The Outcome of Self-expandable Metallic Stent for Malignant Tracheobronchial Stenosis Following Esophageal Stenting

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Abstract
Background: Tracheobronchial stenosis following esophageal stenting is rare. We aim to explore the outcome of SEMS for malignant tracheobronchial stenosis following esophageal stenting.

Methods: Clinical and imaging data of 20 patients (12 males, 8 females) with malignant tracheobronchial stenosis following esophageal stenting from Jan 2014 to Jan 2019 were retrospectively analyzed. Data of the location of tracheobronchial stenosis, stent types, Borg score before and after airway stenting, indication of esophageal stent placement, interval between double stents placement and survival time after airway stenting were collected.

Results: A total of 20 stents (13 Y-shaped stents, 7 tube stents) were successful placement in all patients without procedure-related complications happened. Seven of them are tracheal stenosis, 5 carina stenosis and 8 multiple stenosis. The mean Borg score before and after airway stenting are 6.6±1.1 and 1±0.5 (P<0.001). The interval between double stents placement in patients who received chemoradiotherapy is 146.29±106.77 days, while in palliation therapy is 41.83±146.29 days(P<0.05). The mean survival time after esophageal stenting in patients who received chemoradiotherapy is 232.79 ±97.71 days, while in palliation therapy is 163 ± 113.50 days(P=0.230).

The mean survival time after airway stenting in patients who received chemoradiotherapy is 86.5 ±52.47 days, while in palliation therapy is 121.17 ± 113.48 days(P=0.461).

Conclusion: The application of SEMS in malignant tracheobronchial stenosis following esophageal stenting is safe and effective. Chemoradiotherapy is a factor affect the interval between double stents placement.

Background
Tracheobronchial stenosis following esophageal stenting is rare. It is estimated that esophageal stent related complications are nearly 11–46.2%, commonly are retrosternal pain, hemorrhage, pneumonia, fever, fistula, perforation and pressure necrosis, while trachea compress after esophageal stent placement account for 1%[1-5].

In patients with advanced or recurrent esophageal cancer, surgical resection was impossible.

Malignant esophageal stenosis could deteriorate the life quality of patients and bring malnutrition.
Self-expandable metallic stents (SEMS) placement is an effectively way in diminishing intrinsic obstructive symptoms. Because they can recover the passage of food quickly. Esophageal fistula and malignant extrinsic compression also the indication for esophageal stent placement[6].

In cases with esophageal cancer invading trachea and bring malignant stenosis, double stenting or parallel stenting was development to deal with it. Several studies have demonstrated the feasibility and safety of this method[7-12]. Generally, tracheal stent was placed first to prevent the expansion of esophageal stent aggravate tracheal stenosis and bring dyspnea. Then esophageal stent was placed to recover the passage of food and improve the quality of life. However, in cases without severe stenosis, the placement of tracheal stent could be delayed until the indication of tracheal stent emerged. After all the placement of tracheal stent could bring a series of complications.

After esophageal stenting, tracheal stenosis could occurrence with tumor growth. The remove of esophageal stent is not a good method to reduce the compression of trachea. Tracheal stent placement is the only way to palliative restore the patency of airway. Here, we introduce the experience of tracheal SEMS placement for tracheobronchial stenosis following esophageal stent expansion and tumor growth.

**Methods**

This is a retrospective study. Informed consent was obtained from all the participating subjects, and the ethics committee approved our study. Between January 2014 and January 2019, 20 consecutive patients who received SEMS placement for tracheobronchial stenosis following esophageal stenting were enrolled in this study. The patient group was consisted of 8 females and 12 males, aged 51–85 years (mean 67 ± 10.12 years). All of them are esophageal squamous cell carcinoma. The characteristics of these 20 patients are shown in Table 1.
Table 1
Characteristics of the patient

|                              | No   |
|------------------------------|------|
| Gender                       |      |
| Male                         | 12   |
| Female                       | 8    |
| Location of stenosis         |      |
| T                            | 7    |
| C                            | 5    |
| T + C + L                    | 2    |
| C + L                        | 3    |
| T + C                        | 3    |
| Indication for ES            |      |
| Fistula                      | 5    |
| Stenosis                     | 15   |
| Treatment before ES          |      |
| Palliative treatment         | 6    |
| Chemoradiotherapy            | 14   |
| Borg score                   |      |
| Before stenting              | 6.6 ± 1.1 |
| After stenting               | 1 ± 0.5 |
| Type of TS                   |      |
| Tube                         | 7    |
| Y-shaped                     | 13   |
| Interval between 2 stents    |      |
| Palliative treatment         | 146.29 ± 106.77 days |
| Chemoradiotherapy            | 41.83 ± 146.29 days |
| Complication                 |      |
| Esophageal fistula           | 1    |

T: Trachea, C: Carina, L: Left main bronchus, ES: Esophageal stenting, TS: Tracheal stent.

