Ultrasound imaging features of bronchial anthracofibrosis: A case–control study

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Abstract

To determine the ultrasound imaging characteristics of patients with bronchial anthracofibrosis (BAF) and identify clinical markers for prevention and treatment. We randomly selected 1243 participants (113 with BAF) who underwent bronchoscopy and received treatment at our institution between April 2018 and October 2019. BAF was classified as flat, deep-seated retracted, or black mucosal protruding based on microscopic findings. Ultrasound probes were used to determine the maximum thickness of the tube walls and submucosa. The average values of the submucosal and bony tissue areas in the BAF subtypes were compared. The BAF group included 13 participants with a history of tuberculosis (11.5%) and 57 participants with biofuel exposure (50.4%). The average exposure time was 17.4 ± 6.2 years; BAF accounted for 10% of the bronchoscopies performed. The maximum tube-wall thicknesses of the deep-seated retracted (17.3 ± 5.7) and black mucosal protruding (19.3 ± 5.4) groups were significantly greater than those of the flat group (12.5 ± 5.0; P < .05). The maximum thicknesses of the submucosa in the deep-retracted (9.8 ± 3.0) and black mucosal protruding (14.5 ± 5.0) groups were significantly greater than that of the flat group (6.6 ± 3.5; P < .05). The ratios of bone tissue in the flat and black mucosal protruding groups were 33.3 ± 9.3% and 34.9% ± 12.1%, respectively. The ratio in the deep-seated retracted group (65.2% ± 8.7%) was significantly reduced (P < .05). The flat group showed no significant change (P > .05). Differences in BAF airway remodeling among different subtypes may lead to varying clinical symptoms. Analyzing the characteristics of BAF airway remodeling and the regulatory pathway may provide new clues for treatment.

Abbreviations: BAF = bronchial anthracofibrosis, BMI = body mass index, EBUS = endobronchial ultrasound, TB = tuberculosis.

Keywords: airway remodeling, anthracosis, biofuel, bronchoscopy, chronic obstructive pulmonary disease, pneumoconiosis, ultrasound imaging

1. Introduction

Bronchial anthracofibrosis (BAF) is a pulmonary disease caused by the accumulation of carbon in the lungs due to repeated exposure to air pollution or inhalation of smoke or coal dust particles.[1] The prevalence of BAF in the general population can only be roughly estimated, as diagnosis requires bronchoscopy. Large studies of the prevalence of BAF in the general population can only be roughly estimated, as diagnosis requires bronchoscopy. As auxiliary examinations other than bronchoscopy lack specificity, it is difficult to distinguish BAF from pulmonary tuberculosis (TB), chronic obstructive pulmonary disease, and malignant neoplasms through routine examinations such as pulmonary function tests and computed tomography.[1] A thorough understanding of the clinical characteristics of BAF may facilitate the acquisition of epidemiological data. To date, extensive investigations of the endobronchial ultrasound (EBUS) imaging features of participants with BAF have not been reported. Mirsadraee and Farshchi[2] reported a case of typical anthracosis with a scattered nodular hyperechoic pattern in the subepithelial area of the bronchus or lymph nodes adjacent to the bronchial mucosa. However, in-depth research on this topic is insufficient. Therefore, we analyzed the EBUS imaging features of participants with BAF to provide effective clinical clues for the prevention and treatment of the disease.

2. Materials and Methods

2.1. Participants

This study was approved by the Ethics Committee of the People’s Hospital of the Honghuagang District. The...
requirement for informed consent was waived owing to the retrospective nature of the study. Among the 1243 participants who underwent bronchoscopy and treatment at the Department of Respiratory and Critical Care Medicine at the People’s Hospital of Honghuagang District in Zunyi, China, between April 2018 and October 2019, 113 participants with a diagnosis of BAF were randomly selected for this study. BAF diagnoses were established in accordance with the criteria reported in the literature; that is, typical dark anthracotic pigmentation on the bronchial mucosa visible via electronic bronchoscopy.

