidence of uncurable fistula, which required re-operation or variable treatments under gastroscopy, when compared to the Control Group ( $P = 0.032$ ). Finally, patients in the Tube Group were associated with reduced post AL hospital day ( $P = 0.015$ ) and lower mortality, although there was no significant difference ( $P = 0.188$ ), than in the Control Group.

**Conclusions:** Placement of a MDT can not prevent the AL, but it is an effective method to diagnose AL earlier and facilitate the fistula healing and patient recovery.

## Background

Esophageal cancer is one of the most serious global health problem, especially in developing countries. Surgery is a major component of treatment for patients with locoregional esophageal cancer<sup>[1]</sup>. Improvements in surgical techniques and postoperative care have led to an obvious reduction in surgical complication morbidity and mortality in recent years<sup>[2]</sup>. Nevertheless, as one of the most frequent postoperative complications, anastomotic leakage (AL) is still difficult to completely avoid. According to the literatures, AL occurs in 11.4–21.2%<sup>[3–6]</sup> of cases, with an associated mortality rate between 7.2% and 35%<sup>[7]</sup>. Early diagnosis is essential to facilitate the fistula healing and patient recovery and decrease mortality associated with AL<sup>[8]</sup>.

However, the clinical symptoms of AL, including hyperpyrexia, thoracodynia, chest distress, tachycardia, increased and feculent liquid from the pleural drainage<sup>[8–12]</sup>, are nonspecific and usually appear late, since these symptoms usually emerge secondary to the infection around the fistula, which has already been severe and difficult to drain and flush because of the unsatisfying drainage. After the symptoms onset, several diagnostic modalities are available for AL detection, including esophagography, endoscopy, and the observation of methylene blue in the drainage tube after oral administration<sup>[8]</sup>, that is usually a

few days later than the occurrence of the AL. Therefore, in clinical practice, more effective diagnostic methods for AL are urgently need.

In order to treat AL effectively, several treatment methods have been developed, such as conservative treatment, endoscopic techniques and second operation<sup>[13,14]</sup>. In general, the principles of these management strategies are the closure of the anastomotic fistula, the containment of the leakage, and the adequate drainage of fluid collections<sup>[8]</sup>. Unfortunately, as the abscess cavity resulted from AL is typically very deep, it is challenging to place a drainage tube accurately without a second surgery, as a consequence, the drainage after AL is usually incompleated and the infection around the fistula is difficult to control.

In order to solve the aforementioned problems, we began to place an additional mediastinal drainage tube (MDT) beside the anastomotic stoma in the esophagus bed during the operation since September 2015. In case of leakage, the MDT would realize early diagnosis through the changes in the drainage fluid, and could completely drain the leakage cavity and remove secretions or necrosis by intermittent flushing. In this study, a ten-year retrospective database was used to analyze the early diagnosis and treatment effect of the MDT.

## Methods

In this study, a ten-year retrospective database was used to identify patients who suffered from esophageal or cardia carcinoma and underwent esophageal resection with left or right intrathoracic esophagogastric anastomosis at Thoracic Surgery Department, Hwa Mei Hospital, University of Chinese Academy of Sciences from January 2010 to August 2020. Exclusion criterias were as follows: (☒) patients received esophagectomy under Video-Assisted Thoracic Surgery, (☒) patients with a cervical anastomosis, (☒) the first 10 patients with the MDT were excluded because the most suitable location of the MDT was need to be confirmed. In total, there were 312 recorded cases. Among them, 138 patients with only one pleural drainage tube were devided into the “Control Group” and 174 patients with a pleural drainage tube and an additional MDT were devided into the “Tube Group”.

All the preoperative assessment and surgical procedures were performed according to the NCCN clinical practice guidelines. After resection of the esophagus tumor and dissection of the lymph nodes, the stomach, which was already made into a narrow tube, was pulled into the pleural cavity for anastomosis using an anastomat. At the end of the operation, in the Control Group, a 26-Fr drainage tube was placed into the thoracic cavity above the diaphragm as a pleural drainage tube, while in the Tube Group, in addition to this tube, another 26-Fr drainage tube was placed into the esophagus bed just beside the anastomosis as an MDT. As shown in Fig. 1a, the white arrow indicated the MDT beside the anastomotic stoma and the yellow arrow indicated the pleural drainage tube that above the diaphragm.

