Nonintubated bronchoscopic interventions with high-flow nasal oxygen
A retrospective observational study

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Abstract
To determine the feasibility on maintaining oxygenation of high-flow nasal oxygenation (HFNO) with bispectral index-guided intravenous anesthesia for nonintubated interventional bronchoscopy (NIIB). If desaturation happens, the factors influencing intraprocedural desaturation were also analyzed.

This is a single-center retrospective study on patients receiving NIIB with HFNO and intravenous anesthesia guided by bispectral index levels to the depth of general anesthesia, which were between 40 and 60. Intraprocedural desaturation (SPO\textsubscript{2} < 90\%) and complications (bleeding, delayed discharge, unexpected admission) were collected. Factors affecting desaturation and complications were analyzed including patients’ factors (age, American Society of Anesthesiologists classification, body mass index [BMI]), procedural factors (procedural time, with or without use of cryoprobe), and setting (outpatient or hospitalized).

Records of 223 patients receiving NIIB were collected. The NIIB procedures time was 56.1 ± 26.8 minute. Sixty patients (26.9\%) presented desaturation events. Higher BMI, but not procedure time or setting, was significantly associated with desaturation. The desaturation were resolved after relieving upper airway obstruction but 1 patient required bag–valve–mask ventilation to restore oxygenation. Accidental massive bleeding and inaprocudural desaturation during tracheal and bronchial recannulation with cryoprobe happened in 2 patients and 1 of them was admitted to intensive care unit.

HFNO is feasible to maintain oxygenation during NIIB only if there is effective upper airway management especially for patients with higher BMI. Longer procedural time and different setting did not affect the desaturation rate. Complications and unexpected admission were associated with the use of cryoprobe.

Abbreviations: ASA = American Society of Anesthesiologists, BIS = bispectral index, BMI = body mass index, HFNO = high-flow nasal oxygenation, IB = interventional bronchoscopy, NIIB = nonintubated interventional bronchoscopy, PACU = post-anesthesia care unit, TBC = transbronchial cryobiopsy.

Keywords: anesthetic depth, high-flow nasal oxygen, interventional bronchoscopy

1. Introduction
Interventional bronchoscopy (IB) includes various procedures for the diagnosis or treatment for the pulmonary and mediastinal diseases\cite{1,2}. These procedures such as endobronchial ultrasound transbronchial needle aspiration\cite{2}, has increased rapidly in precise medicine.\cite{3}\textsuperscript{1}\textsuperscript{2}\textsuperscript{3}\textsuperscript{4}\textsuperscript{5}\textsuperscript{6} IBs have been the most powerful and efficient tools for the pathological diagnosis of mediastinal and hilar lymphadenopathy, peribronchial lung lesion, and staging of lung cancers.\cite{4,5} However, the anesthesia for IBs remain challenging on achieving an optimal anesthetic depth for nociception from airways without hemodynamic instability, providing a clear, immobile, operable field without accidental moving, cough or spasm for IB procedures, and maintaining oxygenation with shared airway without intraprocedural desaturation. Severe complications in airways may happen during IB and are extreme challenges to anesthetic management. The risk of iatrogenic bleeding was reported to be higher in transbronchial lung biopsy especially with a cryoprobe.\cite{6}

Adequate anesthetic depth is necessary for IBs but limited data are available on the target anesthetic depth for IB. The 2016

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American College of Chest Physicians guidelines recommend moderate or deep sedation for patients receiving endobronchial ultrasound guided transbronchial needle aspiration.[7] In previous report, moderate sedation was reported to have a higher incidence of anesthesia-related complications, such as hypotension, hypoxemia, cough, arrhythmia, and aspiration, and inadequate sedation compared to general anesthesia besides the comparable diagnostic yield.[8] To indicate the target anesthetic depth for IBs, consciousness monitors such as bispectral index (BIS) may be helpful on determine the optimal intraprocedural anesthetic depth[9] as well as an satisfactory postprocedural recovery[10] especially for outpatients.

Another critical issue regarding anesthesia for IB is to maintain oxygenation with the necessity for an airway free of endotracheal tubes required for satisfactory IB procedural fields. As high-flow nasal oxygen (HFNO) has been applied successfully to maintain oxygenation on bronchoscopy[11,12] and other laryngeal surgery without endotracheal intubations,[13–15] it may be helpful on maintaining oxygenation with non-intubated IB (NIIB). When immobilization is necessary, apneic ventilation could also be performed with HFNO[16] for NIIB. However, the feasibility of applying HFNO on maintaining oxygenation during NIIB and the associated risk factors for procedures requiring longer time has rarely investigated.

In the present study, we retrospectively reviewed the anesthetic and procedural records for NIIB. With intravenous anesthesia guided with BIS levels between 40 and 60, we planned to report the feasibility on maintaining oxygenation during NIIB with HFNO. As the previous studies,[11,17] the primary outcome was set as the desaturation rate. If desaturation or complications such as delayed discharge, unexpected admission, or mortality happened, the management and the following outcomes were recorded. The possible affecting factors including the patient’s, anesthetic, and the procedural factors such as procedural time and the use of cryoprobe to intraprocedural desaturation and complications were also analyzed as the secondary outcomes.

