


## ORIGINAL RESEARCH

# Type and morphology affect the success rate of bronchoscopy for postintubation tracheal stenosis

Mingyuan Yang MS<sup>1</sup> | Hong Li BS<sup>1</sup> | Yunzhi Zhou MS<sup>2</sup> | Huafeng Wei MD<sup>3</sup> | Qinghao Cheng MD<sup>1</sup> 

<sup>1</sup>Center of Anesthesiology and Pain, Emergency General Hospital, Beijing, China

<sup>2</sup>Department of Pulmonary and Critical Care Medicine, Emergency General Hospital, Beijing, China

<sup>3</sup>Department of Anesthesiology and Critical Care, University of Pennsylvania, Philadelphia, Pennsylvania, USA

## Correspondence

Qinghao Cheng, Center of Anesthesiology and Pain, Emergency General Hospital, Beijing 100028, China.

Email: [cqh4000@163.com](mailto:cqh4000@163.com)

## Abstract

**Objective:** With advancements in respiratory interventional techniques, bronchoscopic intervention technology has emerged as a viable approach for managing postintubation tracheal stenosis (PITS). However, there was a paucity of research investigating the potential impact of stenosis characteristics and morphology (such as stenosis degree, length, type, and morphology) on bronchoscopic intervention treatment prognosis for PITS patients. This study was to assess the impact of various preoperative stenosis characteristic factors on the bronchoscopic cure rate among patients.

**Methods:** This is a retrospective study analyzing the medical records of patients with PITS who received bronchoscopic intervention at the tertiary interventional pulmonology center.

**Results:** Among the cases, 115 individuals achieved a success rate of 79.86% for bronchoscopic intervention therapy and were assigned to Group S. On the other hand, 29 cases required surgical intervention, accounting for a surgical treatment rate of 20.14% and were assigned to Group F. The stenosis in the Group F predominantly exhibited irregular shapes with scar granulation accompanied by tracheal chondromalacia collapse. Patients in group S experienced fewer total procedures, rigid bronchoscopy treatment, intraoperative hypoxemia, needed emergency re-bronchoscopy in 24 h and transferred to ICU postoperatively. Patients with pure scar and granuloma, the rate of bronchoscopic success cure was higher than patients with scar granulation accompanied by tracheal chondromalacia (odds ratio: 8.208; 95% confidence interval: 2.755–24.459), and regular stenosis morphology was associated with a higher bronchoscopic success cure rate (odds ratio: 9.463; 95% confidence interval: 3.128–28.623).

Mingyuan Yang and Hong Li contributed equally to this study.

**Trial Registration:** Chinese Clinical Trial Registry on 23/03/2020. Registration number: ChiCTR2000031190.

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**Conclusion:** Irregular airway stenosis, chondromalacia or airway collapse are key factors affecting the success rate of bronchoscopic treatment for post-intubation tracheal stenosis.

**Level of evidence:** 4 (historically controlled studies).

**KEYWORDS**

bronchoscopy intervention, postintubation tracheal stenosis, stenosis length, stenosis morphology, stenosis type

## 1 | BACKGROUND

The annual incidence rate of postintubation tracheal stenosis (PITS) in the general population is approximately five cases per million, and this probability has significantly escalated with the emergence of the COVID-19 pandemic.<sup>1-4</sup> The main etiology is ischemic injury to the airway wall due to high cuff pressure,<sup>5</sup> which appears several hours after intubation with fibrotic changes in the target tissue.<sup>6,7</sup> Surgical trachea-end-to-end resection and anastomosis is considered to be an effective treatment for tracheal stenosis.<sup>8,9</sup> With advancements in respiratory interventional techniques, bronchoscopic intervention technology has emerged as a viable approach for managing airway stenosis,<sup>10-13</sup> demonstrating an impressive efficacy rate up to 98.6% in patients with PITS. Dorris et al.<sup>14</sup> reviewed that bronchoscopic intervention is often attempted as the first approach to avoid surgical interventions in cases of PITS that are less severe and extensive.