When the patient returned to the ward, the two tubes were connected to a water sealed bottle, respectively. To check the position of the tubes, a chest X-ray was obtained at postoperative Day 1. In the Control

Group, the pleural drainage tube would be retained till the patient could eat normally, while in the Tube Group, the pleural drainage tube would be removed when no air leak as observed and the volume of drainage was below 150 ml per day, and the mediastinal drainage tube would be removed until the patient could eat normally. Esophagography, also known as contrast swallow examination, was applied in the patient with suspected AL, and according to which, the diagnosis of AL was confirmed by a radiologist and a thoracic surgeon together. As shown in Fig. 1b, when the AL occurs, the contrast agent was completely drained out through the MDT without widespread, which was indicated by the red arrow. The white arrow indicated the MDT.

Patients received health education, including a pain score method of numerical rating scale (NRS) at admission. A chart card with a 10-cm-long horizontal line with word anchors at each end, ranging from 0= “no pain” to 10= “worst pain” was used to assess a postoperative pain score. The pain score at rest was evaluated three times per day (7am, 3 pm and 11 pm), and included in our hospital information system.

## Statistical analysis

Categorical variables were examined by  $\chi^2$  test. Continuous data were expressed as the mean  $\pm$  standard deviation (SD). Before comparison, the continuous variables of two groups were examined by the Levene test. If the variances were not equal, the Brown-Forsythe test was performed, and if the variances were equal, one way ANOVA was employed. Calculations were performed using the SPSS statistical package, version 20.0 (SPSS Inc, Chicago, IL, USA).

## Results

As presented in Table 1, there were 270 male and 42 female patients with ages from 40 to 76 years ( $64.42 \pm 4.96$  years). On the basis of the NCCN clinical practice guidelines, 203 patients underwent the esophagogastric anastomosis through the right thoracic cavity, while 109 patients received the operation through the left thoracic cavity. According to whether a MDT was placed, the enrolled patients were divided into two groups. Specifically, 138 patients with only one 26-Fr pleural drainage tube were divided into the “Control Group” and 174 patients with a pleural drainage tube and an additional 26-Fr MDT were divided into the “Tube Group”. All the patients received homogeneous postoperative care and nutrition support according to the treatment principles. Among the recruited 312 patients, 26 patients (8.3%) suffered from AL, including 11 patients (8.0%) in the Control Group and 15 patients (8.6%) in the Tube Group. There was no significant difference in the AL rate between the two groups ( $P = 0.837$ ), which demonstrated that placing an MDT could not change the incidence of AL. In terms of postoperative pain associated with the drainage tube, patients in the Tube Group had a similar pain score on post-operative day 1 ( $P = 0.629$ ), 2 ( $P = 0.347$ ), 3 ( $P = 0.157$ ), 4 ( $P = 0.799$ ) and 5 ( $P = 0.190$ ) when compared with patients in the Control Group.

Table 1  
Demographic and perioperative features of the patients.

	Control Group	Tube Group	P value	Total
<b>Age</b>	64.51 ± 5.13	64.36 ± 4.83	0.790	64.42 ± 4.96
<b>Gender</b>			0.739	
Male	118 (85.5%)	152 (87.4%)		270 (86.5%)
Female	20 (14.5%)	22 (12.6%)		42 (13.5%)
<b>Smoking</b>			0.204	
No	25 (18.1%)	22 (12.6%)		47 (15.1%)
Yes	113 (81.9%)	152 (87.4%)		256 (84.9%)
<b>Surgical approach</b>			0.812	
Right	91 (65.9%)	112 (64.4%)		203 (65.1%)
Left	47 (34.1%)	62 (35.6%)		109 (34.9%)
<b>Anastomic leakage</b>			0.837	
No	127 (92.0%)	159 (91.4%)		286 (91.7%)
Yes	11 (8.0%)	15 (8.6%)		26 (8.3%)
<b>Postoperative pain score (NRS*)</b>				
Day 1	3.94 ± 1.27	4.01 ± 1.25	0.629	3.98 ± 1.26
Day 2	3.30 ± 1.04	3.41 ± 0.90	0.347	3.36 ± 0.97
Day 3	2.86 ± 0.86	2.98 ± 0.69	0.157	2.93 ± 0.77
Day 4	2.78 ± 0.96	2.76 ± 0.63	0.799	2.77 ± 0.79
Day 5	2.16 ± 0.70	2.26 ± 0.64	0.190	2.21 ± 0.66
* <b>NRS</b> : Numerical Rating Scale.				

