REVIEW

Journal of Clinical Microbiology and Infectious Diseases (*JCMID*) 2024, Volume 4, Number 2: 41-49
E-ISSN: 2808-9405

Post-Bronchoscopy Infections: A Literature Review

Tri Wijayanti Permatasari[1], Anis Karuniawati[2*]

Published By : the Indonesian Society for Clinical Microbiology

[1]Program of Clinical Microbiology Residency, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia;
[2]Department of Microbiology Faculty of Medicine, Universitas Indonesia - dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

*Corresponding to:
Anis Karuniawati;
Department of Microbiology Faculty of Medicine, Universitas Indonesia - dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia
anis.kurniawatimk@ui.ac.id

Received: 2023-10-02
Accepted: 2024-11-19
Published: 2024-12-15

ABSTRACT

Post-bronchoscopy infections are a critical concern in respiratory medicine, given their potential to exacerbate patient morbidity, particularly among immunocompromised individuals or those with pre-existing lung conditions, one of which is infection. The infection arises from lower respiratory tract pathogens, and most infections originate from reprocessing practices. Infection can occur when the bronchoscope comes into contact with the mucosa and blood vessels of the respiratory tract. Bacteremia is a more often post-bronchoscopy infection complication rather than pneumonia. It is commonly involving *Coagulase-negative or positive Staphylococcus, non-hemolytic or hemolytic Streptococcus, Citrobacter species,* and *Klebsiella*. However, in general, the incidence of post-bronchoscopy infection is mainly caused by gram-negative bacteria. Various risks can affect post-bronchoscopy infection that can increase the severity of the disease to death. It is important to increase obedience and precaution against the transmission of infection. Reducing bacterial pathogens and controlling infection are important steps to reduce the post-bronchoscopy infection mortality rate. Therefore, this study aimed to review the post-bronchoscopy infections in detail.

Keywords: post-bronchoscopy, infection, microorganism.
Cite This Article: Permatasari, T.W., Karuniawati, A. 2024. Post-Bronchoscopy Infections: A Literature Review. *Journal of Clinical Microbiology and Infectious Diseases* 4(2): 41-49. DOI: 10.51559/jcmid.v4i2.61

INTRODUCTION

Bronchoscopy is a diagnostic and therapeutic procedure used to visualize the upper and lower respiratory tract directly. There are two types of bronchoscopes used: rigid and flexible.[1,2] In some cases, doctors may also take mucus and tissue samples (biopsy) to address airway blockages or other lung problems. During bronchoscopy, there is a risk of infection when the bronchoscope meets the mucosa and blood vessels.[3–5] Patients undergoing bronchoscopy may experience complications such as hypoxemia, cardiac arrhythmias, myocardial infarction, bleeding, pneumothorax, and infection. The reported complication rates for bronchoscopy range from 5-32%, with a mortality rate of 0-0.8%.[6] Steinfort et al., in 2010, found a 7% rate of bacteremia with oropharyngeal microorganisms and a 35% positive bacterial culture rate from needle-wash specimens.[7]

Post-bronchoscopy infections are a critical concern in respiratory medicine, given their potential to exacerbate patient morbidity, particularly among immunocompromised individuals or those with pre-existing lung conditions. Post-bronchoscopy infections can arise from pathogens in the lower respiratory tract and infections transmitted from inadequate bronchoscope reprocessing practices, leading to outbreaks.[5] In 2019, Gladys et al. reported a multidrug-resistant (MDR) outbreak, with 70% attributed to *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* in the intensive care unit, originating from reprocessed bronchoscopes.[8]

Although post-bronchoscopy infections are rare, there are reports of complications ranging from 0.2% to 5.2%, such as pneumonia, lung abscess, and empyema, occurring after bronchoscopy procedures that can impact patient survival. Post-bronchoscopy respiratory infections are defined as respiratory infections that occur within 24 hours after the bronchoscopy procedure, marked by clinical symptoms of fever, increased proinflammatory mediators, and identification of microorganisms (2.9% positive cultures indicating biopsy-induced bacteremia) from suspected infection specimens. Chest X-rays and computed tomography (CT) scans may reveal new or progressive infiltrates. Bacteremia can occur at a rate of 6.5% without mucosal damage and prior antibiotic use.[9–12]

The potential for infection in post-bronchoscopy patients is influenced by several factors, including age (≥75 years), gender, smoking status, comorbidities, anesthesia drugs, bronchoscopy technique (BAL, bronchial biopsy, lung biopsy), lesion location, size, and final diagnosis, bronchial stenosis, and white blood cell count and CRP concentration before bronchoscopy.[11,13] The intensity of patient exposure to potentially pathogenic microorganisms after the bronchoscopy procedure is a significant consideration. Establishing safe and secure procedures for individuals at risk is a strategy for preventing post-bronchoscopy infections. Therefore, this study aimed to review the post-bronchoscopy infections in detail.

Table 1. Organisms involved in bronchoscopy-related infections[15]

Bacteria	*Mycobacterial*	Fungi
Pseudomonas aeruginosaa	*Mycobacterium tuberculosis*	*Rhodotorula rubra*
Serratia marcescensa	*M. chelonae*	*Aureobasidium* spp.
Klebsiella pneumoniae	*M. avium-intercellulare*	*Blastomyces dermatitidis*
Legionella pneumophila	*M. xenopi*	*Trichosporon cutaneum*
Burkholderia pseudomallei	*M. fortuitum*	*Penicillium* spp.
Proteus	*M. gordonae*	*Cladosporium* spp.
Bacillus	*M. abscessus*	*Phialospora* sp.
Methylobacterium mesophilicum		
Morganella morganii		
Enterobacter cloacae		
Stenotrophomonas maltophilia		