Before esophageal stenting, 14 of them received chemoradiotherapy, while the other 6 patients received palliative therapy. The indication for esophageal stenting were dysphagia (n = 15) and fistula (n = 5). After stenting, the symptom of digestive tract got improved, no procedure related severe complications happened. However, after a period of time, with stent expansion and tumor progression, all the patient complaint dyspnea (Fig. 1A-C). Modified Borg Sore was used to assess the dyspnea of patients. CT was performed to demonstrate the location of stenosis. Meanwhile, the diameter of tracheobronchial and length of stenosis was measured. A suitable tracheal stent was chosen to placement (Fig. 1D).

Tracheal stent insertion:

All the 20 patients received tracheal self-expandable metal stent (SEMS) placement under the guidance of fluoroscopy. Before stenting, 10 mg dexamethasone and anisodamine was used intravenous and intramuscular, respectively. High-flow oxygen was given through a nasal cannula. Blood pressure, heart rate, blood oxygen saturation and ECG were monitored. A 5F multipurpose catheter containing a 0.035inch hydrophilic guide wire was entered the trachea with local anesthesia.
Contrast agent was injected to show the stenosis. Then, a super stiff guide wire was exchanged through the catheter. The delivery system was introduced over the super stiff guide wire to the stenosis site and released. In the cases that stenosis involved carina or main bronchus, two super stiff guide wires were introduced to right and left main bronchus. The delivery system that contained Y-shaped stent was introduced to the trachea. Once the two branches reached the two main bronchus, the stent was released (Fig. 2). Poststenting 1 day, all cases were assessed by modified Borg score again. After stent insertion 3–5 days, the thoracic CT was performed to evaluate the location and expansion of tracheal stent.

Statistical analysis:
Continuous variables are summarized as mean ± standard deviation value. The paired-sample t test was performed to compare the modified Borg score prior to and following stenting. The Wilcoxon signed-rank test was used to analyzed the difference of interval time of double stenting between the group which received treatment and none. The survival time after esophageal and tracheal stenting was calculated using Kaplan-Meier curves. All statistical calculations were performed by SPSS (version 21.0; USA). P value < 0.05 was considered as statistically significant.

Result:
A total of 20 tracheal stents (7 tube stents and 13 Y-shaped stents) were successfully inserted in 20 patients. No procedure-related complications happened. The mean modified Borg score prior to and following SEMS placement are 6.6 ± 1.1 and 1 ± 0.5, respectively. there was a significantly statistic difference between before and after airway stenting(P < 0.001). The interval between double stents placement in patients who received chemoradiotherapy is 146.29 ± 106.77 days, while in who received palliation therapy is 41.83 ± 29.8 days. There was a significantly difference between the two groups(p = 0.007).

All patients died during the follow up. one patient received esophageal stenting due to esophageal fistula formation one month after airway stenting. Two patients performed esophageal stenting again for restenosis at 12 days and 5 months after airway stenting, respectively. One patient received another tracheal stent after airway stenting 9 months due to restenosis. The mean survival time after
esophageal stenting and tracheal stenting are 211.85 ± 104.88 days (range:79–429 days) and 96.9 ± 74.42 days (range:12–317 days), respectively. The mean survival time after esophageal stenting in patients who received chemoradiotherapy is 232.79 ± 97.71 days, while in palliation therapy is 163 ± 113.50 days. There was no statistic difference between the two groups(P = 0.230). The mean survival time after tracheal stenting in patients who received chemoradiotherapy is 86.5 ± 52.47 days, while in palliation therapy is 121.17 ± 113.48 days. There was no significant statistic difference between the two groups(p = 0.461) (Fig. 3).

Discussion
This study demonstrated the safety and effectiveness of SEMS placement in palliation therapy of tracheobronchial stenosis following esophageal stenting. We also observed that chemoradiotherapy in esophageal cancer could effectively extending the interval between double stents placement.

