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Practice of oxygenation and respiratory support during fibreoptic bronchoscopy: the OxyFOB study protocol

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ABSTRACT

Introduction Flexible bronchoscopy (FB) is widely used for diagnostic and therapeutic procedures in pulmonary medicine. However, FB can cause respiratory and haemodynamic complications, especially in patients with pre-existing lung and/or cardiovascular comorbidities. Despite the range of oxygenation and ventilatory approaches available to prevent these risks, evidence regarding their real-world application and clinical impact is limited. The OxyFOB study aims to assess the prevalence and outcomes of various oxygenation and ventilatory support strategies used during FB across Europe.

Methods and analysis The OxyFOB study is a large, prospective, international, observational cohort study which aims to involve over 10 000 FB procedures across European centres. Eligible participants include all adults undergoing FB for diagnostic, therapeutic or procedural indications. Data are collected via a standardised electronic case report form and encompass demographic information, procedural details and clinical outcomes. The primary endpoint is the prevalence of oxygenation and ventilatory support strategies: conventional oxygen therapy, high-flow oxygen therapy, continuous positive airway pressure, non-invasive ventilation and invasive mechanical ventilation. Secondary outcomes include periprocedural respiratory and haemodynamic events, patient comfort, dyspnoea and postprocedural complications. Statistical analyses include descriptive statistics, subgroup comparisons and multivariate logistic regression.

Ethics and dissemination The study has received ethical approval from the coordinating centre (protocol n. 22/2022 on the 20 January 2022, by the 'Comitato Etico Sezione Area Centro - Regione Calabria') and all participating sites. Informed consent is given from all patients or their legal representatives. Findings will be disseminated through peer-reviewed publications and presentations at international meetings. Data will be managed and made available on reasonable request to support further research.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Large sample size enhances the prospect of wide validity across multiple European centers and settings, to ensure adequate representation across all subpopulations according to the type of flexible bronchoscopy (FB) procedure (eg, bronchoalveolar lavage, brushing, TransBronchial Needle Aspiration (TBNA), Endobronchial Ultrasound (EBUS)).
⇒ Real-world observational design reflects routine clinical practice and variability in FB procedures, especially with regard to preliminary guidance to optimise oxygenation and ventilatory strategies for different patient subpopulations.
⇒ Comprehensive data collection includes both clinical outcomes and patient-reported measures (eg, dyspnoea, comfort).
⇒ Centralised data quality oversight minimises errors and ensures consistency.
⇒ As an observational study, causal relationships cannot be firmly established due to potential confounding and selection bias.

Trial registration number ClinicalTrials.gov ID: NCT05681962. Registered January 2023.

INTRODUCTION

First described by Ikeda *et al*,[1] flexible bronchoscopy (FB) is a medical procedure used to visualise the lower airways and perform diagnostic or therapeutic interventions in a large spectrum of respiratory diseases. FB is employed in the diagnostic approach to persistent cough, management of lung infections and evaluation of non-infective infiltrates through procedures like bronchoalveolar lavage (BAL), endobronchial brushing and both bronchial and transbronchial lung biopsies in neoplastic and non-malignant

lung disorders, removing mucus plugs or foreign bodies and addressing airway bleeding.

With the proper precautions, FB is a generally safe procedure.[2] Studies report a mortality rate ranging between 0.01% and 0.04% and a major complication rate between 0.08% and 0.3%.[3–5] However, most patients undergoing FB have underlying conditions that can compromise gas exchange, such as pneumonia, interstitial lung diseases or neoplasms; the arterial partial pressure of oxygen does in fact often decrease to varying degrees, which may increase the risk of respiratory distress.[6 7] Desaturation may be secondary to a wide array of conditions, such as: alveolar derecruitment, ventilation-perfusion (V/Q) mismatch and alveolar hypoventilation,[8–10] the latter mainly due to alterations in respiratory pattern as a side effect of sedative drugs[11–14] and their effects on the critical closing pressure of the upper airways, which may collapse.[15 16] Also worth mentioning, intraprocedural suctioning reduces end-expiratory lung volume, which may therefore reduce lung compliance and cause V/Q mismatch and venous admixture.[17–19] The occurrence of FB-related complications is greater during interventional procedures such as bronchial and transbronchial biopsies; moreover, individual team expertise is a further, independent variable influencing the incidence of FB-related complications in clinical practice.[8 20]

