Prospective Analysis of Clinical Characteristics and Risk Factors of Postbronchoscopy Fever*

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Study objectives: To assess the clinical characteristics of fever after fiberoptic bronchoscopy (FOB) and to identify the independent risk factors of postbronchoscopy fever.

Study design: Prospective study.

Setting: Tertiary care university hospital.


Measurements and results: Five hundred eighteen adults were included in this study. The incidence of postbronchoscopy fever was 5%, and the mean onset time of the fever was 8.7 ± 1.1 h after FOB (mean ± SEM). In most cases, the fever subsided spontaneously within a day, with a mean fever duration of 14.0 ± 3.1 h. No organisms were isolated from blood culture specimens drawn at the time of fever compared to levels prior to FOB. Univariate analysis showed that fever was related to multiple factors, such as the radiologic extent of involvement, consolidation, abnormal bronchoscopic findings, biopsy, lavage, the amount of saline solution or drug administered, the duration of the procedure, the severity of bleeding, and a final diagnosis of pulmonary tuberculosis. However, after multivariate analysis, the final diagnosis of pulmonary tuberculosis and the severity of bleeding were identified as independent risk factors.

Conclusions: Fever after FOB occurs relatively frequently but transiently in immunocompetent adults. Independent risk factors for the development of this complication seem to be related to the diagnosis of pulmonary tuberculosis and the severity of bleeding during FOB.

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Key words: bacteremia; bleeding; bronchoscopy; fever; tuberculosis

Abbreviations: AFB = acid-fast bacilli; BALF = BAL fluid; CI = confidence interval; FOB = fiberoptic bronchoscopy; IL = interleukin; RR = relative risk; TNF = tumor necrosis factor

Fiberoptic bronchoscopy (FOB) has become the procedure of choice for the examination of the lower respiratory tract since its introduction in 1968. The reported frequency of mortality ranges from 0 to 0.5%. arrhythmia, bleeding, bronchospasm, and pneumothorax occur rarely. In contrast, fever following FOB has been frequently reported. Postbronchoscopy fever usually begins a few hours after FOB and subsides spontaneously within a day. The reported frequency of this complication ranges from 1 to 20%. According to previous reports, postbronchoscopy fever is associated with advanced age, the presence of abnormal bronchoscopic findings, documented endobronchial obstruction, bronchoscopic intervention for malignancy, BAL, bronchial brushing, endotoxin contamination during bronchoscopy, instillation of topical anesthetic through the bronchoscope, abnormal differential cell counts in the BAL fluid (BALF), and bacterial growth in the BALF culture. However, these studies which were undertaken to investigate the risk factors of

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postbronchoscopy fever, were performed in different situations. For example, the underlying diseases of the study populations, the definitions of fever, and the diagnostic techniques used during the procedure differ between studies. Moreover, fever following FOB can be influenced by multiple factors, and these factors can be interrelated. Therefore, we chose to evaluate these possible risk factors in a prospective manner and assess them in a multivariate statistical model.

Since many patients were found to have positive blood culture findings after rigid bronchoscopy, transient bacteremia has been considered to be responsible for postbronchoscopy fever; however, bacteremia was rarely detected in immunocompetent patients undergoing FOB. On the other hand, postbronchoscopy fever was related to elevations of proinflammatory cytokines, such as tumor necrosis factor (TNF)-α, interleukin (IL)-1β, and IL-6, suggesting that postbronchoscopy fever may be related to the release of pyrogenic mediators rather than bacteremia. Thus, fever after FOB may develop more frequently in patients with diseases associated with high levels of underlying pyrogenic cytokines. However, to our knowledge, no study has been reported on the relationship between the development of fever and underlying pulmonary disease in patients who underwent FOB.

In this prospective study, we assessed the incidence, clinical characteristics, and possible risk factors of fever following FOB. We found that the postbronchoscopy fever, which occurred in 5% of patients, was transient and not related to bacteremia. The independent risk factors of fever were identified as the final diagnosis of pulmonary tuberculosis and the severity of bleeding during FOB.