The general demographic data of the study participants, such as age (years) and sex, were recorded. The following clinical data were also collected: history of TB, exposure or nonexposure to biofuels, duration of biofuel exposure (years), smoking history, body mass index, and history of comorbidities such as diabetes, ischemic heart disease, stroke, chronic liver disease, chronic kidney disease, or hyperlipidemia.

2.2. Routine bronchoscopy
Bronchoscopy is the gold standard for the diagnosis of anthracofibrosis. In the present study, an EB-530T electronic bronchoscope (Fujifilm, Japan) was used for the examination and imaging of all participants (as far as possible, up to the segmental bronchi and trachea). In accordance with the criteria reported in the literature, the participants were classified as having a flat BAF, deep-seated retracted BAF (originating from an anthracotic lymph node beside the bronchus), or black mucosal protruding BAF (with or without narrowing of the bronchi) based on bronchoscopy images. In addition to black lesions, other pathological changes (e.g., bronchial swelling or obliteration) visible under bronchoscopy and their locations were recorded.

2.3. EBUS
The EBUS system (PB2020-M) and the supplies used in this study were purchased from Fujifilm (Japan). During each EBUS examination, a mini-probe (external diameter: 1.9 mm, acoustic frequency: 20 MHz) was inserted into the 2.8-mm forceps channel, and ultrasound images were obtained through the working channel of a video endoscope (SP-900). Examinations were performed using the 360° sweep B-scan ultrasound mode and the results were recorded on a computer.

Single-blind analysis of the EBUS images was performed using the ImageJ software (version 1.48c, NIH, USA). The measured and analyzed parameters included the bronchial diameter (calculated using the average value of 2 vertical diameter measurements in each airway), internal perimeter, maximum bronchial wall thickness, and maximum submucosal thickness. For all airways, the average values of diameter, internal perimeter, lumen area, submucosal area, and bony tissue area were calculated. The same observer analyzed 14 EBUS images 3 times at intervals of ≥1 week to assess the repeatability of the measurements.

2.4. Statistical analyses
Data analysis was performed using Statistical Package for the Social Sciences (version 23.0; International Business Machines Corp., Armonk, NY). Continuous variables are expressed as mean ± standard deviation, and categorical variables are expressed as numbers and percentages. Comparisons of continuous variables between 2 groups were performed using the independent samples t test, comparisons of continuous variables between multiple groups were performed using analysis of variance, pairwise comparisons of continuous variables were performed using the least significant difference test, comparisons of categorical variables between groups were performed using the χ² test, and pairwise comparisons of categorical variables were performed using Bonferroni correction. Statistical significance was set at a P value of <.05.

3. Results
3.1. General data
In total, 113 participants with BAF with a mean age of 66.2 ± 9.3 years were included in the present study; 53 participants (46.9%) were men, the mean body mass index was 21.6 ± 3.7 kg/m², and 42 participants (37.2%) were smokers. Thirteen participants (11.5%) had a history of TB, which may be associated with a high prevalence of TB in the region where this study was conducted, and 57 participants (50.4%) had been exposed to biofuels for a mean duration of 17.4 ± 6.2 years. The comorbidities of the participants were as follows: diabetes mellitus (n = 4; 3.5%), ischemic heart disease (n = 22; 19.4%), chronic liver disease (one participant, 0.14%), chronic kidney disease (one participant, 0.14%), and hyperlipidemia (n = 26; 23.0%).

3.2. Bronchoscopy results
Under bronchoscopy, participants with flat BAF (Fig. 1A) exhibited an unobstructed lumen with normal morphology, absence of evident mucosal hyperemia, edema, thickening, and a sharp-appearing bronchial carina. In participants with deep-seated retracted BAF (Fig. 1B), we observed evident fibrous tissue proliferation, slight distortion of the lumen, stenosis of the affected bronchi (commonly occurring as external compression-type stenosis), slight hyperemia in the mucosa, and a sharp-appearing bronchial carina. Additionally, difficulties were encountered during the participants’ biopsy procedures. Bronchoscopy of participants with black mucosal protruding BAF (Fig. 1C) revealed severe distortion of the lumen, evident lumen stenosis often accompanied by bronchial obliteration, evident mucosal hyperemia, edema, and thickening, a broadened and deformed bronchial carina with occasional mucosal ulceration or necrosis, and high bleeding tendency upon contact with the bronchoscope. Significant postbiopsy bleeding was observed (4 participants experienced bleeding during bronchial brushing), and bleeding control was relatively difficult. However, effective control was achieved after the subsequent treatment. Among the 113 participants with BAF, 31 (27.4%) had a flat BAF, 38 (33.6%) had a deep-seated retracted BAF, and 44 (38.9%) had a black mucosal protruding BAF.