Dysphagia is a common symptom in malignant esophageal cancer patients, which deteriorate the quality of life and cause malnutrition. Esophageal SEMS placement is an effectively way in diminishing intrinsic obstructive symptoms. Because they can recover the passage of food quickly. The membrane part of trachea connect esophagus closely. With the expansion of esophageal stent and tumor growth, it is easy to be invasion when tumor growth. As a complication of esophageal stent placement, Łochowski et al[1] reported that the incidence of trachea compress after esophageal stent is about 1% (9/1309), and they described complications as early complication and late complication. It is said that early complications resulting from the procedure of stent placement and late complications resulting mostly from the patient’s cancer. In our study, the interval of double stents placement is from 16 to 308 days. The tracheal stenosis not result from the procedure of esophageal stent placement. Thus, we conclude that the tracheobronchial stenosis was caused by esophageal stent expansion and tumor growth.

Malignant tracheobronchial stenosis is an intractable and often life-threatening disease. Verma[13] and colleagues reported that the median survival in advanced esophageal cancer with central airway obstruction is about 2.8 months. Non-pulmonary malignant tracheal stenosis are more likely to cause extraluminal obstruction. Laser and other bronchoscopic intervention except stent placement
may benefit little\textsuperscript{14}. Stent placement combined with bronchoscopic intervention can provide a safe and effective palliative treatment for patients with malignant airway stenosis\textsuperscript{15}. The mean survival time after tracheal stenting in patients who received chemoradiotherapy is 86.5 ± 52.47 days, which is similar with the 2.8 months median survival time. While in patient who received palliation therapy, the median survival time is 121.17 ± 113.48 days. SEMS placement is the only intervention in advanced esophageal cancer with central airway obstruction. The overall mean survival time after SEMS placement in tracheobronchial stenosis following esophageal stenting is 96.9 ± 74.42 days in this study. It is higher than the 2.8 months median survival time. Indeed, the placement of SEMS prolong the median survival time of patients with malignant tracheobronchial stenosis following esophageal stenting.

In our study, chemoradiotherapy play an important role in extending the interval between double stents placement. In other’s studies, the combination of chemoradiotherapy and esophageal stent placement play a negative role on esophagus. Lu et al.\textsuperscript{16} reported that the rate of esophageal fistula formation during or after chemoradiotherapy was 7.5% in the SEMS plus chemoradiotherapy group and 2.6% in the chemoradiotherapy group. Patients treated with SEMS placement followed by chemoradiotherapy had higher risk of esophageal fistula formation. Reijim et al.\textsuperscript{2} reported that stent-related major complications have increased, which seems to be mainly associated with more frequent use of chemoradiotherapy prior to SEMS placement. These major complications were defined as life-threatening or severe complications, including perforation, hemorrhage, pneumonia, fever, fistula, or pressure necrosis. While, in our study, only one patient formed trachoesophageal fistula after double stents placement.

Patients with advanced esophageal cancer and airway invasion have no indication for surgical resection. Tracheal stent placement may be the best way to restore patency. After double stents placement, the life-threatening complications is 20%, including deaths following esophagotracheal fistula, massive hematemesis and airway restenosis\textsuperscript{8, 16}. While, in our study, except massive hematemesis, both the esophagotracheal fistula and airway restenosis have encountered. One
tracheal restenosis and one tracheoesophageal fistula formation. The management of this complications are palliative therapy. Another longer covered esophageal stent for tracheoesophageal fistula and another longer tracheal stent for tracheal restenosis. The present study was limited by its retrospective design. Secondly, the sample size is small, making it hard to draw a definitively conclusion. However, considering the fact that tracheal stenosis caused by esophageal cancer and stent is rare, we do believe that the data is sufficient to demonstrate the feasibility.

Conclusion
In conclusion, the application of SEMS in malignant tracheobronchial stenosis following esophageal stenting airway stenting is safe and effective. Chemoradiotherapy is a factor affect the interval between double stents placement.

Abbreviations
SEMS: Self-expandable metallic stent. CT: Computed tomography.

Declarations
Ethics: This study obtained approval from the institutional review board of the first affiliated hospital of Zhengzhou University. Written informed consent was obtained from all patients.

Availability of data and materials: Please contact author for data requests.

Consent for publication: Not applicable.