**Materials and Methods**

**Study Subjects**

We conducted a prospective study of adult patients undergoing FOB at Seoul National University Hospital in Seoul, Korea. The study was approved by the hospital ethics committee, and informed consent was obtained from all subjects. Between July 2001 and April 2002, 801 subjects underwent FOB. Subjects were excluded from the study for the following reasons: use of immuno suppressive agents or corticosteroids, positive HIV findings, body temperature > 37.5°C during the 24 h prior to FOB, intubation or mechanical ventilation, therapeutic bronchoscopy (foreign body removal, bronchial toilet, or stenting), discharge within 24 h of FOB, surgical or diagnostic procedures within 24 h of FOB, and use of antibiotics (including antituberculosis chemotherapy) during the 72 h period prior to the study.

**Bronchoscopy**

FOB and diagnostic techniques were performed as recommended by the American Thoracic Society and the British Thoracic Society. All study subjects were admitted to monitor body temperature. The procedures were carried out using a flexible fiberoptic bronchoscope (models BF-1T240, BF-1T200, or BF-3C20, size 3.6 to 5.9 mm; Olympus Optical; Tokyo, Japan). Physicians reported on the performance of specific diagnostic procedures, the doses of medications administered, and the duration of procedure. Volumes of instilled normal saline solution and retrieved amounts of bronchial washings or BAL were also measured. The severity of bleeding was rated on a 2-point scale: none-to-mild bleeding, as just touch bleeding or less, and moderate-to-severe bleeding, ie, more than touch bleeding, which required suctioning or the local instillation of a 1:20000 solution of epinephrine HCl (Jae-II, Seoul, Korea). After FOB, patients were kept under observation for 24 h and body temperature was monitored every 4 h. Fever was defined as an axillary body temperature ≥ 37.8°C.

**Laboratory Evaluations**

CBC counts, spirometry, simple chest radiographs, sputum examinations for acid-fast bacilli (AFB), and sputum cytology were performed before FOB. Chest CT scans were performed in 507 of 518 subjects. Samples obtained during the FOB, such as washing fluid or biopsy tissue, were submitted for bacteriologic, cytologic, and pathologic evaluations. When fever developed after FOB, two sets of blood cultures (both aerobic and anaerobic), CBC, and simple chest radiography were performed.

**Statistical Analysis**

All statistical analyses were performed using SPSS for Windows Release 10.0.1 (SPSS; Chicago, IL). Data are presented as mean ± SEM. To identify the factors that contribute to postbronchoscopy fever, we performed χ² analysis for categorical data, and independent sample t tests for numerical data; and logistic regression analysis was then used to re-examine factors with p < 0.05 in the previous tests. Variables with p < 0.05 were considered to be independent risk factors of fever.

**Results**

**Clinical Characteristics of Patients With Fever After FOB**

Five hundred eighteen subjects were enrolled in the study, and fever during the first 24 h after FOB developed in 26 subjects (5.0%) [Table 1]. In patients in whom fever developed, the mean peak body temperature was 38.5 ± 0.1°C (37.8-39.9) and peak body temperature was reached within 12 h of FOB. The most common diagnoses were thoracic neoplasm (26/26), lung abscess (17/26), bronchiectasis (14/26), and lung cancer (6/26). The course of fever was transient in all subjects. Episodes of fever were resolved within 72 h of FOB.

**Table 1—Clinical Characteristics of Febrile Patients After Bronchoscopy**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of fever</td>
<td>26/518 (5.0)</td>
</tr>
<tr>
<td>Peak body temperature (range), °C</td>
<td>38.5 ± 0.1 (37.8-39.9)</td>
</tr>
<tr>
<td>Onset of fever (n = 26), h</td>
<td>8.7 ± 1.1</td>
</tr>
<tr>
<td>Duration of fever (n = 25), h</td>
<td>14.0 ± 3.1</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>0/15 (0)</td>
</tr>
<tr>
<td>New infiltrates in chest radiograph</td>
<td>1/19 (5.3)</td>
</tr>
</tbody>
</table>

*Data are presented as No./total (%) or mean ± SD. One subject was excluded because of continuous fever after bronchoscopy.
temperature was 38.5°C (range, 37.8 to 39.9°C), and the mean fever onset time was 8.7 ± 1 h after FOB. In most cases, the fever subsided spontaneously within a day, with a mean fever duration of 14.0 ± 3.1 h. Accompanying symptoms at the time of fever were cough in 42.3% (11 of 26 subjects), sputum in 38.5% (10 of 26 subjects), chill in 34.6% (9 of 26 subjects), and dyspnea in 3.8% (1 of 26 subjects). Bacterial organisms were not detected in blood culture specimens drawn at the time of fever. Simple chest radiographs obtained before and after FOB were unchanged, except in one patient, who showed a new infiltrate on chest radiography. Rapidly progressive pneumonia developed in this patient, who died despite antimicrobial therapy and supportive care on the 26th day following bronchoscopy.