In non-intubated patients, the fibrescope occupies approximately 10% of the tracheal cross-sectional area and 15% of that of the cricoid ring. This partial obstruction increases airway resistance, thereby elevating the patient's work of breathing during the procedure.[17] In patients with bronchial hyperreactivity, periprocedural bronchospasm can occur as a complication of FB, potentially leading to airway narrowing and respiratory distress.[21]

These respiratory changes typically resolve after FB; however, in cases of severe parenchymal lung diseases, recovery may take anywhere from 15 min to several hours. This delay may necessitate oxygen therapy or escalation of postprocedural respiratory support and unexpected hospital and/or intensive care unit (ICU) admission.[8 17]

During FB, complex transient and contrasting haemodynamic modifications may also occur: if on one hand cardiac output may increase by up to 50% due to sympathetic stimulation, typically returning to baseline within 15 min after the procedure,[17 22] on the other changes in intrathoracic pressure, resulting from increased inspiratory effort, affect venous return and afterload, potentially reducing cardiac output.[23] Those events can precipitate heart failure in patients with underlying cardiovascular conditions, and ECG changes may occur in up to 21% of awake patients over 60 years of age.[24] Different strategies of oxygenation and ventilatory support have been applied in spontaneously breathing patients and compared in patients receiving FB to prevent respiratory failure or worsening of gas exchange.[25] However, despite a relevant number of available studies, most investigations focus on physiological parameters rather than clinically relevant outcome variables with heterogeneous populations with respect to severity, type of procedure and supportive means.[25]

To assess this gap, we therefore designed this multicentre international prospective observational study to assess the real-life prevalence of oxygenation and ventilatory strategies during FB in different case scenarios, stratifying patients by baseline comorbidities, type of FB procedure and hospital setting, in order to explore whether specific subgroups of patients may benefit from distinct oxygenation or ventilatory strategies during the procedure. In addition, we will evaluate the safety, tolerability and clinical outcomes across different oxygenation and ventilatory support strategies.

METHODS AND ANALYSIS

Study design

This is a prospective international observational cohort study conducted across Europe. The study protocol is designed and reported in this article according to the Strengthening the Reporting of Observational Studies in Epidemiology Statement.[26] The study was approved by the Ethics Committee of the coordinating centre (protocol n. 22/2022 on 20 January 2022, by the 'Comitato Etico Sezione Area Centro - Regione Calabria'). All participating centres obtained the local ethical committee approval. This study was prospectively registered on ClinicalTrials.gov (NCT05681962; principal investigator: Federico Longhini) in January 2023. The flow chart of the Oxy-FOB study is depicted in figure 1.

Recruitment started on 15 February 2023. The study is currently ongoing with 6852 patients recruited patients in 63 active centres across Europe as per 7 May 2025. Additional centres are being included to enhance representativeness and further strengthen the study's conclusions. We expect to complete the recruitment by the end of 2026.

Study population

We consider eligible all consecutive adult (ie, ≥18 years old) patients requiring a FB procedure for the main diagnostic, therapeutic or procedural indications. Diagnostic indications include: evaluation of pulmonary infections, investigation of lung masses or nodules, assessment of interstitial lung diseases, diagnosis of central airway obstruction, evaluation of haemoptysis to localise bleeding and determine its cause, biopsy of mediastinal or hilar lymphadenopathy and the diagnosis and therapeutic lavage of pulmonary alveolar proteinosis.

Therapeutic indications include: airway clearance and secretion management, foreign body removal, balloon dilation of airway stenosis, endobronchial valve placement for lung volume reduction in emphysema, management of haemoptysis, and therapeutic lavage for alveolar proteinosis.

