Heliyon 9 (2023) e22326

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Bronchial balloon dilatation combined with cryotherapy for tuberculous cicatricial central airway stenosis, with Adobe Photoshop for the degree measurement: A multicenter, retrospective study

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A R T I C L E I N F O

Keywords:
Cicatricial central airway stenosis
Balloon dilatation
Cryotherapy
Photoshop image processing technology

A B S T R A C T

Objective: To explore bronchial balloon dilation (BD) combined with cryotherapy and Photoshop (PS)-base image processing technology in the interventional treatment of tuberculous cicatricial central airway stenosis (CCAS).
Methods: This multicenter, retrospective study analyzed the clinical data of patients with CCAS from six hospitals in Henan, China between June 2019 and October 2022.
Results: A total of 307 patients were included, including 152 (62 males) treated with BD alone and 155 (54 males) treated with BD combined with cryotherapy. One month after treatment, compared with the BD group, the total response rate [133 (85.8) vs. 105 (69.1), $P < 0.001$] and occurrence of restenosis at 1-monthaftertreatment [22 (14.2 %) vs. 47 (30.9 %), $P < 0.001$] in BD & cryotherapy group were significantly higher; furthermore, the inner diameter of the airway stenosis (8.1 ± 0.9 mm vs. 6.4 ± 1.5 mm, $P < 0.001$), the cross-sectional area of the airway stenosis (51.6 ± 7.8 mm^2 vs. 33.1 ± 11.6 mm^2, $P < 0.001$), FEV1 (5.26 ± 0.42 L vs. 4.32 ± 0.31 L, $P < 0.001$), and PEF (5.72 ± 0.36 L/s vs. 4.56 ± 0.42 L/s, $P < 0.001$) in BD & cryotherapy group showed significantly more improvements. Moreover, Pearson's correlation analysis showed significantly strong positive correlation ($r = 0.818$, $P < 0.001$) between the cross-sectional area of airway stenosis measured by PS-base image processing technology and the inner diameter of airway stenosis measured by chest CT.
Conclusion: BD combined with cryotherapy for the interventional treatment of CCAS might be superior to BD alone. PS-base image processing technology might be used as a supplement strategy for measuring the degree of central airway stenosis.

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https://doi.org/10.1016/j.heliyon.2023.e22326
Received 13 July 2023; Received in revised form 18 October 2023; Accepted 9 November 2023
Available online 14 November 2023

1. Introduction

Cicatricial central airway stenosis (CCAS) is the most common acquired benign airway stenosis [1]. In China, it is more common in tracheobronchial tuberculosis [1–4]. Tuberculous CCAS occurs in the scar repair stage of bronchial tuberculosis. The bronchial mucosal tissue is replaced by hyperplastic fibrous tissue to form scars. Fibrous tissue hyperplasia and scar contracture cause bronchial lumen stenosis [5,6]. The central airway includes the trachea, the left and right main bronchus, and the right middle trunk bronchus. Airflow limitations of these parts result in central airway stenosis; a pathological condition affecting both adults and children and likely to be underdiagnosed [1]. Central airway stenosis seriously affects and threatens the patient's quality of life and requires surgical treatment. In recent years, with the development of interventional pulmonary disease and the maturity of balloon dilatation, high-frequency electrotome, laser, argon plasma coagulation (APC), freezing, airway stent implantation and other technologies, bronchoscopic interventional therapy has become the main method to treat benign airway stenosis [5,6].

The bronchial balloon dilatation is the most important technique for the treatment of benign airway stenosis [3,5,7], while often less morbid, are more likely to require re-intervention and may have an impact on the success of subsequent surgery [8] Spray cryotherapy (SC) is a new thermal energy platform that has been used extensively in the gastrointestinal tract and more recently reported in the airway [9–11]. Because the integrity of the extracellular matrix remains largely intact at the current dosimetries used with SC [11] and because an intact stroma provides the structural framework for appropriate wound repair, a fundamental shift in the wound response results in a more normative healing process [12,13]. This has been observed in different tissues treated with this technology. Following this type of thermal injury, there is felt to be a more favorable wound response with less long-term scarring, which may be beneficial for patients with benign airway strictures [11,14]. Healing with less fibrosis may allow a reduced number of re-interventions as well as prolong the symptom-free time between interventions. Although the connective network remains intact, it does become malleable at the dosimetries commonly used, allowing for remodeling of the connective matrix while preserving the fundamental architecture of the tissue [15]. Few studies have reported the treatment of benign tuberculous CCAS with bronchial balloon dilatation combined with cryotherapy.