Associations of Postbronchoscopy Fever With Clinical and Laboratory Findings

No differences in demographic characteristics, ie, smoking history or baseline pulmonary function tests, were observed between patients with fever (fever group) and those without fever (nonfever group) [Table 2]. To determine whether fever development is related to chest radiographic findings, the chest radiographic findings were classified as follows: (1) nodular lesion (single or multiple, each lesion < 3 cm); (2) mass (≥ 3 cm); (3) consolidation; (4) atelectasis; and (5) others (ground glass, bronchial lesion, fibrotic band, cavitary lesion, etc). On the CT scans, the extent of involvement was rated by summing the involved areas. Subjects were then categorized based on the involvement of one subsegment or less, or of more than one subsegment. Consolidation was more common in the fever group (19.2%) than in the nonfever group (6.7%; relative risk [RR], 3.31; 95% confidence interval [CI], 1.17 to 9.34; p = 0.034). Other chest radiologic findings were not different between the fever group and nonfever group (Fig 2). Extensive pulmonary involvement (more than one subsegment) was more common in the fever group (80.0%) than in the nonfever group (52.5%; RR, 3.26; 95% CI, 1.34 to 9.80; p = 0.007).

We next compared bronchoscopic procedures between the two groups. The following parameters were more common in the fever group than in the nonfever group: abnormal bronchoscopic findings (69.2% vs 48.6%; RR, 2.38; 95% CI, 1.02 to 5.58; p = 0.04), the duration of the procedure > 10 min (84.6% vs 51.6%; RR, 5.15; 95% CI, 1.75 to 15.17; p = 0.001), bronchial washing or BAL (100% vs 75.4%; p = 0.004), biopsy (53.8% vs 24.6%; RR, 3.58; 95% CI, 1.61 to 7.94; p = 0.001), moderate-to-

![Figure 1. Peripheral blood WBC and differential counts](http://publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/20385/ 06/16/2017)

**Table 2—Demographic Characteristics and Baseline Pulmonary Function Tests**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Nonfever Group</th>
<th>Fever Group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>56.4 ± 0.6</td>
<td>54.2 ± 3.1</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Male/female sex, No.</td>
<td>318/174</td>
<td>19/7</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Smoker/nonsmoker, No.</td>
<td>262/230</td>
<td>15/11</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Pack-years</td>
<td>15.2 ± 0.9</td>
<td>16.7 ± 3.8</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>FEV1, predicted %</td>
<td>87.1 ± 1.1</td>
<td>83.4 ± 2.5</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>FVC, predicted %</td>
<td>88.2 ± 0.8</td>
<td>86.2 ± 3.4</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>FEV1/FVC, %</td>
<td>72.2 ± 0.5</td>
<td>71.1 ± 1.9</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD unless otherwise indicated.
severe bleeding (57.7% vs 19.3%; RR, 5.70; 95% CI, 2.54 to 12.81; p < 0.001), the total amount of saline solution or drug administered (p = 0.002), and the dose of lidocaine instilled (p = 0.016) [Table 3, Fig 3]. In contrast, the amount of fluid retrieved was similar for the two groups (Table 3).

Microbiological examinations were performed on the bronchial washing fluid or BALF. The incidence of bacterial organism isolation was not different between the two groups (57.1% vs 47.5%, p = 0.05). However, the incidence of positive AFB smears or of positive mycobacterial culture findings (from sputum, lavage fluid, or endobronchial biopsy specimens) was significantly higher in the fever group (26.9%) than in the nonfever group (11.5%; RR, 3.03; 95% CI, 1.61 to 7.57; p = 0.023) [Table 4]. Among the patients with pulmonary tuberculosis (n = 48), the number of patients who showed positive AFB smear prior to FOB was 15. The incidence of fever was higher in these patients (5 of 15 patients, 33.3%) than in patients who showed negative AFB smear results prior to FOB and had tuberculosis diagnosed after FOB (2 of 33 patients, 6.1%; p < 0.05).