Procedural indications include: BAL for diagnostic purposes, as well as guidance for transbronchial lung biopsy or needle aspiration.

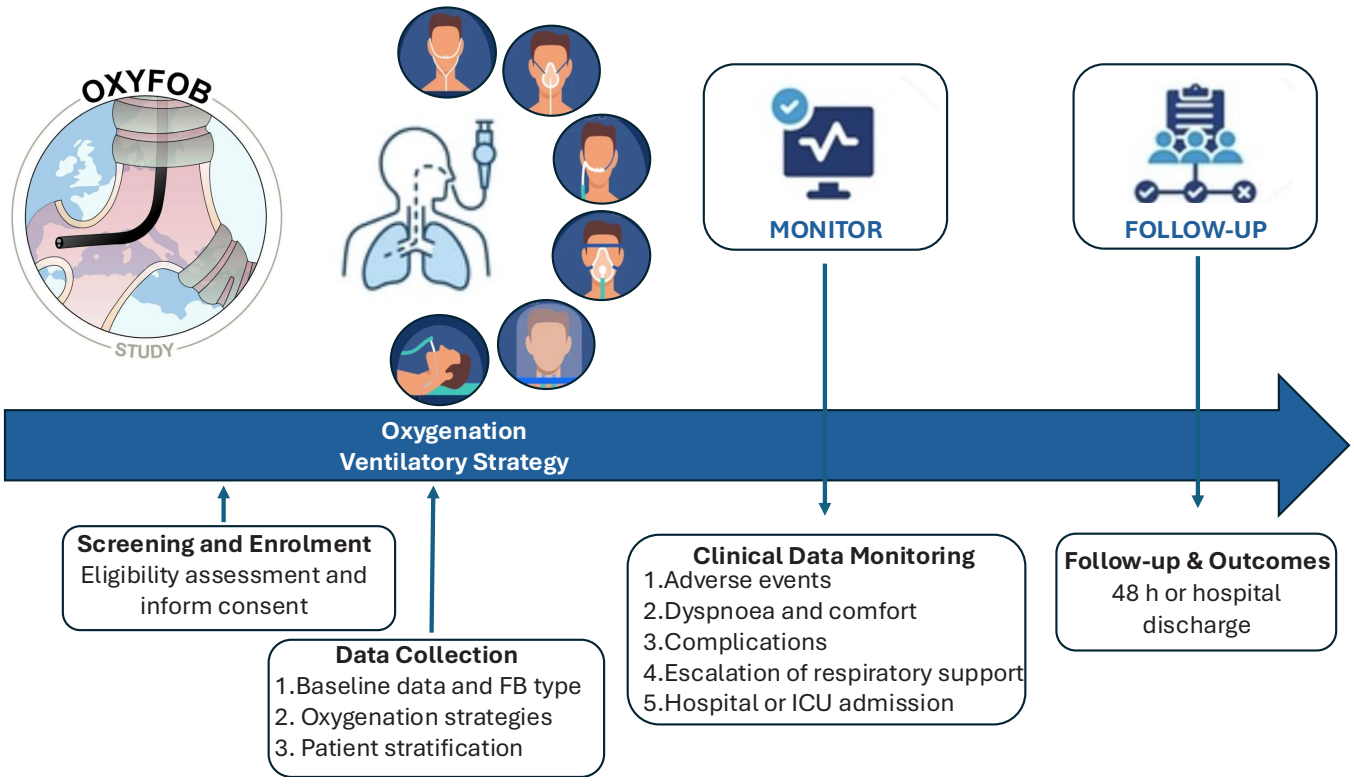

Figure 1 Study flow from patient enrolment to outcome assessment during and after the FB procedure. FB, flexible bronchoscopy; ICU, intensive care unit.