3.3. EBUS examination results
EBUS examinations using a mini-probe revealed the following manifestations in the airways of the healthy control and BAF groups: the healthy control group (Fig. 2A) showed uniform aeration patterns in the peripheral lung tissue, the flat BAF group (Fig. 2B) showed uniform aeration patterns in the lung tissue; the deep-seated retracted BAF group (Fig. 2C) showed disordered lung tissue signals with scattered calcification patterns, and the black mucosal protruding BAF group (Fig. 2D) showed soft tissue patterns in the lung tissue. Figure 3 shows ImageJ 18.0-magnified ultrasound images and transbronchial lung biopsy specimens of an airway with BAF.

As shown in Figure 4, magnified ultrasound images of the bronchial walls of participants in various groups revealed the following manifestations: the healthy control group showed a regular circular distribution of the airway wall, occasional shadows on the cartilage rings, uniform mucosa, and uniformly dense submucosal tissue; the flat BAF group
showed a decreased mucosal area compared with the healthy control group and an uneven thickening of submucosal tissue; the deep-seated retracted BAF group showed a decreased mucosal area compared with the healthy control group, significant thickening of the cartilage layer, and an uneven calcification on the airway wall; the black mucosal protruding BAF group showed a decreased mucosal area, an uneven thickening of submucosal tissue, and a disorderly arrangement of cartilage tissue.

Table 1 shows the airway wall indicators of the various BAF subgroups measured after the magnification of the ultrasound images using ImageJ 18.0. The maximum wall thicknesses of the flat BAF, deep-seated retracted BAF, and black mucosal protruding BAF groups were 12.5 ± 5.0, 17.3 ± 5.7, and 19.3 ± 5.4 mm, respectively, with multigroup comparisons showing significant differences ($F = 14.946$, $P = .000$). Pairwise comparisons showed that the maximum wall thicknesses of the deep-seated retracted BAF and black mucosal protruding BAF groups were significantly
higher than those of the flat BAF group ($P < .05$); the difference in maximum wall thickness between the deep-seated retracted BAF and black mucosal protruding BAF groups was not significant ($P = .090$). The maximum submucosal thicknesses of the flat BAF, deep-seated retracted BAF, and black mucosal protruding BAF groups were $6.6 \pm 3.5$, $9.8 \pm 3.0$, and $14.5 \pm 5.0$ mm, respectively, with multigroup comparisons showing significant differences ($F = 36.819, P = .000$). Pairwise comparisons revealed that the bony tissue area of the deep-seated retracted BAF group was significantly higher than that of the other 2 groups ($P < .05$), the bony tissue area of the black mucosal protruding BAF group did not differ significantly from that of the flat BAF group ($P = .508$). The proportions of bony tissue area in the flat BAF, deep-seated retracted BAF, and black mucosal protruding BAF groups were $33.3\% \pm 9.3\%$, $65.2\% \pm 8.7\%$, and $34.9\% \pm 12.1\%$, respectively, with multigroup comparisons showing significant differences ($F = 113.473, P = .000$). Pairwise comparisons revealed that the bony tissue area of the deep-seated retracted BAF group was significantly higher than that of the other 2 groups ($P < .05$), the bony tissue area of the black mucosal protruding BAF group did not differ significantly from that of the flat BAF group ($P = .508$). The proportions of submucosal area in the flat BAF, deep-seated retracted BAF, and black mucosal protruding BAF groups were $64.8\% \pm 9.1\%$, $30.4\% \pm 8.8\%$, and $58.6\% \pm 11.7\%$, respectively, with multigroup comparisons showing significant differences ($F = 36.819, P = .000$). Pairwise comparisons revealed that the bony tissue area of the deep-seated retracted BAF group was significantly higher than that of the other 2 groups ($P < .05$), the bony tissue area of the black mucosal protruding BAF group did not differ significantly from that of the flat BAF group ($P = .508$).
showing significant differences ($F = 120.031, P = .000$). Pairwise comparisons indicated that the differences between the 3 groups were significant ($P < .05$).