The incidence of fever after FOB was evaluated according to the final diagnosis. Pulmonary tuberculosis was significantly more common in the fever group (26.9%) than in the nonfever group (8.3%; RR, 4.05; 95% CI, 1.61 to 10.21; p = 0.006). In contrast, lung cancer, pneumonia, bronchiectasis, metastatic lung cancer, or nontuberculous mycobacterium were not associated with fever development (Table 5). In the present study, the incidence of fever in subjects with a diagnosis of tuberculosis (14.6%) was significantly higher than others (Fig 4). Furthermore, in patients with positive mycobacterial culture findings, or positive smear results for AFB, clinically and radiologically advanced disease (smear positive tuberculosis, presence of cavitary lesion or multidrug-resistant Mycobacterium tuberculosis) was more common in the fever group (71.4%) than

Table 3—Comparison of Diagnostic Procedures and Bleeding During FOB Between the Fever Group and the Nonfever Group*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Nonfever Group (n = 492)</th>
<th>Fever Group (n = 26)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal bronchoscopic findings</td>
<td>239 (48.6)</td>
<td>18 (69.2)</td>
<td>0.04</td>
</tr>
<tr>
<td>Duration of procedure &gt; 10 min†</td>
<td>254 (51.6)</td>
<td>22 (84.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Bronchial washing or BAL</td>
<td>371 (75.4)</td>
<td>26 (100)</td>
<td>0.004</td>
</tr>
<tr>
<td>Bronchial washing or BAL recovery, %‡</td>
<td>51.6 ± 1.2</td>
<td>51.1 ± 2.7</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Biopsy</td>
<td>121 (24.6)</td>
<td>14 (53.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>Moderate-to-severe bleeding§</td>
<td>95 (19.3)</td>
<td>15 (57.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Data are presented as No. (%) or mean ± SD.
†The duration that the bronchoscope is in the patient, measured in minutes.
‡Recovery % = 100 × the amount of fluid retrieved/the amount of saline solution administered.
§More than touch bleeding that required suctioning or local instillation of a 1:20,000 solution of epinephrine HCl.
in the nonfever group (25.9%; relative risk, 6.61; 95% CI, 1.15 to 38.07; \( p = 0.032 \) by Fisher exact test) [Table 4].

**Predictors of Fever**

By univariate analysis, the following variables were determined to be risk factors of fever following FOB: the duration of the procedure, biopsy, washing, or BAL, the radiologic extent of involvement, consolidation, abnormal bronchoscopic findings, bleeding, the amount of saline solution or drug administered, the dose of lidocaine instilled, and the diagnosis of pulmonary tuberculosis. However, these variables may be interrelated, for example, the severity of bleeding can affect the duration of the procedure; likewise, whether or not biopsy was performed may affect the severity of bleeding. Before performing multivariate analysis, we examined the associations between the variables using the Spearman correlation coefficient (rs), which found that the following variables were significantly interrelated: the duration of the procedure and the severity of bleeding (rs = 0.401), the severity of bleeding and biopsy (rs = 0.735), and the amount of saline solution and drug administered and lavage (rs = 0.737). Therefore, to avoid collinearity in the regression analysis, lavage, biopsy, and the duration of the procedure were excluded from the regression analysis.

Logistic regression analysis was conducted using the following variables: the diagnosis of pulmonary tuberculosis, the radiologic extent of involvement, the dose of lidocaine instilled, abnormal bronchoscopic findings, the severity of bleeding, the amount of saline solution and drug administered, and consolidation. Only the diagnosis of pulmonary tuberculosis (RR, 3.316; 95% CI, 1.12 to 9.80; \( p = 0.030 \))

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**Table 4—Results of Bacteriologic Evaluations**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Nonfever Group</th>
<th>Fever Group</th>
<th>( p ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive bacterial culture finding†</td>
<td>56/118 (47.5)</td>
<td>4/7 (57.1)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Positive AFB smear or culture finding‡</td>
<td>54/471 (11.5)</td>
<td>7/26 (26.9)</td>
<td>0.023</td>
</tr>
<tr>
<td>( M ) tuberculosis positive</td>
<td>35 (7.4)</td>
<td>7 (3.8)</td>
<td></td>
</tr>
<tr>
<td>AFB stain positive in endobronchial biopsy specimen</td>
<td>6 (1.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nontuberculous mycobacterium positive</td>
<td>13 (2.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinically and radiologically advanced mycobacterial disease</td>
<td></td>
<td>14/54 (25.9)</td>
<td>5/7 (71.4)</td>
</tr>
</tbody>
</table>

*Data are presented as No./total (%) or No. (%).
†From BALF or bronchial washing fluid.
‡From sputum, bronchial washing fluid, BALF, or bronchial biopsy specimen.
§Fisher exact test.
¶Smear-positive, cavitary lesion positive and multidrug resistant \( M \) tuberculosis.
and the severity of bleeding during bronchoscopy (RR, 3.23; 95% CI, 1.14 to 9.12; p = 0.027) were identified as independent predictors of fever following bronchoscopy.