The success rate of endoscopic treatment is closely correlated with the specific severity of the lesion, and this heterogeneity arises length of the stenosis.<sup>15</sup> The type of stenosis is also a predictor of patient outcome.<sup>16</sup> An animal study has demonstrated that tracheal stenosis exhibits distinct pathological characteristics at different stages, which in turn necessitate diverse treatment approaches and airway management methods.<sup>17</sup> However, there was a paucity of research investigating the potential impact of stenosis characteristics and morphology on bronchoscopic intervention treatment prognosis for PITS patients.

The hypothesis was formulated that the presence of different preoperative airway stenosis patterns would have an impact on the potential curative effect of bronchoscopy in patients. Therefore, this study retrospectively analyzed the long-term clinical prognosis and preoperative pathological characteristics of PITS patients undergoing bronchoscopy. The objective of this study was to assess the impact of various preoperative stenosis characteristic factors on the bronchoscopic cure rate among patients, aiming to enhance treatment options for individuals.

## 2 | MATERIALS AND METHODS

### 2.1 | Study design

This is a retrospective study analyzing the medical records of patients with PITS who received bronchoscopic intervention therapy at the

tertiary interventional pulmonology center of Emergency General Hospital from April 2013 to September 2019. Ethical approval for this study (Ethical Committee number: K20-9) was provided by the Ethical Committee of Emergency General Hospital, Beijing, China (Chairperson Prof Qingyu Zeng) on 18 January 2020. It was registered in the Chinese Clinical Trial Registry on 23/03/2020 (Registration number: ChiCTR2000031190).

### 2.2 | Patients

The patients were derived from the pulmonology interventional center, Emergency General Hospital, undergoing bronchoscopic intervention therapy under anesthesia from April 2013 to September 2019. Inclusion criteria: (1) diagnoses of PITS, (2) consecutively treated with bronchoscopy interventional therapy, and (3) followed up for at least 1 year after the last treatment. Exclusion criteria: (1) patients with cardiac failure, respiratory failure and coma, (2) history of mental and neurological disorders, sedative or hypnotic drugs and alcohol abuse, and (3) follow-up was less than 1 year or lost. All patients of pulmonology interventional center were informed that the patients' clinical data might be used in clinical studies and signed the informed consent form on admission and before BI. Telephone-based interviews were performed monthly as a part of routine treatment after patients with PITS were discharged, which was the routine for such patients in the pulmonology interventional center. During the telephone follow-up, the interviewers also verbally obtained consent from both patients and their families to gather information data on the patients.

The enrolled patients were categorized into two groups based on the final treatment options. The patients were considered to have recovered if they remained free of symptoms for more than a year after the last bronchoscopic intervention therapy procedure. The patients who achieved successful resolution of airway stenosis through bronchoscopic interventional therapy were categorized into the bronchoscopic success group (Group S), whereas those who underwent successful surgical intervention were categorized into the bronchoscopic failure group (Group F). Different bronchoscopic intervention methods include cryotherapy, balloon dilation, cryotherapy plus balloon dilation, stent placement, laser treatment, electrocautery and argon plasma coagulation. Surgical interventions include T tube insertion, tracheotomy, and surgical tracheal end-to-end anastomosis.

## 2.3 | Data collection

Pre-operative general data, procedural data and post-operative data were collected and analyzed. Pre-operative general data included age, gender, intubation duration, interval days of onset breathless after extubation, stenosis length, stenosis type, stenosis morphology, modified British medical research council (mMRC) score<sup>18</sup> and Karnofsky Performance Status (KPS) score.<sup>19</sup> Procedural data included number of totals, flexible and rigid bronchoscopy, different bronchoscopic treatment methods. Post-operative data includes number of patients with intraoperative hypoxemia, reoperation in 24 h, transfer to ICU, patients' final degree of stenosis, mMRC and KPS scores.