Additionally, at present, there is no unified standard for the determination of the degree of airway stenosis, while a small number of studies so far addressed this limitation. For example, the software SENSA (System for Endoscopic Stenosis Assessment) was previously developed to provide objective stenosis index (SI) measurements, but has not yet been tested in larger studies [2]. Furthermore, chest CT airway three-dimensional imaging technology can make a clear assessment of the location, length, degree of benign central airway stenosis and the small lesions in its vicinity. It has the advantages of being non-invasive, allowing multiple scanning levels and accurate three-dimensional airway simulation imaging [3], but the technology is expensive and time-consuming to operate. With the current strategy of visually estimating central airway stenosis from bronchoscopic images [16], it is of great significance to establish a real-time, accurate, rapid, and simple method to determine the degree of central airway stenosis.

Continuous improvement of image processing software technology allows to better analyze images in clinical settings and evaluate medical observations while offering a simple and low-cost alternative to many traditional methods [17]. In the field of pleural fluid smears, digital image analysis using the Adobe Photoshop software provided quantitative data to reduce variation introduced by different observers to assist pathologists to reach more accurate diagnosis [4]. In another study, to evaluate spiral artery remodeling in normal and pathological human pregnancy, images of spiral arteries were analyzed using the Adobe Photoshop (PS) software [18]. The authors of this study suggested this approach to represent a simpler, more rapid, reproducible, and inexpensive way to assess quantitative data. Additionally, to facilitate the evaluation of response to therapy in choroideremia, PS-base image processing technology was developed [19]. This approach showed better test-retest reliability compared to previously used methods, while also being more feasible. However, no studies reported PS-base image processing technology used for measuring the degree of central airway stenosis.

Therefore, this study aimed to explore the application of bronchial balloon dilatation (BD) combined with cryotherapy for tuberculous CCAS and PS-based image processing technology for measuring the degree of central airway stenosis, preliminarily.

2. Methods

2.1. Objects of study

This multicenter, retrospective study included patients with tuberculous CCAS from six hospitals in Henan Provincial, China between June 2019 and October 2022. All patients underwent bronchoscopic intervention therapy based on systemic anti-tuberculosis treatment. Inclusion criteria: (1) adult patients aged 18–60 years old; (2) patients with clinical and imaging manifestations consistent with tuberculosis and bronchial tuberculosis scar stenosis, and bronchoscopy findings consistent with the expert consensus and guidelines [7], with the degree of stenosis of the affected bronchus lumen≥50 %, according to the definition of benign central airway stenosis interventional diagnosis and treatment expert consensus, with unobstructed distal airway lumen and no damaged lung tissue; (3) patients with pulmonary atelectasis for less than 3 months and corresponding pulmonary function remaining; (4) patients with newly diagnosed pulmonary tuberculosis and tracheobronchial tuberculosis, with sputum culture and bacteriological identification of mycobacterium tuberculosis; (5) patients who received bronchoscopic intervention treatment and follow-up for at least one month. Exclusion criteria: (1) all patients with intraluminal stenosis, dynamic stenosis, extrinsic compression stenosis, and airway softening stenosis that do not belong to scar airway stenosis; (2) all patients with complete airway occlusion and cannot undergo interventional treatment; (3) patients who need to rely on technology such as electrocautery and stents to maintain the patency of narrow airways; (4) patients with severe bleeding tendencies or coagulation disorders; (5) patients with severe cardiopulmonary dysfunction or complications who cannot tolerate bronchoscopic intervention treatment; (6) patients with pulmonary atelectasis for more than 3 months and no significance of bronchoscopic intervention treatment; (7) incomplete data. This study has been approved by the Ethics Committee of Henan Provincial Chest Hospital. All patients gave their written informed consent.