**Discussion**

Previous studies reported on variable incidence of fever after FOB; although the incidence of fever after FOB was 1.2 to 2.5% in adults,9,11 fever developed in 48% of children.14 However, fever after BAL was documented in 21% of healthy volunteers,21 and fever after transbronchial needle aspiration was reported in 10% of 50 cases.10 In the present study, fever developed in 5% of patients within 24 h of FOB. Differences in underlying pulmonary diseases, diagnostic techniques during bronchoscopy, and the definition of fever may account for these discrepancies in the incidence of fever.

The mechanism of fever after FOB has not been elucidated. One factor that may contribute is transient bacteremia. In fact, bacteremia following FOB has been reported in immunocompromised patients.22,23 Although in the present study, prior antibiotic therapy did not affect the incidence of fever after bronchoscopy (no antibiotic group, 5.0%, vs antibiotic group, 4.9%; data not shown in the “Results”), we excluded subjects who were administered antibiotics during the 72-h period prior to FOB, to eliminate the effect of antibiotics on the isolation of bacterial organisms. Subjects receiving immunosuppressive agents or corticosteroids were also excluded from this study. However, no bacterial organisms were isolated from blood cultures at the time of fever. This is in agreement with the findings of previous reports, which demonstrate that bacteremia is rarely detected in immunocompetent subjects who acquire fever after bronchoscopy.9,11,14,17 These results suggest that postbronchoscopy fever is not related to bacteremia at least in immunocompetent subjects. However, one limitation of our study is that we were unable to obtain all the blood samples at the time of fever, and therefore we cannot completely exclude the possibility of bacteremia at the time of fever in the missing cases.

An alternative possible cause of fever after FOB is systemic inflammatory response, which is characterized by fever, tachypnea, tachycardia, and leukocytosis. In the present study, significant increases in

<table>
<thead>
<tr>
<th>Variables</th>
<th>Nonfever Group (n = 492)</th>
<th>Fever Group (n = 26)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung cancer</td>
<td>193 (39.2)</td>
<td>10 (38.5)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>41 (8.3)§</td>
<td>7 (26.9)§</td>
<td>0.0061</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>32 (6.5)§</td>
<td>3 (11.5)§</td>
<td>&gt; 0.051</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>30 (6.1)§</td>
<td>1 (3.8)§</td>
<td>&gt; 0.051</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>21 (4.3)§</td>
<td>0 (0)§</td>
<td>&gt; 0.051</td>
</tr>
<tr>
<td>Esophageal cancer</td>
<td>16 (3.3)§</td>
<td>0 (0)§</td>
<td>&gt; 0.051</td>
</tr>
<tr>
<td>Metastatic cancer</td>
<td>15 (3.0)§</td>
<td>1 (3.8)§</td>
<td>&gt; 0.051</td>
</tr>
<tr>
<td>Nontuberculous mycobacterium</td>
<td>13 (2.6)§</td>
<td>0 (0)§</td>
<td>&gt; 0.051</td>
</tr>
<tr>
<td>Others</td>
<td>144 (29.3)§</td>
<td>4 (15.4)§</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>

*Data are presented as No. (%).
†Fisher exact test.
‡M tuberculosis-positive culture 35 cases; endobronchial biopsy that showed caseating granulomas with acid-fast organisms, 6 cases.
§All M tuberculosis-positive culture.
∥All diagnoses by histologic or cytologic methods.

Figure 4. A final diagnosis and the incidence of fever following FOB.
the total leukocyte and neutrophil counts were observed in the peripheral blood at the time of fever compared to the pre-FOB values. These findings are in agreement with those of previous studies. Proinflammatory cytokines such as TNF-α and IL-1β are now considered central features of systemic inflammation. Indeed, increased circulating IL-6 and granulocyte colony-stimulating factor levels have been reported after BAL. These results suggest that postbronchoscopy fever may be a manifestation of systemic inflammatory response, which can be elicited by a wide variety of insults, such as suctioning, lidocaine instillation, and a range of diagnostic procedures.