### 4. Discussion

BAF was first described as black discoloration of the bronchial mucosa (simple anthracosis) or scattered foci of black spots that retract the mucosa inward owing to the effect of adjacent anthracotic lymphadenopathy and cause changes in bronchial structures. Given the lower prevalence of BAF in Western countries, interest in this disease has gradually declined. However, it is considered a common disease in Asia, as literature has reported the occurrence of a second wave of anthracosis on the continent. Chung et al.\(^\text{[7]}\) considered BAF to be a unique clinical syndrome that distorts and narrows the bronchial lumen in severe cases. Therefore, clinicians have introduced terms such as anthracostenosis\(^{[8]}\) and anthracotic bronchitis\(^{[9]}\) to describe the resultant changes in bronchial structure. In the majority of cases, BAF is accompanied by severe submucosal edema, bronchial stenosis, protruded mucosal folds, and lung collapse.\(^{[9]}\) Owing to the lack of conclusive epidemiological data and the fact that bronchoscopy is the gold standard procedure for anthracosis diagnosis, it is difficult to estimate the prevalence of BAF in the general population. The prevalence of BAF is lower in Western countries, with Wynn et al.\(^{[10]}\) reporting only 7 BAF cases among 7000 bronchoscopies. Reports of BAF from other continents, such as North America and Africa, are also rare.\(^{[11]}\) Available data from a large series of participants who underwent bronchoscopy for other reasons have shown the prevalence of BAF to be 3.4% to 21%.\(^{[2]}\) Recently, researchers in China have begun to show a keen interest in the clinical presentations of BAF; however, in-depth studies on Chinese populations remain scarce.\(^{[12]}\) Through our retrospective analysis of data from participants who underwent bronchoscopy at our hospital, we determined a BAF prevalence rate of approximately 10% among the total number of bronchoscopies. Therefore, it can be deduced that the disease has a relatively high prevalence in the local population (especially among the elderly), which may be related to the environmental conditions and lifestyle habits of the residents in this region. Further studies on the prevention and treatment of BAF are of significant value in clinical practice.

As reported in the literature, BAF may be classified as flat, deep-seated retracted, and black mucosal protruding types. In addition to black lesions, bronchial swelling with infiltration, erythema, and thickening that may cause obliteration of bronchi may be observed.\(^{[4]}\) The bronchoscopy results of the participants in this study revealed that participants with flat BAF (Fig. 1A) exhibited an unobstructed lumen with normal morphology; absence of evident mucosal hyperemia, edema, and thickening; and a sharp-appearing bronchial carina. In participants with deep-seated retracted BAF (Fig. 1B), we observed evident fibrous tissue proliferation, slight distortion of the lumen, stenosis of the affected bronchi (commonly occurring as external compression-type stenosis), slight hyperemia in the mucosa, and a sharp-appearing bronchial carina. Additionally, difficulties were encountered during the participants’ biopsy procedures. Bronchoscopy of participants with black mucosal protruding BAF (Fig. 1C) revealed evident stenosis of the lumen, evident lumen stenosis often accompanied by bronchial obliteration, evident mucosal hyperemia, edema, and thickening, a broadened and deformed bronchial carina with occasional mucosal ulceration or undesirable deposits, and high bleeding tendency upon contact with the bronchoscope. Significant bleeding after biopsy was observed (four participants experienced bleeding during bronchial brushing), and bleeding control was relatively difficult, although effective control was achieved after subsequent treatment. Among the 113 participants with BAF, 31 (27.4%) had a flat BAF, 38 (33.6%) had a deep-seated retracted BAF, and 44 (38.9%) had a black mucosal protruding BAF. Based on the bronchoscopic features described herein, we deduced that airway fibrosis is not the sole pathological characteristic of BAF. Angiogenesis may be involved in airway remodeling in patients with BAF, thereby leading to a high tendency toward airway wall bleeding. Therefore, further investigation of the structural characteristics of the airway wall in BAF is of significant clinical value.