CLASSIFICATION OF POST-BRONCHOSCOPY INFECTIONS

Clinically, bronchoscopy-related infections are classified as infections caused by lower respiratory tract pathogens (occurrence rate of 3-4%), and most infections originate from reprocessing practice. Lower respiratory tract infections can be acquired by patients with clinical symptoms and signs of infection, and pathogenic microorganisms are found due to infection transmission during bronchoscopy. Infections caused by pathogenic microorganisms can result from endogenous flora (microorganisms present in the patient) or exogenous microorganisms (microorganisms entering through bronchoscopy). The occurrence of infections caused by the transmission of microorganisms between patients or the environment after bronchoscopy is estimated to be very low. Bacteria colonizing the oropharynx or nasal cavity can be aspirated and become a temporary source of bacteremia and pneumonia. Post-bronchoscopy pneumonia can occur (<1%), known as hospital-acquired infection. Post-bronchoscopy bacteremia occurs in 6-8% of patients, most commonly involving *Coagulase-negative or positive Staphylococcus, non-hemolytic or hemolytic Streptococcus, Citrobacter species, and Klebsiella*. Transmission of viral pathogens through flexible endoscopy rarely occurs due to obligate intracellular microorganisms that cannot replicate outside human cells. Therefore, if viral particles are present in the flexible endoscope after the procedure, the viral load cannot increase because they are unable to replicate in vitro.[14]

Endogenous infections from microbes entering the bloodstream or other normally sterile areas result from mucosal trauma or instrumentation and are not related to bronchoscope instrument processing issues. For example, pneumonia is due to oral secretion aspiration when a patient is under anesthesia or bacteremia resulting from microscopic tissue trauma during bronchoscopy. The upper respiratory tract mucosa has a significant number of microorganisms that can be introduced into the lower respiratory tract when the bronchoscope tube is inserted into the lungs through the mouth. In adults, the upper respiratory tract microbiota includes three phyla: *Actinobacteria*, *Firmicutes*, and *Proteobacteria*, including *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Propionibacterium*, *Corynebacterium*, *Moraxella*, and *Propionibacterium acnes*.[16]

Infections originating from the transmission of bronchoscope instrument reprocessing practices are found to have positive cultures in bronchoscopy specimens without clinical evidence of disease. These infections can arise from inadequate instrument reprocessing practices. While not worsening the patient's clinical condition, these findings can slow down the diagnosis process. Infections without clinical evidence require comprehensive epidemiological investigation into bronchoscopy facilities, addressing reprocessing failures until the cause is identified and corrected. A variety of bacteria, mycobacteria, and fungal agents are involved in bronchoscopy-related outbreaks. *Pseudomonas aeruginosa* and *Serratia marcescens* were found to be the causes of most post-bronchoscopy infections. Recent reports include multidrug-resistant infections caused by *Acinetobacter baumannii* and *Klebsiella pneumoniae* through bronchoscopy. Poorly maintained bronchoscopes with microbial growth of 58% can lead to infections. In 2019, the Emergency Care Research Institute (ECRI) observed the recontamination of flexible endoscopes due to mishandling or improper storage. Recontamination is caused by the personnel's failure to change gloves insert, and remove the endoscope from the Automated Endoscope Reprocessor (AER).[17]

Bronchoscope devices have internal, long, and narrow canal structures that can be contaminated with microorganisms during each procedure, allowing biofilm formation. There are reports of biofilm formation on bronchoscopes leading to infections caused by *Pseudomonas aeruginosa*.[18] Biofilm plays a crucial role in causing secondary infections in contaminated medical equipment. Biofilm forms when microorganisms attach to solid surfaces, forming colony structures and extracellular materials serving as nutrient storage for bacteria. Bacteria in biofilm strongly adhere to each other's surfaces through flagella and type IV pili support, forming microcolonies. Microcolonies continue to grow into mature biofilm structures, and cavities within microcolonies are disturbed, leading to cell autolysis. One of the biofilm formation cycles in *P. aeruginosa* is divided into 6 stages: (1) Bacteria attach to the surface and produce extracellular polymer substances (EPS), including polysaccharide proteins, lipids, and DNA. (2) Cell division occurs, and reversible attachment transitions to irreversible attachment. (3) Microcolony formation and cell interaction play a crucial role in biofilm maturation and resistance.

(4) Mature biofilm forms a fungus-like structure that increases antibiotic tolerance. (5) Cavities in the center of microcolonies rupture through cell autolysis. Finally, within 2 hours, released cells transition to a planktonic phenotype, occupying uncolonized spaces. Biofilm protects bacteria from disinfectant activities and can cause inactivation of microbial agents to plasmid-mediated resistance. Biofilm from chronic lung infections shows slow growth and is challenging to culture microbial organisms.[19]

CLINICAL SIGNS AND SYMPTOMS

Post-bronchoscopy infection is a respiratory tract infection that occurs within 24 hours after bronchoscopy with the following criteria: (1) Onset or exacerbation of respiratory symptoms lasting > 24 hours (fever > 37°C, cough, sputum production, chest pain, dyspnea), (2) Increase in leukocytes or C-reactive protein (CRP) compared to before bronchoscopy, (3) New infiltrate or exacerbation on chest X-ray or CT scan with antibiotic administration. Fever in patients with post-bronchoscopy infection ranges from 1.2-16%. Fever above 38°C occurs approximately 4-24 hours after bronchoalveolar lavage (BAL), with 13% associated with acute inflammatory response. Fever <40°C lasts an average of 14 hours but is rarely accompanied by infiltrates on chest X-ray.[6] An acute systemic inflammatory response is marked by elevated levels of circulating cytokines and the activation of alveolar macrophages, resulting in the release of inflammatory mediators such as tumor necrosis factor (TNF)-alpha, interleukin (IL)-1 beta, and IL-6. Bronchoscopy procedures, including forceps biopsy and transbronchial needle aspiration, can trigger the release of these pyrogenic mediators.[20] However, it is unknown whether microbiological components contribute to inflammatory cytokine release.[21,22]