Included subjects will be screened consecutively, and written informed consent will be obtained from all patients, next of kin or legal representatives, as per national laws. Exclusion criteria include pregnancy, breastfeeding, paediatric patients (ie, <18 years old) and patients for whom informed consent cannot be obtained.

Study outcomes and measures

Primary endpoint

The primary outcome of this study is to assess the prevalence of oxygenation and ventilatory strategies during FB in different case scenarios, conducting subgroup analyses based on baseline comorbidities, type of FB procedure and hospital setting. For this purpose, we defined the following oxygenation and ventilatory strategies as follows:

1. Conventional oxygen therapy (COT): administration of oxygen through nasal prongs, oxygen mask (with or without reservoir) and Venturi mask.
2. High flow oxygen therapy (HFOT): administration of high flows (up to 60 L/min) of air/oxygen mixtures, heated at temperatures ranging from 31 to 37°C and fully humidified (up to 44 mg H_2O/L), providing an inspired oxygen fraction (FiO_2) ranging from 21% to 100%.
3. Continuous positive airway pressure (CPAP): application of positive end-expiratory pressure (PEEP) throughout the whole respiratory cycle with a ventilator, flow generator or Venturi system, through interfaces including, but not limited to, mask or helmet.
4. Non-invasive ventilation (NIV): application of a PEEP and an inspiratory pressure support (PS) triggered by the patient, delivered by a ventilator through a mask or helmet.
5. Invasive mechanical ventilation (IMV): application of a ventilatory assistance in controlled or assisted modes through an endotracheal or tracheostomy tube.

Secondary endpoints

Secondary endpoints of the study include evaluating the safety and tolerability of the procedure through the recording of major periprocedural respiratory and haemodynamic adverse events, as well as patient comfort and dyspnoea during the procedure and collecting clinical outcomes associated with different oxygenation and ventilatory support strategies.

Major periprocedural respiratory and haemodynamic adverse events include:

- Peripheral desaturation (defined as peripheral oxygen saturation (SpO_2<90% for at least 10 s) or severe desaturation (defined as SpO_2<80% for any duration).
- Need for interruption of FB.
- Haemodynamic instability, defined as the occurrence of hypotensive (ie, a systolic blood pressure <90 mm Hg) or hypertensive (ie, systolic blood pressure >140 mm Hg) events.
- New-onset cardiac arrhythmias requiring treatment, myocardial infarction and/or electrocardiographic ST alterations.

- Occurrence of neurological events, defined as ischaemic or haemorrhagic stroke, transient ischaemic attack and/or seizures.[9 25 27]

Clinical outcomes consist of:

1. Need for additional respiratory support beyond that initially applied.
2. Occurrence of procedural complications (including, but not limited to, airway bleeding, pneumothorax, pneumomediastinum, bronchial perforation, bronchospasm or laryngospasm).
3. Need for unplanned admission to the emergency department (ED), hospital ward or high-dependency unit/ICU.
4. For hospitalised patients, in-hospital and/or ICU length of stay and mortality.

Measures

Baseline and demographic data include patient age, gender, height, type of admission (outpatient, inpatient, ICU or ER), comorbidities, Charlson Comorbidity Index, smoking habit, previous need for long-term oxygen therapy or home NIV or tracheoventilation. In addition, we will register the baseline values of SpO_2, systolic and diastolic blood pressure, baseline arterial blood gas analysis (ABGs) if available, type of FB performed and indication for the procedure.

During the procedure, we will record the lowest SpO_2, the occurrence of desaturation or severe desaturation, the need for interruption of FB, lowest and highest intraprocedural systolic blood pressure, new-onset cardiac arrhythmias or pathological conditions and neurological events.

At the end of the FB, vital parameters and ABGs (if available), presence of dyspnoea and patient's comfort during the procedure will also be recorded. Both dyspnoea and patient's comfort will be assessed using the 11-point Numeric Rating Scale, as previously reported.