As the AL occurred, hyperpyrexia ( $T \geq 38.5^{\circ}\text{C}$ ) and abnormal drainage fluid from the MDT or pleural drainage tube, including the rapidly increased drainage volume and the change of color and smell, were the earliest and most common symptoms. The drainage volume would suddenly greatly exceed that of the previous day, with the increment of more than 100 to 200 ml per day, and in the meantime, the drainage liquid would become feculent and rancid. As shown in Table 2, in this study, when the AL occurred, hyperpyrexia was observed in all patients, while abnormal drainage fluid was observed in all patients in the tube group, and only 7 patients (7/11, 63.6%) in the control group.

Table 2  
Treatments and outcomes of the patients with AL.

	Control Group	Tube Group	P value
<b>Occurrence time of hyperpyrexia (Day)</b>	5.27 ± 2.35	5.80 ± 1.87	0.693
<b>Abnormal drainage fluid</b>			
Number of patients	7 (63.6%)	15 (100%)	0.022
Occurrence time (Day)	6.86 ± 1.35	3.94 ± 0.88	
<b>AL* management</b>			
Conservative treatment	4 (36.4%)	12 (80.0%)	0.032
Re-operation	3 (27.3%)	0 (0%)	
Endoscopic treatment	4 (36.4%)	3 (20.0%)	
<b>Outcome of AL*</b>			
Patients recovered	8 (72.7%)	14 (93.3%)	
Hospital stay after AL* (Recovery time)	86.50 ± 28.52	56.64 ± 23.64	0.015
Mortality	3 (27.3%)	1 (6.7%)	0.188
* AL: Anastomotic Leakage			

In the tube group, the presentation of hyperpyrexia was a median of 5.80 ± 1.87 days after operation, that was later than the abnormal drainage fluid from the MDT (3.94 ± 0.88 days). However, in the control group, the abnormal drainage fluid from the pleural drainage tube appeared on a median of 6.86 ± 1.35 days after surgery in the aforementioned 7 patients, that was intermittent and occurred later than hyperpyrexia, which appeared on a median of 5.27 ± 2.35 days after surgery. When persistent hyperpyrexia or abnormal drainage fluid was observed, the AL was highly suspected and the esophageal iodology was performed to confirm the diagnosis (Fig. 1). These results suggested that the abnormal drainage fluid was more likely to appear in the MDT than that in the pleural drainage tube (P = 0.022), and the occurrence of the abnormal drainage fluid in the MDT was earlier than that of hyperpyrexia. As a result, the placement of a MDT could be a more sensitive and specific method for early diagnosis of AL.

Then the therapeutic effect of the MDT was analyzed. In the tube group, as the MDT placed during the surgery was next to the anastomotic stoma and was usually located in the abcess cavity, there was no need to place another drainage tube after the the AL occurred. After diagnosed to be AL, all patients in the tube group received normal saline flush through the MDT twice a day, enteral and parenteral nutrition support, and anti-infective therapy, among them, 12 patients (80.0%) recovered without any other treatment, 3 patients (20.0%) received endoscopic therapy, including self-expandable metallic stents and

over-the-scope-clip. However, in the control group, as the pleural drainage tube was not close to the anastomotic stoma, the abnormal drainage fluid was observed in only seven patients (63.6%). All of the patients in the control group underwent CT-guided or ultrasound-guided chest tube placement to manage the abscess cavity, nevertheless, three of them (27.3%) still needed re-operation to eliminate the abscess cavity, place another drainage tube next to the anastomotic stoma, and plus jejunostomy, four patients (36.4%) received endoscopic therapy, and only four patients (36.4%) recovered with conservative therapy alone. Furthermore, the recovery time of the patients in the tube group ( $56.64 \pm 23.64$ ) was significantly shorter than that in the control group ( $86.50 \pm 28.52$  days) ( $P = 0.015$ ). These results suggested that the placement of a MDT could be convenient for draining and cleaning the abscess cavity, that would accelerate the recovery and reduce the complication and re-operation rate in patients suffered from AL.