2.2. Data collection and definition

The detailed procedures for implementing interventional treatment using balloon dilation or balloon dilation combined with cryotherapy were showed in the Supplementary materials. Baseline information, such as gender, age (in years), degree of stenosis (51–75, 76–90, >90), length of stenosis (<1 cm, 1–3 cm), and location of stenosis (left main bronchus, right main bronchus, right middle lobe bronchus), was collected for all patients. The inner diameter and cross-sectional area of the airway stenosis, and pulmonary ventilation indicators (FEV1, PEF), were measured before and 1 month after interventional treatment. The diameter of the narrowest part of the stenosis, the length of the narrow lumen, and the location of the airway stenosis and distal lung parenchyma were observed using bronchoscopy combined with chest CT airway 3D reconstruction. The occurrence of complications, including bleeding, pneumothorax, mediastinal emphysema, and airway perforation, was recorded for patients after interventional treatment. The incidence of airway restenosis was observed during follow-up 1 month later.

2.3. Evaluation of therapeutic efficiency

The therapeutic efficiency were evaluated by the response of interventional therapy for tuberculous CCAS, inner diameter of the airway stenosis, cross-sectional area of airway stenosis, pulmonary function. The response was measuredby: (1) completely response, with a restoration of airway diameter of over 70 %; (2) significantly response, with a restoration of airway diameter of over 50 % but less than 70 %; (3) mildly response, with a restoration of airway diameter of over 40 %, and the endoscope (with a diameter of 4.9 mm) can pass through smoothly; (4) no response, with no significant improvement in airway diameter or even more stenosis after intervention treatment. The total response rate (%) = (number of completely effective cases + number of significantly effective cases + number of mildly effective cases)/total number of cases × 100 %. The immediate response rate was the therapeutic response observed immediately after treatment. After one month of follow-up observation, the recurrence of airway stenosis [5] refers to the shrinkage of the patient's narrowed airway diameter to the level before expansion or even narrower than before, and the recurrence rate is recorded. Complications include bleeding, chest pain, mediastinal emphysema, and airway perforation. In addition, pulmonary function testing, including forced expiratory volume in 1 s (FEV1) and peak expiratory flow (PEF), are important indicators for evaluating airway stenosis [1], so they are used as evaluation indicators before and after treatment. The cross-sectional area of airway stenosis was measured using PS-based image processing techniques. The inner diameter of airway stenosis was measured by chest CT.

2.4. Statistical analysis

SPSS19.0 (IBM Corp., Armonk, N.Y., USA) statistical software was used for data statistical analysis. Continuous variables were expressed as mean ± SD. Paired *t*-test was used to compare airway diameters before and after treatment. Categorical variables were expressed as n (%) and analyzed by chi-square test. A two-sided P value of less than 0.05 was considered statistical significance.

3. Results

A total of 307 patients were included, including 152 (62 males) treated with BD alone (BD group) and 155 (54 males) treated with

Table 1
Baselinecharacteristics.

Variables	BD group (n = 55)	BD & cryotherapy (n = 57)	P
Sex, n (%)			0.282
Male	62 (40.8)	54(34.8)	
Female	90 (59.2)	101(65.2)	
Age [years, n (%)]			0.531
18–29	47 (30.9)	58 (37.4)	
30–39	54 (35.5)	49 (31.6)	
40–49	32 (21.1)	26 (16.8)	
50–60	19 (12.5)	22 (14.2)	
Degree of bronchial stenosis, n (%)			0.603
51–75	66 (43.4)	59 (38.1)	
76–90	74 (48.7)	81(52.2)	
>90	12 (7.9)	15 (9.7)	
Length of bronchial stenosis [cm, n (%)]			
<1	58 (38.2)	46 (29.7)	0.116
1–3	94 (61.8)	109 (70.3)	
Site of bronchial stenosis, n (%)			0.684
Left main bronchus	74 (48.7)	82 (52.9)	
Right main bronchus	53 (34.9)	47 (30.3)	
Right intermediate segmental bronchus	25 (16.4)	26 (16.8)	

BD combined with cryotherapy (BD & cryotherapy group). The baseline characteristics between BD group and BD & cryotherapy group were comparable (all P > 0.05) (Table 1).