Since relying solely on clinical indicators can be insufficient to detect early or evolving hypercapnia, particularly in patients with chronic respiratory conditions, we also collected the arterial partial pressure of CO_2, when available as per clinical practice. This approach is critical for accurately assessing ventilatory adequacy, especially when comparing support strategies such as HFOT, CPAP and NIV during bronchoscopy. Since the study protocol was designed in 2022, only a few (<5%) centres were equipped with end-tidal or transcutaneous CO_2 monitoring at that time; therefore, we chose not to include it as a data point to be collected.

Patients will be asked to define the perceived severity of their condition by providing a number between 0 (no discomfort/no dyspnoea) and 10 (worst possible discomfort/worst possible dyspnoea) on a large printed scale including numbers and descriptors.[28–31]

In addition, we will also record the need for respiratory support escalation beyond that initially applied and the occurrence of complications as previously described. These outcomes will be checked and recorded within the first 48 hours from FB or hospital discharge.

All intraprocedural adverse events will also be analysed to assess their impact on post-procedural clinical outcomes, including the need for respiratory support escalation, unexpected ED, ward or ICU admission, hospital/ICU lengths of stay and mortality.

Data collection

Data will be collected on an electronic case report form (eCRF) based on the Research Electronic Data Capture secure web application. The eCRF consists of five sections:

1. Demographic and pre-procedural physiological parameters.
2. Details of FB procedure.
3. Intraprocedural parameters.
4. Postprocedural parameters.
5. Clinical outcomes.

Local investigators will screen and report all the FB procedures.

Data quality framework

A dedicated team of investigators will ensure data quality by routinely assessing the integrity, completeness, consistency and accuracy of the existing data.[32] All data will undergo thorough verification, and any instances of missing data, potential errors or ambiguous values will prompt contact with local investigators for resolution, ensuring robust and reliable data quality control.[32]

Statistical analysis

Statistical analysis is designed by an independent team of expert statisticians, in collaboration with the steering committee. We plan on collecting data from a convenience sample of 10 000 procedures. The sample characteristics will be described using absolute frequencies and percentages (qualitative variables), mean and SD or median and IQR (quantitative variables), as appropriate. Data normality will be assessed using the Shapiro-Wilk test. Prevalence will be determined and reported with the corresponding 95% CIs. Additionally, the incidence and type of major periprocedural respiratory and haemodynamic adverse events will be calculated along with their 95% CIs.

Differences in quantitative variables between two groups will be evaluated using the unpaired Student's t-test or the corresponding non-parametric test, after assessing the relative assumptions. In the case of groups >2, these differences will be assessed using analysis of variance or Kruskal-Wallis test. Differences in qualitative variables will be evaluated using Pearson's χ^2 test or Fisher's exact test. Multivariate logistic regression modelling will be performed to determine factors associated with oxygenation and ventilatory supports; any variable with significant univariate test or clinical relevance will be selected as a candidate for multivariate analysis. The level of statistical significance will be set at a p value <0.05.

DISCUSSION

This large prospective observational study aims to describe the current clinical practices on oxygenation and ventilatory strategies during FB across Europe in various clinical scenarios. The results will provide insights into the use of different oxygenation and ventilatory support strategies for patients with different indications for FB and varying severity of respiratory failure. By analysing the occurrence of respiratory and haemodynamic impairments, as well as clinical outcomes, this study will identify key patterns across subpopulations supported by COT, HFOT, CPAP, NIV or IMV.

As an observational cohort study, this study can estimate the incidence of clinically meaningful outcomes such as respiratory and haemodynamic impairments, adverse events and unexpected hospital or ICU admission[33] and will therefore provide data useful to potentially suggest the use of one technique over another. The findings could modify clinical practices and lay the groundwork for future randomised controlled trials (RCTs) to validate the efficacy of specific interventions.[34]

To the best of our knowledge, this is the largest ongoing study ever conducted in this population, while the current existing literature predominantly consists of studies with sample sizes of fewer than 100 patients.[25]