Proinflammatory mediators such as leukocytes, CRP, and procalcitonin (PCT) have been suggested as indicators of invasive bacterial infection.[23] Leukocyte counts are within the normal range (<9,000/μL in men and <7,800/L in women) before bronchoscopy, and an increase to >10,000/L is considered significant. When leukocyte counts are already elevated before bronchoscopy, an increase of >2,000/μL from the baseline is considered significant.[22] CRP is within the normal range (<0.5 mg/dL), and an increase to >1.0 mg/dL after bronchoscopy is considered significant. When CRP is already increased (≥ 0.5 mg/dL) before bronchoscopy, an increase of >1.0 mg/dL from the baseline is considered significant. PCT is evaluated as a response to endotoxins released in bacterial infections (IL-6, TNF-α, IL-8, IL-1β), and its elevation is associated with the severity of infection. PCT and IL-8 are good indicators of the success of antibiotic use. Repeat PCT examination is recommended on days 3, 5, and 7 after antibiotic administration.[24,25] A decrease in PCT to <0.25 g/L or at least >80%-90% from the peak is used as a threshold for antibiotic discontinuation.[25] PCT increases within 6 hours after inflammation, with a half-life of 25 to 30 hours, presenting as a predictor of disease severity and can be used to assess antibiotic success. PCT levels are significantly higher in patients with proven bacterial infection when fever occurs after bronchoscopy.[20,26] In cases of viral infection or non-infectious fever, procalcitonin levels are low or normal (<0.15 ng/ml).[27] PCT is a good marker for diagnosing bacterial infection if serum levels increase 3 to 4 hours after infection, much faster than other inflammatory markers such as CRP.[28]

Immune response decline occurs in cancer patients due to leukocyte deficiency, inflammation dysregulation, mucosal disruption, pathogen recognition impairment, and anatomical abnormalities caused by tumors, making cancer patients vulnerable to lower respiratory tract infections.[29] Infections in lung cancer patients can occur after bronchoscopy, accounting for 3% without death and disability. Research conducted in Japan by Asano et al. in 2010 reported a 0.2% diagnostic bronchoscopy-related lung complication rate.[30] Takiguchi et al., in 2017, reported a post-bronchoscopy pneumonia rate in lung cancer patients of 4.1%.[31] In both studies, risk factors influencing pneumonia were advanced age (≥70 years), smoking, lesion location, and size affecting pneumonia.[32] Pathogenic microorganisms involved in infection include *Peptostreptococcus*, *Streptococcus anginosus*, Group A *Streptococcus*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Haemophilus influenzae*, and some difficult-to-identify pathogens.[33,34]

In a study conducted by M. Shimoda et al., 61% of 344 patients with post-bronchoscopy lung infections were found to have risk factors, including elevated leukocyte and CRP levels, low serum albumin levels, tumor necrosis and cavitation, as well as large tumor diameters. Post-obstruction pneumonia, defined as a new infiltrate or consolidation around the target lesion observed during bronchoscopy, is a notable complication. This condition frequently occurs in patients with advanced and progressive neoplasms and is associated with significant morbidity and mortality. Post-obstructive community-acquired pneumonia (PO-CAP) is prevalent among patients with a smoking history (93%) and those with chronic obstructive pulmonary disease (43%). Symptoms often include fever, chills, weight loss, cough, sputum production, dyspnea, hemoptysis, and pleuritic chest pain. Leukocytosis is detected in 40% of blood tests, cavitation in chest imaging in 17%, and bacterial infections in 10% of microbiological examinations. Pneumonia associated with advanced lung malignancy (PO-AM) is reported in 45-55% of cases. As the condition progresses, mucus retention distal to the obstruction leads to alveolar filling with mucus and serum from alveolar capillaries, resulting in infection and an acute inflammatory response. Obtaining diagnostic specimens is challenging due to the infection's distal location and the lack of sputum production in most patients.[35]

MICROBIOLOGICAL EXAMINATION OF THE LOWER RESPIRATORY TRACT

Laboratory diagnosis of respiratory tract infections is necessary to provide prompt and adequate management to control infections in patients and reduce the length of hospital stays. Lower respiratory

Table 2. Microorganisms cause post-obstructive pneumonia in cancer patients[31]

Gram-positive bacteria
Staphylococcus aureus (including MRSA)
Viridans group streptococci (60% are susceptible to penicillin non-susceptibility)
Beta-hemolytic streptococci (group A, B, C, F, and G)
Gram-negative bacteria
Escherichia coli
Klebsiella species
Enterobacteriaceaea lainnya
Pseudomonas aeruginosa
Strenotrophomonas maltophilia
Acinetobacter species
Nonfermenting Gram-negative bacilli (NFGNB)
Anaerobic Bacteria
Peptococcus spp. and *Peptostreptococcus* spp.
Fusobacterium nucleatum
Bacteroides melaninogenicus
Fungi
Candida spp.

tract infections include infections that occur in the bronchi, bronchioles, alveoli, and lungs. Lower respiratory tract infections can be caused by a variety of pathogens, including bacteria, viruses, and fungi. Diagnostic methods for identifying the causative microorganisms include microscopic examination, culture, serology, and molecular techniques. Among these, culture remains the most widely used conventional method and is regarded as the gold standard for diagnosis. Molecular-based techniques, on the other hand, are particularly valuable for detecting viruses and atypical bacteria.[36]

The collection of specimens is a critical step in ensuring the quality of respiratory samples, which directly influences laboratory diagnostics and patient management. Accurate microbiological diagnosis relies heavily on the timing of specimen collection, as it plays a vital role in interpreting results effectively. Respiratory specimens should be collected when symptoms are present since the number of viruses and bacteria may decrease after 72 hours of clinical onset. The transportation and storage methods of samples should be as fast as possible to the laboratory within 1-2 hours, maintaining a temperature of -80°C to -20°C to preserve microbial conditions. If not possible, samples should be stored at 4°C to 8°C and processed on the first or following day if specimens in transport media can be stored at room temperature or 4°C. To detect the virus, they should be transported in appropriate transport media at 2-8°C and frozen at -80°C if the test is delayed for >48 hours. Based on the suspected pathogen etiology, diagnosing respiratory infections requires the appropriate type of specimen and collection method. Specimens suitable for microbiological examination for lower respiratory tract infections include sputum, bronchoscopy specimens, bronchoalveolar lavage (BAL), endotracheal aspiration, and transthoracic lung aspiration. Lower respiratory tract specimens can be contaminated with commensal oropharyngeal microbiota, which can interfere with result interpretation.[36]