One month after treatment, the total response rate (P < 0.001) and occurrence of restenosis at 1-monthaftertreatment (P < 0.001) in BD & cryotherapy group were significantly higher than that in BD group, while the immediate response rate, complications between the two groups were comparable (all P > 0.05, Table 2). In both BD group and BD & cryotherapy group, the inner diameter of the airway stenosis, the cross-sectional area of the airway stenosis, FEV1, and PEF were significantly improved compared with those before treatment (all P < 0.001). Moreover, compared with the BD group, the inner diameter of the airway stenosis (P < 0.001), the cross-sectional area of the airway stenosis (P < 0.001), FEV1 (P < 0.001), and PEF (P < 0.001)in BD & cryotherapy group showed significantly more improvements (Table 3).

Comparison before and after interventional treatment for a typical case of tuberculous cicatricial central airway stenosis measured by PS image processing technology showed that cross-sectional area of the airway stenosis at both of left (63.98 mm^2 vs. 9.24 mm^2) and right (21.02 mm^2 vs. 0.36 mm^2) main bronchus were greatly improved (Fig. 1). Pearson's correlation analysis showed significantly strong positive correlation ($r = 0.818$, $P = 0.000$) between the cross-sectional area of airway stenosis measured by PS image processing technology and the inner diameter of airway stenosis measured by chest CT, indicating that PS-base image processing technology might be used as a supplement strategy for measuring the degree of central airway stenosis.

4. Discussion

This study suggested that BD combined with cryotherapy for the interventional treatment of CCAS might be superior to BD alone. Moreover, PS-base image processing technology might be used as a supplement strategy for measuring the degree of central airway stenosis. These findings might provide cues for alternative treatment for CCAS and measuring the degree of central airway stenosis.

In this study, the total response rate of BD along was significantly inferior to that of BD combined with cryotherapy in bronchial intervention therapy. The reason may be that the scar ring is thicker. After the balloon dilation, damage to the airway wall and/or mucosal tearing can be observed, as well as varying degrees of congestion and edema [20]. When treated by BD alone, post-traumatic repair was observed after tears of airway walls and/or mucosa, manifested by granulation tissue hyperplasia and scar proliferation. While when treated by BD combined with cryotherapy, the cryoprobe is inserted through the biopsy channel of the bronchoscope, and the metal tip of the probe is placed at the site of the original stenosis where balloon dilation was performed, and multi-point freezing is implemented, and which can reduce the proliferation of granulation tissue and improve collagen synthesis, reduce scar proliferation, improve physiological indicators such as airway stenosis internal diameter and cross-sectional area, FEV1, PEF, and reduce the risk of restenosis. Cryotherapy is widely used in the intervention therapy of benign airway stenosis and is less likely to damage the cartilage [1,6,16–18]. This is consistent with the results of this study, further confirming that the use of balloon dilation combined with cryotherapy is superior to the use of balloon dilation alone in the treatment of cicatricial central airway stenosis, and may provide a viable treatment option for the clinical management of tuberculous CCAS.

The use of digital imaging technology and software is gradually increasing in clinical settings due to its improved accessibility and means for standardization. Especially, the widely used Adobe PS-based image processing software allowed clinicians to reliably analyze images and data of pleural fluid smears and spiral arteries, amongst others [8,9]. While the study here used the Adobe PS software to measure distances in images of the airway tract, other studies used the same tool to measure visual distances of various body parts. Marca et al. used the Adobe PS software to outline root and canal perimeters for area measurement, which the study found to be more correct [21]. Another study analyzed images before and after surgery of the nasal bone to assess changes in nasal shape [22]. The authors measured heights and lengths as well as angles of different nasal parts with the Adobe PS software and found this method to be more rapid and simpler. Furthermore, to evaluate disease progression or response to therapy in patients suffering from choroideremia, a PS-based approach was developed [19]. The authors measured the area of preserved retinal pigment epithelium and compared the measurements with a traditional method and suggested the PS-based quantification to be more feasible and reliable.