Respiratory and haemodynamic impairments during FBs are common events that can worsen the patients' clinical conditions, potentially leading to unplanned hospital admission during out-patient procedures, or ICU admission and escalation of respiratory support after the procedure.[25] A previous systematic review showed that patients with poorer baseline lung function have higher oxygen requirements during FB and an increased risk for post-procedural worsening of respiratory failure.[25] The pooled data analysis revealed that HFOT performs better than COT in terms of oxygenation outcomes for patients with lower oxygen requirements, while NIV appeared to be more effective than HFOT in those with more severe respiratory failure. However, insufficient evidence prevents definitive recommendations regarding the superiority of one oxygenation strategy over another. Nevertheless, improving intra-procedural oxygenation remains a critical safety concern for patients undergoing FB and has the potential to improve key clinical outcomes, such as reducing the need for hospital or ICU admission due to post-procedural respiratory failure, though these benefits require further investigation.[25] Currently, other RCTs are ongoing to compare different strategies in specific patient populations.[35 36]

Strengths and limitations

Our study has several strengths and limitations worth discussion.

One of the main strengths is the design that reflects real-world practices and outcomes, fully addressing our primary aim. The large sample size enables pooling of data from multiple centres across Europe, ensuring the inclusion of patients from diverse geographic, cultural and healthcare settings, thereby enhancing the generalisability of the findings.[37] The study was designed to ensure adequate representation across all subpopulations according to the type of FB procedure (eg, BAL, brushing, TBNA, EBUS), providing each group with an adequate number of patients.

Although RCTs remain the standard of reference for establishing causality, observational studies provide valuable insights into real-world practice, can help to identify the effect of interventions in specific subpopulations and can serve as a valid reference when planning future RCTs.[38 39] Therefore, once this study is completed and published, it will provide the basis for RCTs comparing different oxygenation or ventilatory support techniques in specific patient populations, with the aim of reducing the occurrence of respiratory and haemodynamic adverse events during FB. Another strength of this study is the presence of a data quality team that routinely checks the collected data to reduce the possibility of missing or low-quality data.[32]

Finally, this study is highly innovative, providing preliminary guidance on optimising oxygenation and ventilatory strategies for different patient subpopulations. The findings could significantly influence and improve clinical practices, helping clinicians to refine their approaches, reduce costs associated with complications and minimise unexpected hospital or ICU admissions.

Concerning limitations, the observational design may be more susceptible to confounding factors, making it challenging to establish causal relationships. Moreover, not all patients may be enrolled, leading to potential selection bias. However, through careful implementation of rigorous data quality measures and the use of advanced statistical methods to adjust for biases and confounders, many of the conventional limitations of observational studies can be mitigated.[40] Indeed, a selection bias in participating centres may have occurred, limiting the generalisability of the findings. However, participating centres are representative of different levels of care, settings and geography. Furthermore, this study will not gather information on the direct long-term consequences of periprocedural adverse events on specific patient outcomes, as the aim of the study was to prospectively collect data on short-term adverse events.

A further potential limitation of our study is related to the collection of FB data both from stable and acutely unstable critically ill patients in different settings (from the bronchoscopy unit to the ICU), driven by heterogeneous indications and expected outcomes. However, we believe that this may also be considered as a strength, as it contributes to the ambitious goal of building a comprehensive 'road map' for how different physicians manage FB in real-world

practice, providing insights on safer oxygenation tools and tailored approaches for each clinical scenario.

Ethics and dissemination

The study received approval from the Ethical Committee of the coordinating centre (protocol no. 22/2022, approved on 20 January 2022, by the 'Comitato Etico Sezione Area Centro - Regione Calabria') and, in accordance with local regulations, by all relevant local Ethical Committees. Informed consent is obtained from all participants or their consultee before enrolment. For participants lacking capacity, consent is sought from a personal or nominated consultee. The study adheres to good clinical practice guidelines and current data protection regulations, ensuring the ethical conduct of research and the protection of participant rights. The results of the study will be disseminated at the end of enrolment through a manuscript that will be submitted for publication in an international peer-reviewed scientific journal.

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