The length of stenosis was categorized into two conditions: less than 2 cm and  $\geq 2$  cm. Stenosis types include simple scar granulation and scar granulation accompanied by tracheal chondromalacia collapse. The stenosis morphology was classified as either regular or irregular in shape. Stenoses with circle or oval shape were categorized as regular, whereas those with triangle and funnel shapes were considered irregular. The number of patients with intra-operative hypoxemia was calculated that patients who were considered to have hypoxemia during any bronchoscopic intervention session. The number of patients with post-operative transfer back to ICU was calculated that patients who were transferred back to ICU after any bronchoscopic intervention session. Similarly, patients were classified as having undergone 24-h surgery if they necessitated an additional emergency procedure within the first 24 h following their latest surgery.

## 2.4 | Statistical analysis

SPSS was used for data statistical analysis. Measurement data are presented in the form of mean  $\pm$  standard deviation, and counting data are presented in terms of quantity and percentage. Statistical counting data between two groups were compared by chi-square test. The measurement data between groups were compared by univariate analysis of variance. The correlation between preoperative stenosis factors and bronchoscopic treatment success condition was investigated by Pearson analysis and Binary logistics regression. When  $p < 0.05$ , the data was considered statistically different.

## 3 | RESULTS

A total of 201 patients were diagnosed with PITS from April 2013 to September 2019. In all, 17 patients were lost to follow-up and 40 patients were still undergoing bronchoscopic intervention therapy. Among the cases, 115 individuals achieved a success rate of 79.86% for bronchoscopic intervention therapy and were assigned to Group S. On the other hand, 29 cases required surgical intervention, accounting for a surgical treatment rate of 20.14% and were assigned to Group F. The flow diagram illustrating these findings is presented in Figure 1.

There was no significant difference in age, gender, intubation duration, interval days of onset wheezing after extubation, preoperative degree of stenosis, stenosis length and mMRC score between two groups ( $p > .05$ , respectively). While preoperative KPS score of patients in group F was significantly higher than that in group S ( $p = .048$ ). Stenosis type and morphology were statistically different between two groups ( $p = .000$ ,  $p = .000$ ). The stenosis in the failure group predominantly exhibited irregular shapes with scar granulation accompanied by tracheal chondromalacia collapse. The details are shown in Table 1.

The patients in group S experienced fewer total procedures and rigid bronchoscopy ( $p = .026$ ,  $p = .004$ ). There was no significant difference in details different treatment methods, including cryotherapy, balloon dilation, cryotherapy plus balloon dilation, stent implantation, laser treatment, electrocautery and argon plasma coagulation ( $p > .05$ , respectively). The details are shown in Table 2.