Furthermore, microscopic examination is a beneficial test for assessing sample quality before culturing to prevent errors in result interpretation. Microscopic examination provides initial information, such as the number of polymorphonuclear cells (PMNs) found, and the presence of characteristic bacterial morphology in microscopic examination results can provide an early indication of culture results and guide treatment. Gram staining and microscopic examination are essential steps in evaluating the suitability of samples from patients suspected of having lower respiratory tract infections. Specimen quality is assessed based on the number of epithelial cells and polymorphonuclear neutrophils (PMNs) observed in the Gram stain smear. The presence of inflammatory markers and bacterial characteristics, such as shape, arrangement, quantity, and intra- or extracellular location, can indicate infection. For aspiration pneumonia, Gram stain smears typically show numerous PMNs and intracellular respiratory bacteria (often Streptococcus and anaerobic bacteria), which must be differentiated from contaminating respiratory microbiota. The results of Gram staining should highlight bacteria with features resembling common respiratory pathogens, enabling clinicians to interpret findings accurately and guide potential empirical therapy. Communicating these findings to physicians ensures timely and effective management. While electron microscopy can be used to diagnose respiratory viral infections, it has significant limitations. These include operator fatigue, long processing times, the need for advanced technical skills, strict experimental controls, and a high concentration of virus particles ($>10^5$/mL). Completion times range from 3 to 16 hours, including specimen preparation. Due to these challenges, direct application of electron microscopy to clinical samples is not recommended as a routine diagnostic tool. Instead, it is better suited for identifying viruses that cause cytopathic effects following cultivation.[43]

For mycobacterial examination, acid-fast staining with Ziehl-Neelsen and Kinyoun stains is performed. Immunofluorescence (IF) antibody staining on specimens is more challenging and less specific, replaced mainly by nucleic acid amplification techniques (NAAT). Stains such as alcofluor white, methenamine silver, Giemsa, and periodic acid-Schiff (PAS) can be used for tissue and other specimens, such as fungi and parasites. Potassium hydroxide (KOH) solution can be used to lyse tissue and epithelium around fungi to observe fungal hyphae. If fungal infection is suspected, lactophenol cotton blue (LPCB) stain is used to examine growth and identify fungi.[37]

Bacterial cultures are a vital method for identifying pathogenic bacteria in the respiratory tract, including atypical bacteria, but they require technical

expertise and significant time to produce results. The accuracy of this method depends on specimen quality at the time of sampling and is compromised if the patient has already started antibiotic therapy. Aerobic, facultative anaerobes, and obligate anaerobic bacteria can be cultured, followed by biochemical tests to identify colonies. Both qualitative and quantitative bacterial cultures are utilized.[36]

1. Qualitative Bacterial Cultures
   Specimens are inoculated onto media like blood agar and MacConkey agar, incubated at 5% CO_2 for 24-48 hours. For atypical bacteria, selective media are used: Hemophilus spp.: Chocolate agar at 35°C, 5% CO_2 for 24-48 hours. Legionella spp.: Charcoal yeast extract with antimicrobials, incubated aerobically at 35°C for 5-10 days. *Chlamydophila spp*.: Antibiotic-containing media, stored at 4°C (24-48 hours) or -70°C for extended periods. *C. trachomatis and C. psittaci: Cultured in McCoy cells. C. pneumoniae:* Cultured in Hep-2 cells. *Burkholderia cepacia*: Selective agar and oxidative-fermentative polymyxin B bacitracin lactose media. *M. pneumoniae*: Mycoplasma-glucose or methylene blue-glucose agar up to 3 weeks. *S. aureus*: Mannitol salt agar. *Nocardia spp*.: BCYE agar at 35°C for up to 3 weeks. Due to the slow growth of organisms like *Chlamydophila* and *Mycoplasma species* and the complexity of culturing processes, molecular tests are preferred for faster and more accurate diagnostics.[36]
2. Quantitative Bacterial Cultures
   Quantitative cultures are critical for diagnosing *ventilator-associated pneumonia* (VAP), aspiration pneumonia, and infections in immunocompromised patients or those with cystic fibrosis. For bronchoalveolar aspirate (BAS), the detection of $>10^6$ CFU/mL suggests active infection, while lower amounts may indicate contamination. Similarly, bronchoalveolar lavage (BAL) samples with $<10^4$ bacteria/mL likely represent contamination, while counts $>10^5$ bacteria/mL confirm active infection. Overall, bacterial cultures remain indispensable in clinical microbiology, but their limitations necessitate complementing them with molecular diagnostic techniques to ensure timely and accurate results.[36]

Phenotypic identification systems can be semi-automatic, with reactions prepared manually, or automatic instruments (Vitek, Phoenix, MicroScan TREK) that can achieve sophistication in identifying organisms and conducting antimicrobial susceptibility testing. The Vitek system (sensitivity and specificity 95-96%) has cards for identifying anaerobes, *coryneforms*, and fungi. Organisms are identified by generating a score or percentage, and a low score indicates that identification has not been achieved. This can happen if there is no match in the database, possibly due to poor preparation. The detection of major respiratory viruses by observing cytopathic effects in cell cultures remains the gold standard. Degenerative changes in monolayer cells serve as evidence of viral presence. However, viral cultures demand technical expertise, are time-consuming, have a high false-negative rate, and are limited to specialized laboratories. Due to these challenges, molecular tests are often favored for faster and more accurate virus identification.[37]

Antigen detection methods are widely utilized in healthcare due to their affordability and rapid turnaround time (<30 minutes). For influenza and respiratory syncytial virus (RSV), these tests demonstrate sensitivity ranging from 44% to 95% and specificity of 90-95% when compared to cell culture. In bacterial diagnostics, they enable quick identification of pathogens from respiratory, blood, and urine samples, particularly for *S. pyogenes, S. pneumoniae, M. pneumoniae, C. pneumoniae, and Legionella species*. For detecting group *A Streptococcus*, sensitivity ranges between 60% and 95%. Meanwhile, immunochromatography-based urine antigen tests (UAT) for Legionella spp. exhibit 70-80% sensitivity and nearly 100% specificity, offering rapid and reliable results for diagnosing Legionella infections. These attributes make antigen detection an essential tool in clinical settings, especially when timely diagnosis is critical.[38]