In this study, various clinical parameters were associated with fever after FOB by univariate analysis. However, only the final diagnosis of pulmonary tuberculosis and the severity of bleeding were identified as independent risk factors of fever by multivariate analysis. Fever developed more frequently in patients with tuberculosis than in patients with lung cancer. Furthermore, among those subjects positive for mycobacterial studies, clinically and radiologically advanced disease was more common in the fever group than in the nonfever group. Although the mechanism of this discrepancy was not found during this study, it might be related to the basal levels of systemic inflammation associated with disease. Indeed, it has also been reported that patients with elevated IL-1β serum concentrations prior to the procedure are more likely to acquire fever than patients with normal baseline cytokine levels. It has also been reported that levels of TNF-α and IL-1β are elevated in BALF of patients with active pulmonary tuberculosis, and that this is correlated with disease extent. However, various levels of pyrogenic cytokines in the BALF of patients with lung cancer have been reported. Therefore, differences in pyrogenic cytokine levels in the alveolar compartment may affect the incidence of fever. However, the treatment with antituberculosis medication did not affect the incidence of fever. In the analysis of this study, the subjects who were receiving antituberculosis chemotherapy were excluded. When the subjects who were receiving antituberculosis medication before FOB were included in the analysis, the incidence of fever was not significantly different between patients who were receiving antituberculosis medication (4 of 23 subjects, 17.4%) and patients who finally received a diagnosis of tuberculosis but were not receiving antituberculosis medication (7 of 48 patients, 14.6%; p > 0.05).

The severity of bleeding was also identified as an independent risk factor of postbronchoscopy fever by the present study. Although the mechanism as to how bleeding during FOB can contribute to fever is uncertain, such a mechanism may also be related to systemic inflammation. According to previous reports, hemorrhage evokes systemic and pulmonary inflammation. Thus, there is a possibility that the direct invasion of bacteria or the influx of cytokines into systemic circulation may occur as the severity of bleeding increases during FOB, since the severity of bleeding may correspond to the influx of cytokines or bacteria into the peripheral circulation. BAL, the amount of saline solution or drug administered, and the dose of lidocaine instilled were identified as risk factors in the present study. This is in agreement with a previous study showing that the instillation of fluid into the airways was the main stimulus for the release of cytokines, and prilocaine bolus instillation in FOB patients induced a significant elevation of serum IL-1β and a dramatic increase of serum IL-6, whereas in patients who inhaled a prilocaine aerosol only a minor increase of serum IL-6 was observed. Thus, the more fluid is instilled into the airways, especially into the alveoli, the more and/or stronger macrophages are activated to produce and release cytokines. Furthermore, it is possible that when BAL is performed in an infected or inflamed area, more pyrogenic cytokines are released. This may also account for our findings of a higher incidence of fever among those with abnormal bronchoscopic findings, with consolidation, or with the extensive radiologic involvement. Biopsy was also a risk factor for fever after FOB. However, it is not evident how biopsy influences the development of fever after FOB. In our study, bleeding and the biopsy were significantly related. In the fever group, moderate-to-severe bleeding occurred in 12 of 14 patients who underwent biopsy. Therefore, bleeding rather than biopsy may contribute to the development of fever. Although the duration of the procedure was also one of risk factors after FOB in this study, it was influenced by multiple factors: biopsy, BAL, and bleeding. Therefore, the duration of the procedure was excluded in the final regression analysis.

In the present study, one patient died in association with the bronchoscopic procedure. The patient was a 73-year-old man suspected of having primary lung cancer. A chest CT scan showed that the lesion was centrally located and extensive. After FOB, non-small cell lung cancer with systemic metastasis was diagnosed. Although no bacteremia was reported in this patient, it seems like the pneumonia developed after FOB because fever and a new infiltrate at the site of BAL developed. A possible cause of pneumonia may be contamination occurring in association with the bronchoscopic procedure. The patient’s condition worsened in spite of rigorous antibiotic therapy and full supportive care, and he
died of respiratory failure due to pneumonia while receiving mechanical ventilation.

To our knowledge, this is the first prospective study to investigate the risk factors of fever after FOB according to basal demographic characteristics, chest radiologic findings and bronchoscopic abnormalities, the performance of various diagnostic procedures, and diagnosis. In summary, transient fever was a relatively frequent adverse event following FOB, and independent risk factors for the development of this complication seem to be related to the diagnosis of pulmonary tuberculosis and the severity of bleeding during FOB.

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