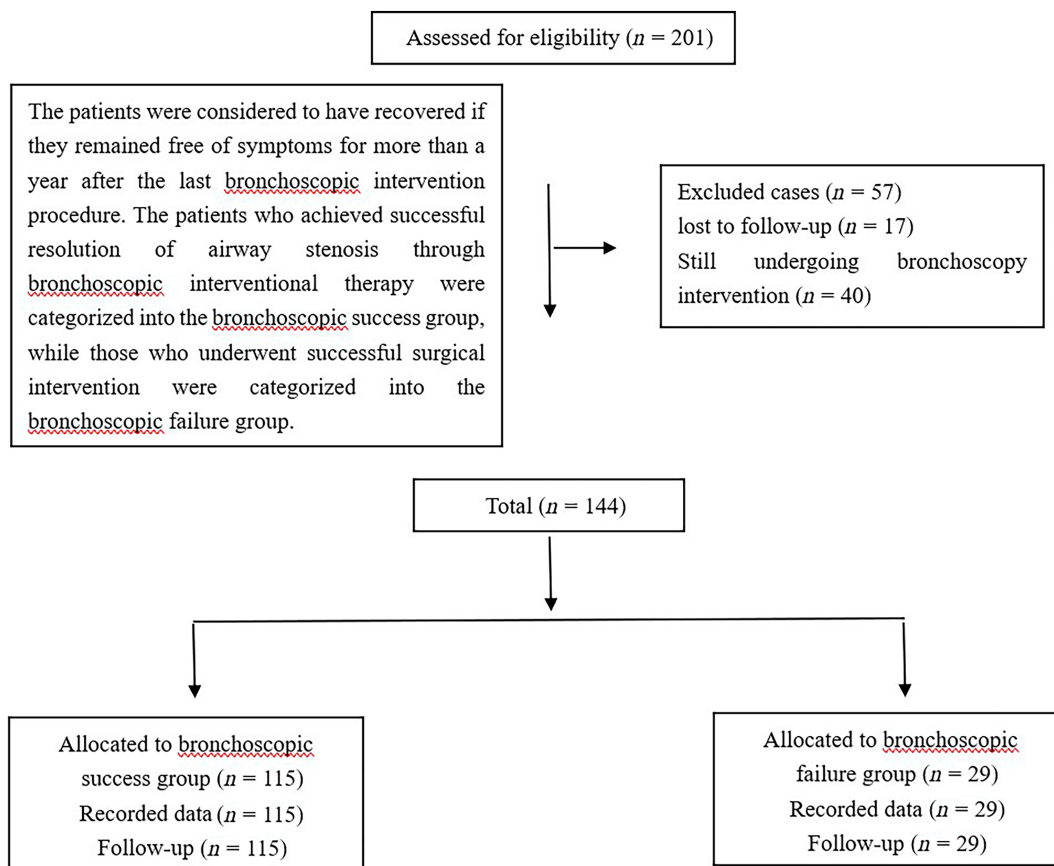
The number of patients who had experienced intraoperative hypoxemia, re-bronchoscopy in 24 h and transfer back to ICU were significantly different between two groups ( $p = .009$ ,  $p = .000$ ,  $p = .012$ ). Fewer patients in group S experienced intraoperative hypoxemia, needed emergency re-bronchoscopy in 24 h and were transferred to ICU postoperatively. Postoperative KPS score of patients in group S was significantly higher than that in group F ( $p = .006$ ). There was no significant difference in postoperative mMRC score and postoperative degree of stenosis between two groups ( $p > .05$ , respectively) (shown in Table 3).

Pearson analysis results showed that ultimate bronchoscopic success cure was significantly correlated with stenosis type ( $p = .000$ ) and stenosis morphology ( $p = .000$ ). In PITS patients with pure scar and granuloma, the rate of bronchoscopic success cure was higher than patients with scar granulation accompanied by tracheal chondromalacia (odds ratio: 8.208; 95% confidence interval: 2.755–24.459;  $p = .000$ ), and regular stenosis morphology was associated with a higher bronchoscopic success cure rate (odds ratio: 9.463; 95% confidence interval: 3.128–28.623;  $p = .000$ ) (shown in Figure 2).

## 4 | DISCUSSION

With the outbreak of COVID-19, more and more patients experienced PITS after long-term tracheal intubation,<sup>3,4</sup> especially for COVID-19 patients with prolonged intubation and obesity.<sup>1</sup> Despite technical improvements and specialized care for the management of critically ill patients, the incidence of PITS is still high as a severe complication after tracheal intubation. Veder et al.<sup>20</sup> found that cuffed tubes were still an important related risk factor.