Serological testing plays a pivotal role in the diagnosis of respiratory infections caused by slow-growing or difficult-to-culture microorganisms, including *Mycoplasma pneumoniae (M. pneumoniae), Chlamydia pneumoniae (C. pneumoniae), Legionella species*, and viral pathogens. These tests rely on the detection of a four-fold increase in IgG or combined IgG and IgM antibody titers across two serum samples collected at least 7 to 10 days apart. While IgM testing is generally less sensitive and specific than assessing a four-fold change in antibody titers, it remains an essential diagnostic tool for pathogens that cannot be readily cultured. There are severa diagnostic applications of it:

1. Respiratory Pathogens
   Serological tests facilitate the identification of common respiratory pathogens, including *Respiratory Syncytial Virus* (RSV), *Adenovirus* (ADV), *Influenza A and B, Parainfluenza Virus* (PIV) types 1-3, and mixed infections. Specific antibodies typically emerge approximately two weeks after the onset of infection, necessitating acute-phase and convalescent-phase serum collection.
2. Sample Collection Protocol
   Acute-phase serum should be obtained as soon as possible after symptom onset, ideally within the first week. Convalescent-phase serum should be collected at least two weeks after symptom resolution to assess seroconversion.
3. Atypical Bacteria
   M. pneumoniae: Enzyme immunoassay (EIA) is the reference method for detecting IgM or IgG antibodies, with IgM titers peaking between 4 and 6 weeks post-symptom onset. *C. pneumoniae*: Microimmunofluorescence (MIF) is regarded as the gold standard, offering high sensitivity and specificity by measuring both IgG and IgM antibodies. *L. pneumophila*: Diagnostic options include microagglutination, immunofluorescence assay (IFA), and enzyme-linked immunosorbent assay (ELISA). IFA serves as the reference standard, with sensitivity ranging from 75% to 80% and specificity exceeding

99%. *Bordetella pertussis*: ELISA is the preferred method, enabling the detection of antibodies against pertussis toxin.

Although serological testing is invaluable for detecting pathogens that are challenging to culture, its diagnostic utility is constrained by the need for paired acute and convalescent serum samples to confirm a four-fold rise in antibody titers. Moreover, sensitivity ranges between 14% and 77%, and specificity varies from 49% to 97% when compared to polymerase chain reaction (PCR). Consequently, serology is best employed as a complementary tool rather than a standalone method, particularly in cases requiring rapid diagnosis. These considerations underscore the importance of integrating serological testing with molecular diagnostic techniques for optimal patient outcomes.[38]

Nucleic acid amplification tests, including polymerase chain reaction (PCR), are used to amplify specific small amounts of DNA present in clinical specimens (sensitivity and specificity 100%). This allows for the detection of organisms with low DNA quantities, where the type, quantity, and quality of the obtained specimens significantly influence results.[39] False positive or false negative results may arise if proper precautions in handling genetic material to prevent contamination are not meticulously followed. Species-specific polymerase chain reaction (PCR) tests have been developed for numerous pathogenic bacteria, offering higher accuracy and sensitivity than traditional culture-based diagnostics. An alternative approach, multiplex PCR, allows simultaneous targeting of multiple pathogens in a single reaction, reducing the risk of false positive and false negative results associated with conventional PCR. Furthermore, quantitative PCR (qPCR) using fluorescence-based Real-Time detection (RT-qPCR) has been introduced to enhance the accuracy and precision of pathogen identification. This method provides faster turnaround times, making it a valuable tool for rapid and reliable diagnostics in clinical microbiology.[40] Multiplex PCR is another option that can target more than one desired agent in a single reaction, effectively addressing false positive and false negative results obtained using conventional PCR.

The BioFire FilmArray Pneumonia Panel (PN Panel) and Pneumonia Plus Panel (PNplus Panel) are FDA-approved diagnostic tools designed to detect viruses, bacteria, and antimicrobial resistance markers in lower respiratory tract specimens, such as sputum and bronchoalveolar lavage (BAL) fluid. The PN Panel demonstrates a sensitivity of 100% and a specificity of 87.2% for these specimen types, making it a highly effective diagnostic method. Additionally, it offers early insights into potential antimicrobial resistance, providing valuable data for clinical decision-making. The panel detects key resistance markers, such as mecA/mecC genes associated with methicillin resistance, with positive and negative predictive values ranging from 87.5% to 95.9%. It also identifies broad-spectrum beta-lactamase enzymes, particularly CTX-M, which is commonly associated with *E. coli* and *Klebsiella spp*. These organisms are significant contributors to urinary tract and bloodstream infections in the community. CTX-M results are reported when *Enterobacteriaceae, Acinetobacter spp.,* or Pseudomonas aeruginosa are detected, as these pathogens are known carriers of extended-spectrum beta-lactamase (ESBL). The inclusion of these features highlights the panel's utility in guiding targeted antimicrobial therapy and addressing resistance concerns effectively.[40]

ANTIBIOTIC THERAPY

The use of the antibiotic azithromycin given for 3 days (500mg/day) post-bronchoscopy is effective in preventing post-bronchoscopy respiratory tract infections. Kanazawa et al. compared the administration of cefcapene 300mg/day with azithromycin 500mg/day for 3 days post-bronchoscopy and found that azithromycin reduced the incidence of infection by 0.7%. Azithromycin concentrations in the lungs are present for 5 days after a single dose of 500mg. Azithromycin has good pharmacokinetics for penetrating sputum and bronchial mucosa.[41] Azithromycin has been recommended as the first-line treatment for community-acquired pneumonia because it is effective against *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Mycoplasma pneumoniae*.