2. Methods

This study was approved by the Institutional Review Board (no. 20201001SRNIB) of the Research Ethics Committee, National Taiwan University Hospital. For patients undergoing IB from February to September in 2020 in the bronchoscopic examination room at our institution. All patients received preanesthetic evaluation and signed the informed consent forms for the anesthesia and bronchoscopic interventions. Anesthetic planning was reviewed and the cases with planned intubation for IB would not include in our analyzation. Anesthetic records of all scheduled IBs were reviewed and records which were lack of body weight or height, or the BIS data were excluded. Bronchosopic examinations without any intervention were excluded, too. IB diagnostic and treatment procedures included TBNA with or without rapid on-site examination, cryobiopsy probe (for transbronchial cryobiopsy [TBC] and airway cryo-recannulation), electrooscural snare tumor resection.

The anesthesia for IB was performed with monitoring including electrocardiography, noninvasive blood pressure and BIS. Patients received HFNO with 10L/min oxygen throughout the procedures. The intravenous anesthesia was performed with midazolam, alfentanil, and propofol infusion. BIS levels were maintained in the level of general anesthesia between 40 and 60[10] throughout NIIB with HFNO. After NIIB and anesthetic emergence, patients were sent to post-anesthesia care unit (PACU).[19] Delayed discharge was defined by stay in PACU for more than 2 hours.

Data for all patients who received NIIB with HFNO was collected including age, sex, inpatient or outpatient, body mass index (BMI), procedure type, procedure time, American Society of Anesthesiologists (ASA) classifications, anesthetic method, duration, BIS value, desaturation (defined as SpO2 < 90% for >1 minute). Complications such as iatrogenic bleeding, delayed discharge from postoperative care unit (longer than 2 hours), and unexpected admission were recorded. Data analyzation was done by an independent author who did not participate in the anesthesia of IB procedures.

The incidence of intraprocedural desaturation was analyzed with all possible affecting factors. Patients’ factors (such as age, BMI, ASA classifications), settings (outpatient or hospitalized), procedural factors (including procedure time, diagnostic intervention or treatment, with or without cryoprobe) were all analyzed. Based on BMI, the patients were defined as underweight (BMI < 18.5 kg/m²), normal (BMI between 18.5 to 23.9 kg/m²), overweight (BMI between 24 to 26.9 kg/m²), or obese (BMI ≥ 27 kg/m² or more) per the definitions provided by the Health Promotion Administration, Ministry of Health and Welfare, Taiwan.

The chi-square test or 1-sided Fisher exact test were used to compare independent binomial groups, and results with \( P < .05 \) were considered significant. Correlations between continuous variables were analyzed using Spearman correlation coefficient and logistic regression. The software used for analyzation was IBM SPSS Statistics version 22.

3. Results

We had viewed total 260 records and excluded 4 of those missed the BIS levels and 4 of those were lacking of the height or weight for the calculation of BMI. There were 4 records of standard bronchoscope for the morphology survey, which did not be included in our analyzation. The rest 248 records were composed with those underwent IB under general anesthesia (IB) with endo-tracheal tube or supraglottic airway (SGA) insertion \( (n = 25) \), and non-intubated IB (NIIB) under TIVA with THRIVE and BIS monitor \( (n = 223) \) (Fig. 1). The demographic, anesthetic, and procedural data were summarized in Table 1. Most patients \( (185/223, 83.0\%) \) who received NIIB procedures were outpatients.

The ASA classifications, intraprocedural desaturation, and complications were presented in Table 2. The time for NIIB procedures was \( 56.1 \pm 26.8 \) minute \( \pm SD \). Desaturation occurred in 60 of 223 NIIB procedures \( (26.9\%) \), and most of these events were managed with increasing the oxygen flow rate or upper airway management, such as upper airway manipulation, positioning, and inserting a nasal airway. Only 1 desaturation event interrupted the procedure by requiring bag–valve–mask ventilation, and after which the procedure was completed smoothly without prolonged stay at the postoperative recovery care unit. Accidental iatrogenic bleeding happened in 2 patients. Blood clot was removed smoothly after inserting a laryngeal mask airway in 1 patient without delaying of recovery and discharge from PACU. Accidental massive bleeding occurred during cryoprobe tracheal and bronchial recannulation in the other patient. The patient was intubated and transferred to intensive care unit after blood clot removal.
and discharged 3 days later. However, he developed apnea at home; thus, 1 instance of mortality occurred in our cohort within 30 days after the procedure. There was another case that was converted to intubated bronchoscope during the interventions due to the preexisted poor pulmonary condition of right upper lobe consolidation. He was extubated after the intervention without the need of prolong staying in PACU.