With the continuous advancement of endoscopic technology, the treatment options for PITS have become increasingly diverse. Although surgery has been considered the gold standard of treatment, its significant invasiveness and prolonged recovery period often deter many patients. In contrast to traditional surgical procedures, bronchoscopic treatment necessitates multiple interventions and extended duration; however, it offers relatively minimal patient



**FIGURE 1** Flow diagram.

Group	Group S ( $n = 115$ )	Group F ( $n = 29$ )	<i>p</i> -Value
Age, years	46.42 ± 19.17	49.59 ± 15.88	.413
Male, <i>n</i> (%)	87 (75.7)	20 (69.0)	.481
Intubation duration, days	9.90 ± 7.40	13.79 ± 16.53	.060
Time of onset of breathless, days	28.29 ± 27.14	18.72 ± 20.41	.078
Preoperative mMRC score	3.17 ± 0.80	2.86 ± 1.03	.133
Preoperative KPS score	59.66 ± 16.79	66.26 ± 15.70*	<b>.048</b>
Preoperative degree of stenosis, %	77.76 ± 13.86	72.74 ± 17.86	.161
Stenosis length			
<2 cm, <i>n</i> (%)	98 (85.2)	24 (82.8)	.742
≥2 cm, <i>n</i> (%)	17 (14.8)	5 (17.2)	
Stenosis type			
Scar + granuloma, <i>n</i> (%)	102 (88.7)	13 (44.8)*	<b>.000</b>
Scar + granuloma + collapse, <i>n</i> (%)	13 (11.3)	16 (55.2)*	
Stenosis shape			
Regular shape, <i>n</i> (%)	100 (87.0)	11 (37.9)*	<b>.000</b>
Irregular shape, <i>n</i> (%)	15 (13.0)	18 (62.1)*	

**TABLE 1** Comparison of general and airway characteristics between two groups.

Note: Bold values indicates statistically significant  $p < 0.05$ .

Abbreviations: KPS, Karnofsky Performance Status; mMRC, modified British medical research council.

\*was statistically significant compared with Group S.

**TABLE 2** Comparison of bronchoscopy treatment characteristics between two groups.

Group	Group S (n = 115)	Group F (n = 29)	p-Value
Number of BI, n	7.37 ± 6.60	11.38 ± 13.98	<b>.026</b>
Number of flexible bronchoscopes, n	7.30 ± 6.75	9.21 ± 12.19	.261
Number of rigid bronchoscopes, n	0.74 ± 1.47	1.93 ± 3.26	<b>.004</b>
Cryotherapy, n	2.42 ± 5.67	3.17 ± 3.74	.498
Balloon dilation, n	0.97 ± 1.70	1.07 ± 3.38	.831
Cryotherapy + balloon dilation, n	3.97 ± 5.33	5.48 ± 10.81	.283
Stent implantation, n	0.25 ± 0.57	0.41 ± 0.98	.251
Laser treatment, n	0.67 ± 1.05	1.10 ± 1.29	.060
Electrocautery, n	0.56 ± 0.99	0.55 ± 0.78	.981
Argon plasma coagulation, n	0.57 ± 1.38	0.28 ± 0.80	.266

Note: Bold values indicates statistically significant  $p < 0.05$ .

**TABLE 3** Comparison of adverse events and post-operative stenosis characteristics between two groups.

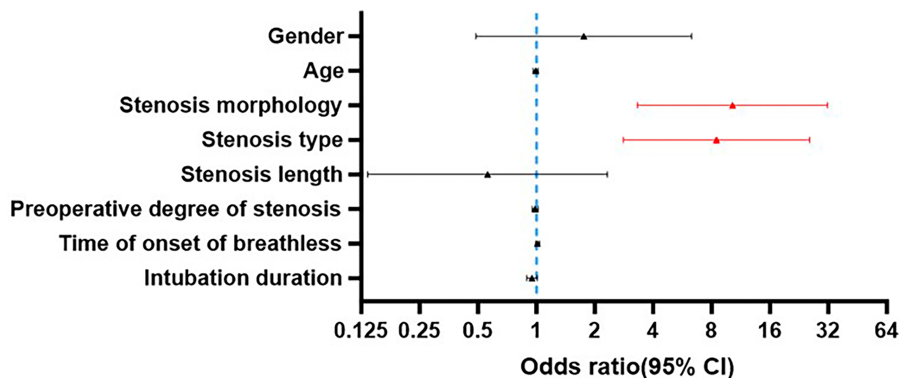
Group	Group S (n = 115)	Group F (n = 29)	p-Value
Number of patients with intraoperative hypoxemia, n (%)	56 (48.7%)	22 (75.9%)*	<b>.009</b>
Number of patients with re-bronchoscope in 24 h, n (%)	10 (8.7%)	10 (34.5%)*	<b>.000</b>
Number of patients with transfer to ICU, n (%)	3 (2.6%)	4 (13.8%)*	<b>.012</b>
Postoperative mMRC score	0.90 ± 0.51	1.10 ± 0.72	.090
Postoperative KPS score	86.26 ± 13.79	77.59 ± 19.58*	<b>.006</b>
Postoperative degree of stenosis, %	26.87 ± 12.36	26.21 ± 13.99	.802