PREVENTION OF INFECTION

Reducing pathogen exposure is the most crucial action to prevent infection. Hospital-acquired pathogens can be prevented through hand hygiene, the use of personal protective equipment, good room ventilation (7-15 air exchanges per hour), and routine decontamination.[42,43] All personnel involved in bronchoscopy cleaning and decontamination must receive specific training in infection control practices and decontamination processes. Decontamination and disinfection are performed at the beginning and end of use. Infection control can involve high-level disinfection, intermediate-level disinfection, and low-level disinfection.[6] Infection control can be done using high-level disinfection. According to this classification, bronchoscopes are classified as semi-critical medical devices according to Spaulding's classification, and high-level disinfection is recommended.[43]

The disinfection process involves the destruction of living pathogenic microorganisms, including most viruses but not all bacterial spores. Disinfection generally uses chemicals to clean instruments and other inanimate objects. FDA-approved chemicals for high-level disinfection (HLD) include 2% glutaraldehyde, peracetic acid, and ortho-phthalaldehyde. Glutaraldehyde actively removes organic material and destroys viruses, bacteria, including mycobacteria, and spores. Alkaline glutaraldehyde is more effective than acidic glutaraldehyde in killing viruses and bacteria. The American College of Chest Physicians (ACCP) recommends bronchoscope disinfection for 20 minutes in 2% alkaline glutaraldehyde at 20 °C.[44]

High-level disinfection can be done manually or using an automated endoscope reprocessor (AER). When using AER, it is essential to ensure that instruments are used as recommended by the manufacturer.[4] Cleaning should be done immediately after bronchoscopy to prevent organic residue hardening.

All parts of the instrument should be removed and checked for damage. Regular maintenance and disinfection of related equipment should be performed according to the protocol. Reusable instruments should be recorded for each use, routine care, and storage as recommended by the manufacturer. If a drying cabinet or storage space is not available, bronchoscopes should be decontaminated no more than 3 hours before the procedure to eliminate pathogen colonization. Bronchoscopes should be cleaned in a designated cleaning area, and the room used should be separated from clean areas to prevent cross-contamination.[6]

Compliance and vigilance are the most important actions to prevent infection transmission. All healthcare workers involved in bronchoscopy should wear personal protective equipment, including gowns, gloves, masks, and eye protection. A comprehensive investigative team approach to outbreaks in bronchoscopy facilities requires a healthcare service team. Team members include the healthcare facility's person responsible, infection control specialists, infectious disease consultants, microbiology and molecular techniques trained laboratory personnel, epidemiologists, and biomedical staff. Microbiology laboratories should regularly monitor isolates to distinguish patterns indicative of outbreaks. All healthcare facilities performing bronchoscopy should be well-recorded. If a bronchoscopy-related outbreak occurs, it should be reported to the infection control department, local health department, and government. Patients and bronchoscopy personnel potentially exposed to infection during an outbreak should also be notified.[43]

Bronchoscopy poses challenges in infection prevention, and anesthesia experts in the ICU have used disposable flexible bronchoscope (SUFB) to reduce infection. The advantages of using SUFB include reducing the risk of cross-infection, minimizing post-procedural side effects, and lowering bronchoscope repair costs 50.9%.[5,43] However, the use of SUFB is limited to bronchoscopy intubation and simple therapeutic aspiration. SUFB should not be stored and reused, even in the same patient, due to the risk of cross-contamination like the use of repeated bronchoscopes.[45]

PROPHYLAXIS

Antibiotic prophylaxis does not reduce the frequency of fever, changes in leukocytes, CRP, and serum levels of pyrogenic cytokines. In a study by J.S Park and Lee in 2011, the administration of amoxicillin-clavulanate prophylaxis in post-bronchoscopy patients was effective against normal oropharyngeal bacterial flora and had good bioavailability with a rapid onset 30 minutes after consumption.[21]

PROGNOSIS OF POST-BRONCHOSCOPY INFECTION

The prognosis for patients with post-bronchoscopy infections is complex and influenced by multiple factors, including individual risk profiles, the type of infection, and overall health. While post-bronchoscopy infections are relatively rare, they can result in significant morbidity, particularly among vulnerable groups such as individuals with lung cancer or weakened immune systems. Research highlights the prevalence of post-bronchoscopy infections, such as pneumonia, with studies noting an infectious fever rate of approximately 2.56% after the procedure.[46] Contributing factors include poor nutritional status, which weakens immune defenses and heightens susceptibility to infections.[10] Additionally, demographics like smoking status have been associated with a higher risk of pneumonia, although findings on this are inconsistent.[3]

CONCLUSIONS

Gram-negative bacteria most commonly cause post-bronchoscopy incidents and can impact patient morbidity and mortality. Infections are generally caused by bacteria identified through microbiological examinations, which can be recognized by symptoms and clinical signs accompanied by an increase in proinflammatory markers 24 hours post-bronchoscopy. Bronchoscopy is a specialized procedure that requires extensive training, including knowledge, implementation of safety standards, and proper maintenance procedures to reduce the incidence of infection. The microbiology laboratory plays a role in identifying pathogenic microorganisms causing infections and preventing infection outbreaks related to bronchoscopy in healthcare facilities. Post-bronchoscopy infections depend on the integrity of the patient's immune defense mechanisms, procedural actions, compliance, and vigilance to prevent infection transmission.

DISCLOSURE

Author contribution

All of the authors contribute to this manuscript preparation.

Conflict of interest

None.

Funding

None.

REFERENCES

1. Spiro SG, Silvestri GA, Agustí A. Clinical Respiratory Medicine. 4th ed. Elsevier; 2012. 154–173 p.
2. Becker HD. A Short History of Flexible Bronchoscopy. In: Flexible Bronchoscopy. Wiley; 2020. p. 1–19.
3. Sato Y, Murata K, Yamamoto M, Ishiwata T, Kitazono-Saitoh M, Wada A, et al. Risk factors for post-bronchoscopy pneumonia: a case-control study. Sci Rep. 2020;10(1):19983. Available from: https://pubmed.ncbi.nlm.nih.gov/33204000
4. Mehta AC, Prakash UBS, Garland R, Haponik E, Moses L, Schaffner W, et al. American College of Chest Physicians and American Association for Bronchology [corrected] consensus statement: prevention of flexible bronchoscopy-associated infection. Chest. 2005;128(3):1742–55. Available from: https://pubmed.ncbi.nlm.nih.gov/16162783
5. Barron SP, Kennedy MP. Single-Use (Disposable) Flexible Bronchoscopes: The Future of Bronchoscopy? Adv Ther. 2020/09/17. 2020;37(11):4538–48. Available from: https://pubmed.ncbi.nlm.nih.gov/32944885
6. Du Rand IA, Blaikley J, Booton R, Chaudhuri N, Gupta V, Khalid S, et al. British Thoracic Society guideline for diagnostic flexible bronchoscopy in adults: accredited by NICE. Thorax. 2013;68(Suppl 1):i1–44. Available from: http://dx.doi.org/10.1136/thoraxjnl-2013-203618
7. Steinfort DP, Johnson DF, Irving LB. Incidence of bacteraemia following endobronchial ultrasound-guided transbronchial needle aspiration. European Respiratory Journal. 2009;36(1):28–32. Available from: http://dx.doi.org/10.1183/09031936.00151809