At last, the comparison of mortality between the two groups was analyzed. Among the 26 patients who had AL, 1 patient (6.7%) died of severe anastomotic hemorrhage in the tube group, while 3 patients (27.3%) died of respiratory failure or systemic infection secondary to the empyema in the control group, which suggested that the placement of a MDT could reduce the mortality rate after AL. There was no statistical difference in mortality associated with AL between two groups ( $P = 0.188$ ), perhaps because there were limited number of AL cases in this study.

## Discussion

AL after esophagectomy is a severe postoperative complication with potential poor prognosis. In recent years, a wide range of measures to prevent AL has been suggested, including improvement in anastomotic techniques<sup>[15-17]</sup> and gastric tube formation<sup>[18,19]</sup>, utilization of pedicled omental flaps<sup>[20,21]</sup> or mobilized pleura<sup>[22]</sup>, avoiding excessive tension at the anastomosis<sup>[23]</sup>, intraoperative perfusion monitor<sup>[24,25]</sup>, efficient gastric decompression<sup>[26]</sup>, and meticulous perioperative management. Nevertheless, among them, only few interventions are supported by strong clinical evidence, and then anastomotic leakage has still been an important postoperative complication.

Because of the lack of typical symptoms and effective real-time monitoring method, early diagnosis of introthoracic esophageal AL remains to be a problem. A wide variety of clinical manifestations have been included as early symptoms to diagnose AL, such as hyperpyrexia, thoracodynia, chest distress and tachycardia<sup>[8-12]</sup>. According to the literatures, hyperpyrexia, which results from systemic infection secondary to the sepsis cavity around the anastomotic fistula, may be the earliest symptom of AL in most cases<sup>[8,23,27]</sup>, nevertheless, sometimes the first symptom may only be mild tachycardia or atrial fibrillation<sup>[9,12]</sup>. Unfortunately, the occurrence of hyperpyrexia or tachycardia is nonspecific for diagnosis and prone to be neglected in clinical practice, worse still, these symptoms usually appear several hours or even several days later than that of the AL. In contrast, abnormal liquid from the pleural drainage tube, including the rapidly increased drainage volume and the change of color and smell, can be a specific symptom for AL diagnosis, however, due to the postoperative pleural adhesion and the distance between the anastomotic stoma and the pleural drainage tube, it also appears relatively late or even never appears

in most cases. To solve the problems mentioned above, we hypothesized that, once the AL occurs, increased and feculent liquid could be immediately drained out through a tube, which was placed just beside the anastomotic stoma in the esophagus bed during the operation, and could be easily observed to make a diagnosis. As a result, in this study, the occurrence of abnormal fluid from the MDT was earlier than that of hyperpyrexia, that endowed the MDT with better sensitivity and specificity.

As to AL treatment, there has been no widely accepted or standardized strategy till now. In general, the basic principles of treatments are the closure of the anastomotic fistula, containment of the leakage, drainage of fluid collections and effective control of infection<sup>[8]</sup>. Re-operation is one of the most effective treatment to manage the anastomotic fistula, nevertheless, because of the poor physical status of the patients with AL, even in the absence of a consensus guideline, current strategies are still prone to shift from aggressive surgery to more conservative approaches<sup>[13]</sup>, such as endoscopic treatment<sup>[14]</sup>. Self-expandable metallic stents was applied through endoscopy to cover the fistula and reduce the leakage<sup>[28]</sup>. Over-the-scope-clip system could restrain the leakage by closing the fistula directly<sup>[29,30]</sup>. There were also reports about endoluminal suturing techniques<sup>[31]</sup> or use of sealants<sup>[32,33]</sup> for AL treatment. Nevertheless, without complete drainage and clearance of the sepsis cavity, the efficacy of the aforementioned strategies would be significantly restricted. To address this problem, endoluminal vacuum therapy was developed to remove secretions by continuous negative pressure suction<sup>[34-36]</sup>, however, in most cases, the local infection around the anastomotic fistula had already been severe when this therapy was applied, and vacuum through esophageal lumen could not completely eliminate the sepsis cavity outside. In this study, an MDT was placed just beside the anastomotic stoma during operation and was demonstrated to prevent the retention of the fluid from the fistula, decrease bacterial contamination, alleviate the local infection, and be convenient for flushing, so as to promote granulation tissue proliferation and fistula closing.