Note: Bold values indicates statistically significant  $p < 0.05$ .

Abbreviations: KPS, Karnofsky Performance Status; mMRC, modified British medical research council.

\*was statistically significant compared with Group S.

**FIGURE 2** Variables associated with bronchoscopy cured results of binary logistic regression analysis. Odds ratios were reported with 95% confidence intervals.



discomfort.<sup>11,21,22</sup> Consequently, a considerable number of patients prefer noninvasive bronchoscopic intervention treatment as their primary choice, with surgery being considered only if the former proves ineffective.<sup>8,23-26</sup>

A study had reported limited efficacy of bronchoscopic intervention in treating complex, long-standing cartilage lesions.<sup>27</sup> The severity of complex tracheal stenosis is primarily influenced by factors such as the degree, length, type and morphology related variables. All these variables can affect the passage of gases through the stenosis into the lungs for oxygenation.<sup>28</sup> The success rate of bronchoscopic intervention treatment for PITS in this study was found to be 80%, which

analysis of data from previous patients with PITS and found that the type and morphology of stenosis observed in patients prior to treatment were the primary determinants for selecting the appropriate treatment approach.

The mean length of airway stenosis ranged from 1.6 to 1.8 cm,<sup>29,30</sup> so the patients were divided into two groups based on the length of stenosis, with an interval of 2 cm. A study had suggested that shorter tracheal stent lengths were associated with lower risks of recurrent tracheal stenosis after removal. Although the length of the tracheal stent is related to the length of tracheal stenosis, it cannot fully represent the length of stenosis.<sup>31</sup> Professor Sun and his

colleagues discovered that the length of airway stenosis did not exhibit a noteworthy disparity between the group of patients who achieved successful outcomes and those who experienced failure after undergoing bronchoscopic intervention for scarring central airway stenosis.<sup>27</sup> Through the retrospective analysis conducted in this study, no significant difference was found in the length of stenosis between the two groups. The length of stenosis was also not found to be an independent factor affecting the bronchoscopic cure rate.

The stenosis types in this study were categorized into two groups: one consisted of simple scar with granulation hyperplasia, whereas the other group included chondromalacia or collapse of the tracheal membrane along with scar granulation hyperplasia. Long-term intubation may even soften the trachea.<sup>32</sup> Collapse of the airway in the expiratory phase of spontaneous breathing can cause increased airway flow limitations and worsen airway obstruction, especially when patients cannot breathe on their own and muscle relaxants are used. The proportion of patient with chondromalacia or collapse of group F was more than group S. The surgical treatment is more frequently required for patients with chondromalacia or membrane collapse, and the bronchoscopic cure rate exhibits a significant decrease.