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Authors' contributions: YHL, HXW and RJZ designed study. YHL, ZHZ, KWR and LHB performed study. YHL, ZML, ZNL, JFL, XLZ, JJC collected and analyzed data. All authors wrote the paper and finally approved of the version to be published.

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References
[1] Łochowski M, Brzeziński D, Rębowski M, et al. Complications after treating esophageal strictures with prostheses and stents - 20 years' experience[J]. Videochir Inne Tech Maloinwazyjne, 2016,11(4): 295-299.
[2] Reijm A, Didden P, Schelling S, et al. Self-expandable metal stent placement for malignant esophageal strictures - changes in clinical outcomes over time[J]. Endoscopy, 2018.

[3] Aneeshkumar S, Sundararajan L, Santosham R, et al. Erosion of esophageal stent into left main bronchus causing airway compromise[J]. Lung India, 2017,34(1): 76-78.

[4] Binkert C, Petersen B. Two fatal complications after parallel tracheal-esophageal stenting[J]. Cardiovasc Intervent Radiol, 2002,25(2): 144-147.

[5] Paganin F, Schouler L, Cuissard L, et al. Airway and esophageal stenting in patients with advanced esophageal cancer and pulmonary involvement[J]. PLoS One, 2008,3(8): e3101.

[6] Rhee K, Kim JH, Jung DH, et al. Self-expandable metal stents for malignant esophageal obstruction: a comparative study between extrinsic and intrinsic compression[J]. Dis Esophagus, 2016,29(3): 224-228.

[7] De Olabozal J, Roberts J, Hoeltgen T, et al. Double stenting to prevent airway compression in proximal malignant esophageal strictures[J]. Am J Gastroenterol, 2001,96(9): 2800-2801.

[8] Fu YF, Lv LL, Xu H, et al. Double Stent Insertion for Combined Malignant Airway and Esophageal Stenoses: Feasibility, Safety, and Long-Term Outcome[J]. J Laparoendosc Adv Surg Tech A, 2016,26(1): 11-16.

[9] Herth FJ, Peter S, Baty F, et al. Combined airway and oesophageal stenting in malignant airway-oesophageal fistulas: a prospective study[J]. Eur Respir J, 2010,36(6): 1370-1374.

[10] Lechleire S, Antonietti M, Di Fiore F, et al. Double stenting of oesophagus and airways in palliative treatment of patients with oesophageal cancer is efficient but associated with a high morbidity[J]. Aliment Pharmacol Ther, 2007,25(8): 955-963.

[11] Nasir BS, Tahiri M, Kazakov J, et al. Palliation of Concomitant Tracheobronchial and Esophageal Disease Using a Combined Airway and Esophageal Approach[J]. Ann Thorac Surg, 2016,102(2): 400-406.

[12] Nomori H, Horio H, Imazu Y, et al. Double stenting for esophageal and tracheobronchial stenoses[J]. Ann Thorac Surg, 2000,70(6): 1803-1807.

[13] Verma A, Goh SK, Tai DYH, et al. Outcome differences between recanalized malignant central airway obstruction from endoluminal disease versus extrinsic compression[J]. Lasers in medical science, 2019,34(5): 955-962.

[14] Li Y, Ren J, Chen J, et al. Letter about outcome differences between recanalized malignant central airway
obstruction from endoluminal disease versus extrinsic compression]. Lasers in medical science, 2019, 34(8): 1723.

[15] Niu JM, Zhang J, Qiu XJ, et al. Comparison of clinical features and stent placement outcomes between airway stenosis caused by primary pulmonary malignancies and that caused by primary non-pulmonary malignancies]. Chin Med J (Engl), 2019, 132(4): 431-436.

[16] Lu YF, Chung CS, Liu CY, et al. Esophageal Metal Stents with Concurrent Chemoradiation Therapy for Locally Advanced Esophageal Cancer: Safe or Not?[J]. Oncologist, 2018, 23(12): 1426-1435.

Figures
Figure 1

A, Enhanced CT suggest esophageal cancer and strictures. B, Esophageal stent placement restore the pantancy of esophagus. C, Tracheal stenosis caused by esophageal tumor growth and stent expansion.

D, Tracheal stent placement restore the pantancy of trachea.
Figure 2

Esophageal stent and tracheal stent (A, Y-shaped; B, tube) on fluoroscopy.
Survival time after esophageal stenting (A) and airway stenting (B) in patients received palliative treatment and chemoradiology.