The manifestations described above are merely macroscopic features that are observed during bronchoscopy. Currently, in-depth studies on the airway wall structures of participants with BAF are scarce. Mirsadraee and Farshchi\(^{[13]}\) performed EBUS in a patient with BAF and observed a scattered, nodular, hyperechoic pattern in the subepithelial area of the bronchus or lymph nodes adjacent to the bronchial mucosa. However, the authors could only achieve a preliminary understanding of the structural features of large airways owing to the limitations of the medical equipment. In recent years, the clinical application of mini-probes in EBUS has provided favorable conditions for the assessment of distal small airways.\(^{[14]}\) To determine the structural characteristics of small airways in BAF, we performed EBUS in participants with BAF and observed the presence of severe calcification and mucosal remodeling around the airways. Subsequently, Image 18.0 was used to magnify the airway images of the various BAF subgroups for the measurement of airway wall indicators. As shown in Table 1 and Figure 3, the maximum wall thicknesses of the deep-seated retracted BAF and black mucosal protruding BAF groups were significantly higher than those of the flat BAF group, and the same was observed for the maximum submucosal thickness. Compared with the proportion of the submucosal area (64.8% ± 9.1%) in the flat BAF group, the proportion (30.4% ± 8.8%) in the deep-seated retracted BAF group was significantly lower, but the proportion (58.6% ± 11.7%) in the black mucosal protruding BAF group did not differ significantly from that of the flat BAF group. The limitation of this study is that a definite conclusion cannot be drawn owing to its small sample size. It can be deduced that different airway remodeling features may exist among the different BAF subtypes in the study; however, the acquisition and analysis of ultrasound images and pathological examinations of participants with different types of BAF on a larger scale may

### Table 1

| | Flat bronchial anthracofibrosis | Deep-seated retracted bronchial anthracofibrosis | Black mucosal protrusion bronchial anthracofibrosis | $F$ value $P$ value |
|---|---|---|---|---|
| N | 31 (27.4%) | 38 (33.6%) | 44 (38.9%) | $120.031$ $< .05$ |
| Maximum wall thickness (mm) | 12.5 ± 5.0 | 17.3 ± 5.7 | 19.3 ± 5.4 | $14.964$ $< .05$ |
| Maximum submucosal thickness (mm) | 6.6 ± 3.5 | 9.8 ± 3.0 | 14.5 ± 5.0 | $36.819$ $< .05$ |
| Proportion of submucosal area (%) | 64.8 ± 9.1 | 30.4 ± 8.8 | 58.6 ± 11.7 | $120.031$ $< .05$ |
| Proportion of bony tissue area (%) | 33.3 ± 9.3 | 65.2 ± 8.7 | 34.9 ± 12.1 | $113.473$ $< .05$ |

SD = standard deviation.
provide conclusive evidence of airway structural changes associated with the disease.

5. Conclusions

In conclusion, different types of BAF exhibit different features under bronchoscopy, and differences have also been observed in airway walls upon further examination using EBUS. Therefore, differences in airway remodeling among various BAF subtypes may lead to the manifestation of different clinical symptoms. Further studies are required to elucidate the mechanisms by which airway remodeling in BAF causes different clinical symptoms. An adequate understanding of the airway remodeling characteristics and regulatory pathways of BAF may provide new clues for the treatment of this disease.

Author contributions

Xiaoyan Cai; data collection: Qingshong Zeng and Li Zou; study design: Zuoli Du; data analysis: Xiaofeng Lu; manuscript preparation: Xiaofeng Lu and Daishun Liu; manuscript review: Guoqi Zhou.

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