Stenosis morphology is another critical predictor of patient outcome. Irregular stenosis was the main shape in group F and regular stenosis was the main shape in group S. Severe collapse and irregular stenosis made it impossible to place a stent. In addition to that, only central airway collapse can be alleviated, whereas distal airway and small airway collapse cannot be alleviated. The findings of other studies also suggested that open surgery was recommended for patients with tracheal stenosis characterized by disappearance or softening of tracheal cartilage.<sup>15,33-35</sup>

Stenosis degree had been discussed and considered to be a major factor affecting ventilation in patients with airway stenosis.<sup>36-38</sup> The results of a 10-year retrospective study on patients with subglottic stenosis revealed a significant correlation between the severity of stenosis and the likelihood of reoperation, indicating that higher degrees of stenosis are associated with an increased probability for requiring subsequent treatment intervention.<sup>39</sup> The pre- and post-operation degree of stenosis did not exhibit a significant difference between the two groups, and correlation analysis revealed no statistical association between the degree of stenosis and ultimate bronchoscopic cure.

In addition to the aforementioned pathological and morphological characteristics of stenosis, there were also various factors that may impact treatment options and prognosis. Age and gender had been found to have a significant association with the incidence of PITS. Asik and Birkent found that the possibility of tracheal stenosis should be considered in patients over 40 years of age especially with a history of other diseases.<sup>40</sup> While Veder et al.<sup>20</sup> believed youth was the risk factor of PITS. In this study, the results showed no statistical difference in age between the two groups. It indicates that age may have a certain influence on the occurrence of tracheal stenosis, but different ages have little influence on the treatment prognosis of patients with known PITS. Another previous study had found that simple PITS

were more prevalent in women, while complex PITS common in men.<sup>41</sup> Additionally, another study had confirmed that female patients with PITS exhibited improved outcomes following bronchoscopic intervention treatment.<sup>27</sup> However, the present study did not find any significant gender-related differences in the effectiveness of endoscopic treatment.

Prolonged mechanical ventilation ( $\geq 7$  days) may lead to long-term complications such as PITS in addition to pneumonia during hospitalization.<sup>2,42</sup> The time to onset of PITS varies from case to case, ranging from 28 days to 6 months.<sup>2</sup> Is the prognosis worse with longer intubation time and shorter onset interval? Whether they influence each other? In this study, the intubation time and onset time of patients in group F were significantly prolonged, but the differences were not statistically significant compared with group S. Similarly, a cohort study conducted by Ghiani et al.<sup>42</sup> revealed no significant association between intubation duration and tube diameter with tracheal stenosis.

The limitations of this study are the following: (1) first, this study was a retrospective study, in which some data may not be counted or lost, so the factors affecting the prognosis of such patients cannot be comprehensively evaluated. The results of this study will serve as the basis for conducting a prospective investigation on patients with similar conditions, aiming to comprehensively explore their medical history, relevant factors, and pathological characteristics. (2) Additionally, this inclusion criteria exclusively encompassed patients presenting with PITS subsequent to endotracheal intubation, thereby excluding individuals who underwent tracheotomy or cricothyroid membrane puncture. Therefore, patients with tracheal stenosis resulting from cartilage injury were not included in this study. The incorporation of subjects afflicted by tracheal stenosis following cartilage injury would yield a more comprehensive characteristics and facilitate enhanced recommendations and options for a broader patient population. (3) The previous literature had indicated that the presence of subglottic stenosis is a crucial determinant in selecting appropriate treatment strategies. However, this study solely focused on analyzing the length of stenosis. Our findings demonstrate that the length of stenosis does not independently influence the choice of treatment method, and there was no statistically significant difference observed in stenosis length between the two groups. (4) The present study was conducted at a single center; to achieve a substantial increase in the sample size of patients, a multicenter will be implemented. This strategic decision will enhance the potential impact and significance of the research findings.

## 5 | CONCLUSION

The efficacy of bronchoscopic intervention treatment in the application of PITS is notable. However, for patients with chondromalacia, collapsed and irregularly shaped stenosis, the success rate of bronchoscopic intervention therapy cure is limited, necessitating potential surgical intervention following multiple attempts.



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## CONFLICT OF INTEREST STATEMENT

All authors have no conflicts of interest.

## DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## ORCID

Qinghao Cheng  <https://orcid.org/0000-0001-8294-5777>

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