8. Galdys AL, Marsh JW, Delgado E, Pasculle AW, Pacey M, Ayres AM, et al. Bronchoscope-associated clusters of multidrug-resistant Pseudomonas aeruginosa and carbapenem-resistant Klebsiella pneumoniae. Infect Control Hosp Epidemiol. 2019;40(1):40–6.
9. Aguñín PR. Infectious complications following bronchoscopy: does sedation play a role? Journal of Lung, Pulmonary & Respiratory Research. 2018;5(4):112–8. Available from: http://dx.doi.org/10.15406/jlprr.2018.05.00174
10. Shimoda M, Yamana K, Yano R, Saitou M, Fujiwara K, Furuuchi K, et al. Analysis of risk factors for the development of a post-bronchoscopy respiratory infection in lung cancer patients. Journal of Infection and Chemotherapy. 2021;27(2):237–42.
11. Agrawal A, Murgu S. Infections After Radial EBUS-Guided Transbronchial Lung Biopsy. Chest. 2020;158(2):458–60. Available from: http://dx.doi.org/10.1016/j.chest.2020.04.030
12. Asano Y, Kashiwagi S, Onoda N, Noda S, Kawajiri H, Takashima T, et al. Platelet–Lymphocyte Ratio as a Useful Predictor of the Therapeutic Effect of Neoadjuvant Chemotherapy in Breast Cancer. PLoS One. 2016;11(7):e0153459.
13. Yu G, Dymond M, Yuan L, Chaturvedi LS, Shiratsuchi H, Durairaj S, et al. Propofol's effects on phagocytosis, proliferation, nitrate production, and cytokine secretion in pressure-stimulated microglial cells. Surgery. 2011/06/15. 2011;150(5):887–96. Available from: https://pubmed.ncbi.nlm.nih.gov/21676422
14. Sharif-Kashani B, Raeissi S, Bikdeli B, Shahabi P, Behzadnia N, Saliminejad L, et al. Sticker reminders improve thromboprophylaxis appropriateness in hospitalized patients. Thromb Res. 2010;126(3):211–6. Available from: http://dx.doi.org/10.1016/j.thromres.2010.05.020
15. Wang K-P, Mehta AC, Turner JF. Flexible Medical Bronchoscopy. 4th ed. Willey Blackwell; 2020. 1–479 p.
16. Rounds S, Dixon A, Schnapp L, Huang Y. The Microbiomein Respiratory Disease. Huang YJ, Garantziotis S, editors. Human Press; 2022. 21–21 p.
17. Culver DA, Gordon SM, Mehta AC. Infection Control in the Bronchoscopy Suite. Am J Respir Crit Care Med. 2003;167(8):1050–6. Available from: http://dx.doi.org/10.1164/rccm.200208-797cc
18. Srinivasan A, Wolfenden LL, Song X, Mackie K, Hartsell TL, Jones HD, et al. An Outbreak of*Pseudomonas aeruginosa*Infections Associated with Flexible Bronchoscopes. New England Journal of Medicine. 2003;348(3):221–7. Available from: http://dx.doi.org/10.1056/nejmoa021808
19. Thi MTT, Wibowo D, Rehm BHA. Pseudomonas aeruginosa Biofilms. Int J Mol Sci. 2020;21(22):8671. Available from: https://pubmed.ncbi.nlm.nih.gov/33212950
20. Hackner K, Riegler W, Handzhiev S, Bauer R, Veres J, Speiser M, et al. Fever after bronchoscopy: serum procalcitonin enables early diagnosis of post-interventional bacterial infection. BMC Pulm Med. 2017;17(1):156. Available from: https://pubmed.ncbi.nlm.nih.gov/29179755
21. Park JS, Lee C-H, Yim J-J, Yang S-C, Yoo C-G, Chung HS, et al. Impact of antibiotic prophylaxis on postbronchoscopy fever: a randomised controlled study. The International Journal of Tuberculosis and Lung Disease. 2011;15(4):528–35. Available from: http://dx.doi.org/10.5588/ijtld.10.0386
22. Souma T, Minezawa T, Yatsuya H, Okamura T, Yamatsuta K, Morikawa S, et al. Risk Factors of Infectious Complications After Endobronchial Ultrasound-Guided Transbronchial Biopsy. Chest. 2020;158(2):797–807. Available from: http://dx.doi.org/10.1016/j.chest.2020.02.025
23. Wacker C, Prkno A, Brunkhorst FM, Schlattmann P. Procalcitonin as a diagnostic marker for sepsis: a systematic review and meta-analysis. Lancet Infect Dis. 2013;13(5):426–35. Available from: http://dx.doi.org/10.1016/s1473-3099(12)70323-7
24. Rhee C. Using Procalcitonin to Guide Antibiotic Therapy. Open Forum Infect Dis. 2016;4(1):ofw249–ofw249. Available from: https://pubmed.ncbi.nlm.nih.gov/28480245
25. Schuetz P, Beishuizen A, Broyles M, Ferrer R, Gavazzi G, Gluck EH, et al. Procalcitonin (PCT)-guided antibiotic stewardship: an international experts consensus on optimized clinical use. Clinical Chemistry and Laboratory Medicine (CCLM). 2019;57(9):1308–18. Available from: http://dx.doi.org/10.1515/cclm-2018-1181
26. Farrokhpour M, Kiani A, Mortaz E, Taghavi K, Farahbod AM, Fakharian A, et al. Procalcitonin and Proinflammatory Cytokines in Early Diagnosis of Bacterial Infections after Bronchoscopy. Open Access Maced J Med Sci. 2019;7(6):913–9. Available from: https://pubmed.ncbi.nlm.nih.gov/30976333
27. Harbarth S, Holeckova K, Froidevaux C, Pittet D, Ricou B, Grau GE, et al. Diagnostic Value of Procalcitonin, Interleukin-6, and Interleukin-8 in Critically Ill Patients Admitted with Suspected Sepsis. Am J Respir Crit Care Med. 2001;164(3):396–402. Available from: http://dx.doi.org/10.1164/ajrccm.164.3.2009052