During the bronchoscopy airway images processing, the author found that by examining bronchoscopy airway images of patients before and after interventional treatment, PS-based image processing allows to compare the changes intuitively and accurately in the

Table 2
Response of interventional therapy, occurrence of restenosis and complications.

Outcomes	BD group (n = 152)	BD & cryotherapy (n = 155)	P
Response rate, n (%)			
Immediate response rate	147 (96.4)	148 (95.5)	0.579
Total response rate	105 (69.1)	133 (85.8)	<0.001
Completely response	26 (17.1)	48 (31.0)	–
Significantly response	33 (21.7)	51 (32.9)	–
Mildly response	46 (30.3)	34 (21.9)	–
No response	47 (30.9)	22 (14.2)	–
Restenosis at 1-month after treatment, n (%)	47 (30.9)	22 (14.2)	<0.001
Occurrence of complications, n (%)			
Hemorrhage	42 (27.6)	50 (32.3)	0.376
Chest pain	21 (13.8)	18 (11.6)	0.562
Emphysema mediastinum	0 (0)	0 (0)	–
Airway perforation	0 (0)	0 (0)	–

Table 3
Physiological index.

Variables	BD group (n = 152)		BD & cryotherapy (n = 155)		$P^{\#}$
	Before treatment	After treatment	Before treatment	After treatment	
Inner diameter of the airway stenosis (mm, mean ± SD)	3.5 ± 1.3	6.4 ± 1.5**	3.4 ± 1.2	8.1 ± 0.9**	<0.001
Cross-sectional area of airway stenosis (mm^2, mean ± SD)	9.3 ± 4.2	33.1 ± 11.6**	8.7 ± 3.1	51.6 ± 7.8**	<0.001
FEV1 (L, mean ± SD)	1.36 ± 0.29	4.32 ± 0.31**	1.43 ± 0.46	5.26 ± 0.42**	<0.001
PEF (L/s, mean ± SD)	3.63 ± 0.39	4.56 ± 0.42**	3.47 ± 0.61	5.72 ± 0.36**	<0.001

**means $P < 0.001$, as the comparison between after and before treatment; # means the comparison of after treatment between the two groups.