In addition, postoperative pain and safety is also a major concerns for surgeons and patients. In this study, there was no significant difference in the recorded pain scores or the incidence of AL between the two groups, that made the placement of MDT an adequate method for early diagnosis and effective treatment in intrathoracic AL.

## Conclusions

In conclusion, placing an MDT in the esophagus bed just beside the anastomotic stoma during the operation is a safe and effective method to diagnose and treat the introthoracic AL. The MDT showed excellent sensitivity and specificity in early diagnosis of the leakage and provided an approach for complete drainage and thorough cleaning. In our point of view, the MDT could be strongly recommended to be a routine procedure during esophagectomy.

## Abbreviations

AL

Anastomotic Leakage

MDT

Mediastinal Drainage Tube

NCCN

National Comprehensive Cancer Network

## Declarations

**Ethics approval and consent to participate:** This study was reviewed and approved by human research ethics committee of Hwa Mei hospital, (No. PJ-NBEY-KY-2020-163-01) and the informed consent forms were signed by participants.

**Consent for publication:** The informed consent forms for publication were signed by participants.

**Availability of data and materials:** The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**Competing interests:** The authors declare that they have no competing interests.

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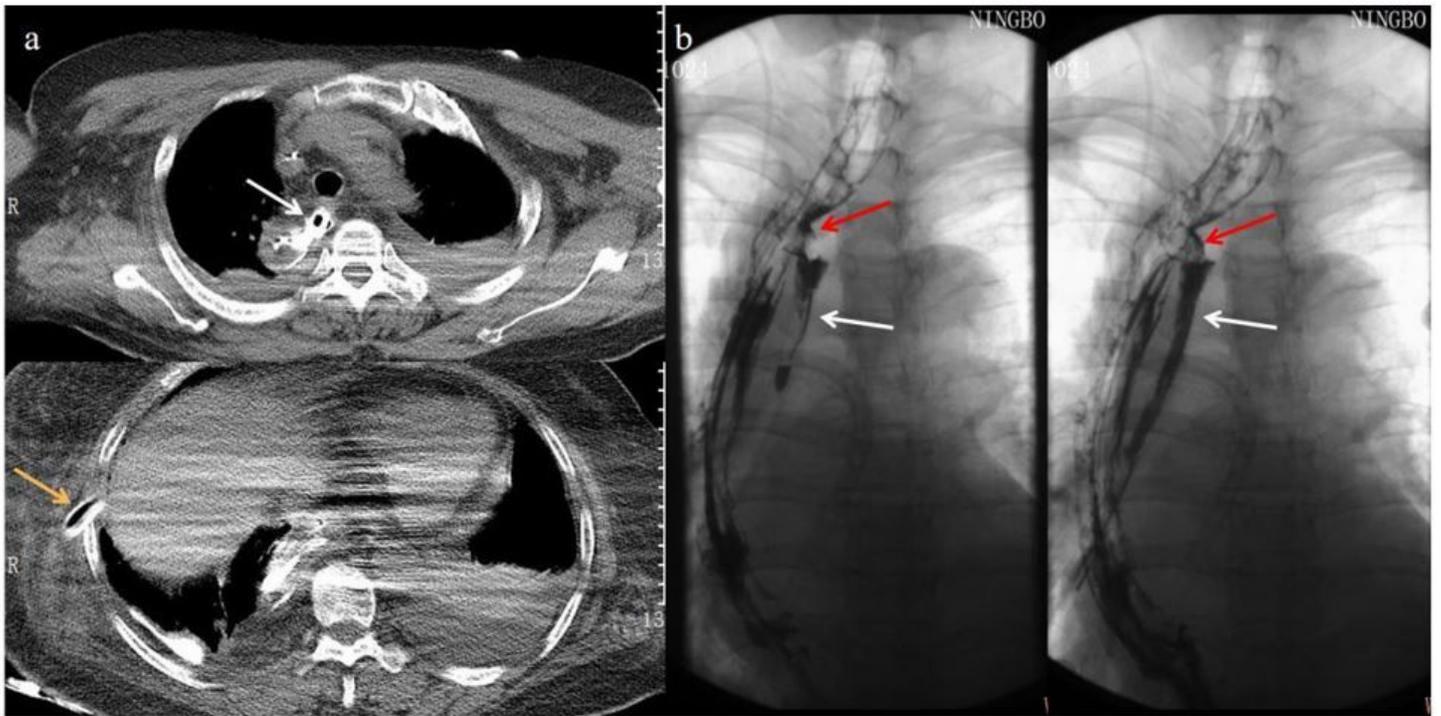
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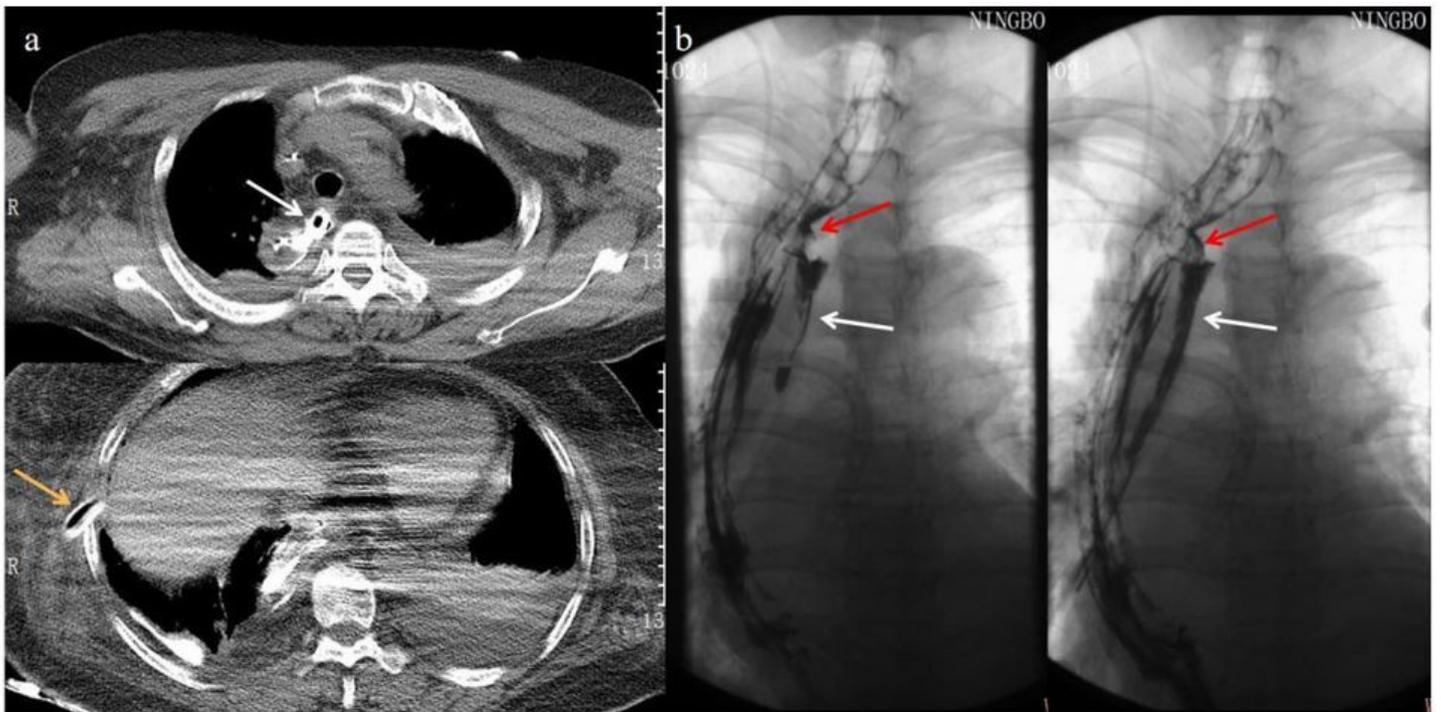
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# Figures



**Figure 1**

The exact location of the drainage tubes (a) and the good drainage effect of the mediastinal drainage tube (b). The white arrow indicates the mediastinal drainage tube. The yellow arrow indicates the pleural drainage tube. The red arrow indicates the anastomotic fistula.



## Figure 1

The exact location of the drainage tubes (a) and the good drainage effect of the mediastinal drainage tube (b). The white arrow indicates the mediastinal drainage tube. The yellow arrow indicates the pleural drainage tube. The red arrow indicates the anastomotic fistula.



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