28. Gilbert DN. Use of plasma procalcitonin levels as an adjunct to clinical microbiology. J Clin Microbiol. 2010/04/26. 2010;48(7):2325–9. Available from: https://pubmed.ncbi.nlm.nih.gov/20421436
29. Wong JL, Evans SE. Bacterial Pneumonia in Patients with Cancer: Novel Risk Factors and Management. Clin Chest Med. 2017/03/01. 2017;38(2):263–77. Available from: https://pubmed.ncbi.nlm.nih.gov/28477638
30. ASANO F, AOE M, OHSAKI Y, OKADA Y, SASADA S, SATO S, et al. Deaths and complications associated with respiratory endoscopy: A survey by the Japan Society for Respiratory Endoscopy in 2010. Respirology. 2012;17(3):478–85. Available from: http://dx.doi.org/10.1111/j.1440-1843.2011.02123.x
31. Takiguchi H, Hayama N, Oguma T, Harada K, Sato M, Horio Y, et al. Post-bronchoscopy pneumonia in patients suffering from lung cancer: Development and validation of a risk prediction score. Respir Investig. 2017;55(3):212–8. Available from: http://dx.doi.org/10.1016/j.resinv.2016.12.007
32. Okachi S, Imaizumi K, Imai N, Shimizu T, Hase T, Morise M, et al. Safety and efficacy of diagnostic flexible bronchoscopy in very old patients with lung cancer. Eur Geriatr Med. 2018;9(2):255–62. Available from: http://dx.doi.org/10.1007/s41999-018-0033-7
33. Fortin M, Taghizadeh N, Chee A, Hergott CA, Dumoulin E, Tremblay A, et al. Lesion heterogeneity and risk of infectious complications following peripheral endobronchial ultrasound. Respirology. 2016;22(3):521–6. Available from: http://dx.doi.org/10.1111/resp.12942
34. Hiraishi Y, Izumo T, Sasada S, Matsumoto Y, Nakai T, Tsuchida T, et al. Factors affecting bacterial culture positivity in specimens from bronchoscopy in patients with suspected lung cancer. Respir Investig. 2018;56(6):457–63. Available from: http://dx.doi.org/10.1016/j.resinv.2018.07.006
35. Rolston KVI, Nesher L. Post-Obstructive Pneumonia in Patients with Cancer: A Review. Infect Dis Ther. 2018/02/01. 2018;7(1):29–38. Available from: https://pubmed.ncbi.nlm.nih.gov/29392577
36. Garcia LS, Isenberg HD, editors. Clinical Microbiology Procedures Handbook. Wiley; 2010.
37. Carroll KC, Hobden JA, Miller S, Morse SA, Mietzner TA, Detrick B, et al. Adelberg's Medical Microbiology [Internet]. Vol. 20, Indian Journal of Medical Microbiology. Elsevier BV; 2019. 1–231 p. Available from: http://dx.doi.org/10.1016/s0255-0857(21)03203-5
38. Kawasaki T, Nakagawa N, Murata M, Yasuo S, Yoshida T, Ando K, et al. Diagnostic accuracy of urinary antigen tests for legionellosis: A systematic review and meta-analysis. Respir Investig. 2022;60(2):205–14. Available from: http://dx.doi.org/10.1016/j.resinv.2021.11.011
39. Huh HJ, Kim JY, Kwon HJ, Yun SA, Lee MK, Ki CS, et al. Performance Evaluation of the PowerChek MERS (upE & ORF1a) Real-Time PCR Kit for the Detection of Middle East Respiratory Syndrome Coronavirus RNA. Ann Lab Med. 2017;37(6):494–8. Available from: https://pubmed.ncbi.nlm.nih.gov/28840986
40. Calderaro A, Buttrini M, Farina B, Montecchini S, De Conto F, Chezzi C. Respiratory Tract Infections and Laboratory Diagnostic Methods: A Review with A Focus on Syndromic Panel-Based Assays. Microorganisms. 2022;10(9):1856. Available from: https://pubmed.ncbi.nlm.nih.gov/36144458
41. Kanazawa H. Efficacy of azithromycin administration in prevention of respiratory tract infection after bronchoscopic biopsy: A randomized, controlled trial. Respirology. 2006;12(1):70–5. Available from: http://dx.doi.org/10.1111/j.1440-1843.2006.00973.x
42. Siegel JD, Rhinehart E, Jackson M, Chiarello L. Management of multidrug-resistant organisms in health care settings, 2006. Am J Infect Control. 2007;35(10):S165–93. Available from: http://dx.doi.org/10.1016/j.ajic.2007.10.006
43. Rutala WA. APIC guideline for selection and use of disinfectants. Am J Infect Control.

1996;24(4):313–42. Available from: http://dx.doi.org/10.1016/s0196-6553(96)90066-8
44. Leers WD. Disinfecting endoscopes: how not to transmit Mycobacterium tuberculosis by bronchoscopy. Can Med Assoc J. 1980;123(4):275–80, 283.
45. Lamb CR, Yavarovich E, Kang V, Servais EL, Sheehan LB, Shadchehr S, et al. Performance of a new single-use bronchoscope versus a marketed single-use comparator: a bench study. BMC Pulm Med. 2022;22(1):189. Available from: https://pubmed.ncbi.nlm.nih.gov/35550062
46. Farrokhpour M, Kiani A, Mortaz E, Taghavi K, Farahbod AM, Fakharian A, et al. Procalcitonin and Proinflammatory Cytokines in Early Diagnosis of Bacterial Infections After Bronchoscopy. Open Access Maced J Med Sci. 2019;7(6):913–9.