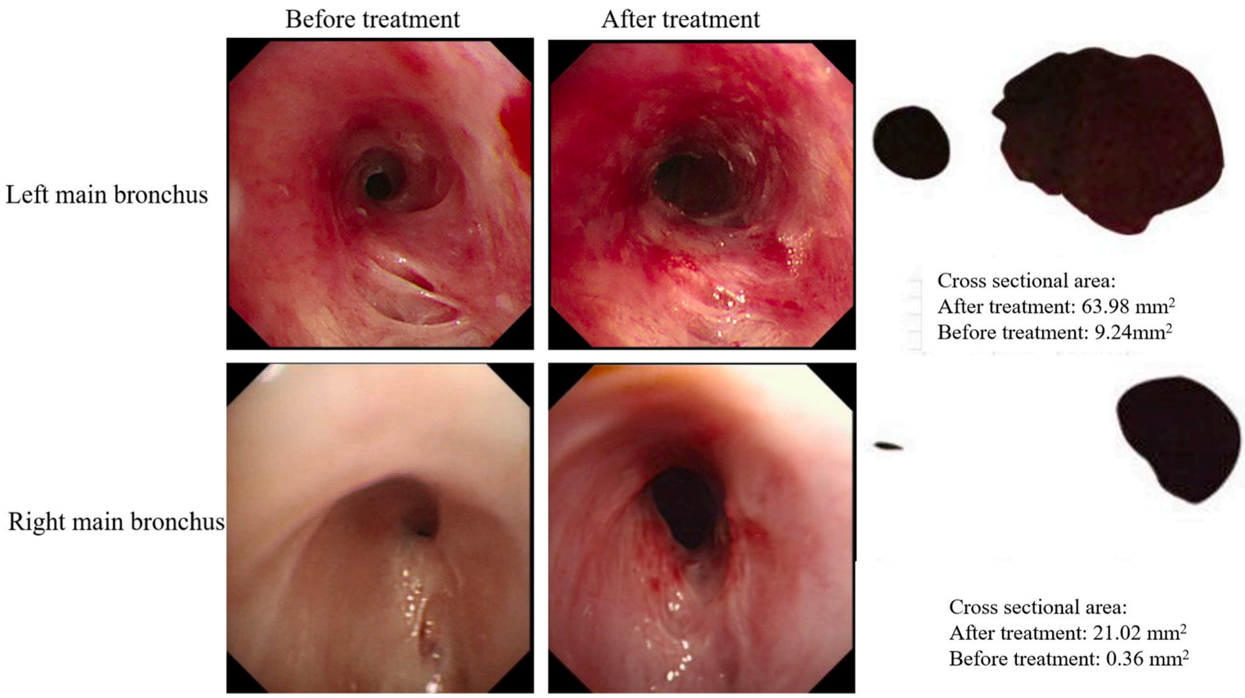

Fig. 1. Comparison before and after interventional treatment for a typical case of tuberculous cicatricial central airway stenosis measured by PS image processing technology.

cross-sectional area of the stenosis. This evaluation is thus objective and accurate and not affected by the subjective consciousness of researchers. Compared with chest CT airway three-dimensional imaging methods [23], our approach is accurate, rapid, simple to operate and of low cost. These advantages render this method worthy of clinical application to determine the degree of central airway stenosis. This will allow to establish a standardized interventional treatment plan to improve the overall level of interventional treatment of central airway stenosis.

With the theory and technology of artificial intelligence maturing, its application in the medical field is expanding. Computer-assisted cell recognition or tumor recognition can be used to detect small and medium-sized particles in cells or body fluids or quantitatively analyze indicators in tissue or bone marrow [24–27]. In the field of endoscope, deep learning algorithm can be used to dynamically identify and capture targets in the field of vision, which can make up for the shortcomings of incomplete visual capture and fatigue of human [28,29]. The method of collecting images of stenosis through bronchoscopy and accurately calculating the cross-sectional area of stenosis through PS-based image processing software was a simple, rapid, accurate, low-cost and dynamic observation method based on computer system. It was not affected by the visual discrimination ability and subjective consciousness of the researcher, and can accumulate a large amount of data, which was also an embodiment of the application of artificial intelligence technology in respiratory endoscopy. It can combine artificial intelligence and endoscopic intervention quality control to achieve dynamic observation and evaluation. Images of the stenosis site were collected under bronchoscopy before interventional therapy, and images of the original site were collected again after interventional therapy. The specific method is to record the length of the bronchoscope into the nasal/oral cavity at the bronchostenosis where the bronchoscope is unable to advance, which could ensure that a picture of the same site is taken before and after the intervention. The cross section of the narrow part was obtained by PS technology, and the area was calculated.

This study has several limitations. Firstly, it was a retrospective study, which needs to be validated prospectively. Secondly, this study has a small sample size, and it is not clear whether it is representative. Thirdly, the use of PS-based image processing was not full statistical analysis in more clinical practice.

5. Conclusion

In conclusion, BD combined with cryotherapy for the interventional treatment of CCAS might be superior to BD alone. PS-base image processing technology might be used as a supplement strategy for measuring the degree of central airway stenosis, which can visually and accurately compare the changes in the cross-sectional area of the stenosis before and after interventional treatment, and objectively and accurately determine the efficacy. Nevertheless, a prospective study with large sample size is need for further confirmation.

Ethic statement

This study has been approved by the Ethics Committee of Henan Provincial Chest Hospital.
All patients gave their written informed consent.

Availability of data and material

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

Funding

None.

CRediT authorship contribution statement

Taomei Lian: Conceptualization, Data curation, Visualization, Writing – original draft, Writing – review & editing. **Chao Liang:** Data curation, Formal analysis. **Shouyuan Yu:** Data curation, Formal analysis. **Zongxin Feng:** Formal analysis, Resources. **Hongwei Ren:** Data curation, Formal analysis. **Ke Xu:** Resources, Software. **Xin Liu:** Conceptualization, Data curation. **Kunying Li:** Data curation, Formal analysis.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledge

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e22326.

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