Table 3 presents the factors influencing intra procedural desaturation in the NIIB group. There was a positive correlation of the rate of desaturation with increased BMI (Spearman correlation coefficient \( r = 0.36 \) and the significance of the independence of the 4 BMI groups was \(<0.001\)). In the logistic regression, the rate of desaturation of the 3 groups with abnormal BMI (underweight, overweight, and obese) was all significantly differing to the reference group (normal BMI). Age, ASA classification, patient setting, and procedure time were not significantly associated with intraprocedural desaturation. Procedure type contributed to increased desaturation risk. Intervventional treatment such as electrosurgical snaring resection and cryoprobe tracheal or bronchial recannulation showed a higher desaturation rate (3 of 6 cases) without statistical significance (\( P = .35 \)). The application of cryoprobe for TBC and recannulation was associated with a significantly higher desaturation rate (\( P < .001 \)). Considering the diagnostic procedures, combination with TBC also had a significantly higher desaturation rate than simple TBNA did (\( P = .019 \)).
Table 2
Anesthesia data and outcomes for patients receiving NIIB.

| Anesthetic records | (n, % of 223 patients) |
|---------------------|------------------------|
| Anesthetic risk by ASA classification ASA | N | % |
| IV | 1 | 0.4 |
| III | 54 | 24.2 |
| II | 166 | 74.5 |
| I | 2 | 0.9 |
| Intraprocedural events | Desaturation (SPO2 < 90%) | 60 | 26.9 |
| Interruption of procedure due to delayed unsolved desaturation | 1 | 0.4 |
| Massive bleeding | 2 | 0.9 |
| Conversion to tracheal intubation | 1 | 0.4 |
| Complications | Delayed discharge | 0 |
| (PACU stay > 2 h) | 1 |
| Unexpected admission | 1 |

ASA=American Society of Anesthesiologists, NIIB=nonintubated interventional bronchoscopy, PACU=post-anesthesia care unit.

4. Discussion

According to the present results, HFNO is feasible to maintain oxygenation during NIIB under BIS guided intravenous anesthesia only if with effective upper airway management. The risk of desaturation was significantly associated with higher BMI and cause an obstructed airway with general anesthesia. However, other such desaturation events were resolved with jaw thrust or nasal airway insertion in the beginning of NIIB. Effective upper airway management remains to be the major work for anesthetic team for NIIB. In 2 studies using HFNO-assisted light or moderate sedation for bronchoscopy examinations (mean procedure times of 20 and 24 minute) without monitoring anesthetic depth, the desaturation rates were 5.5% to 13.3%.[11,17] The possibly deeper anesthesia (BIS levels 40-60) may associated with higher incidence of upper airway obstruction, however, with effective airway management, the desaturation rate were not affected by the procedural time as shown in our study. Though HFNO is beneficial for NIIB with higher oxygenation[12,20] and allowing apneic ventilation,[21,22] our results indicated that HFNO cannot prevent desaturation without patent upper airways. Desaturation may be aggravated by continuous suction by bronchoscopic probes. Procedure time and BMI influence intraprocedural desaturation was reported in a previous study.[17] Our results on NIIB do not suggest that procedure time increases desaturation risk. Perioperative airway management and desaturation events are more frequent for obese patients[23] and are associated with a rapid decrease in oxygenation reserve.[24] Accordingly, supraglottic airway or tracheal intubation may be favorable for obese patients with difficult airway or obstructive sleep apnea.

The required anesthetic depth for IBs is deeper than that for simple bronchoscopy requiring shorter time.[25] The anesthetic depth in this study with BIS levels between 40 and 60 for NIIBs requiring longer time was similar with that suggested in previous study without BIS monitors.[26] Adequate anesthetic depth is required for NIIB with less procedure interruption, desaturation, cough, and agitation[8] during a shared airway procedure.[17] To ensure the precise localization of certain lesion sites and longer procedure time as that in our study, an anesthetic team may be essential for NIIB for maintaining an optimal anesthetic depth without desaturation throughout the procedures.

We also observed that the application of a cryoprobe increased the risk of intraprocedural desaturation. Repeated insertion of bronchoscope during the cryobiopsy might be a factor for desaturation. The specimen of TBC was not possible to retrieve

Table 3
Factors associated with intraprocedural desaturation in NIIB patients.

| Factors | Categories | Numbers | Desaturation N/% | \( P \) |
|---------|------------|---------|------------------|------|
| Settings | Outpatient | 185 | 47/25.4% | .26 |
| Hospitalized | 38 | 13/34.2% |
| Patient factors | Age (N/%) | | | |
| ≥65 y/o | 99 | 30/30.3% | .31 |
| <65 y/o | 124 | 30/24.2% |
| BMI | | | | |
| <18.5 | 17 | 0/0 | .001* |
| 18.5 to <24 | 124 | 23/18.0% | Normal BMI = ref. group |
| 24 to <27 | 51 | 17/32.7% | <.001* |
| ≥27 | 32 | 20/62.5% | <.001* |
| ASA classification | | | | |
| ≥3 | 55 | 18/32.7% | .26 |
| ≤2 | 168 | 42/25.0% |
| Procedural time (min) | < mean | 118 | 29/24.6% | .41 |
| Mean = 56.1 min | ≥mean | 105 | 31/29.5% |
| Intervention-related factors (N/% in this group) | Procedures performed | Diagnostic interventions | 217 | 57/26.3% | .35 |
| All NIIB procedures with or without cryoprobe | Interventions | 6 | 3/50% | .000016* |
| With cryoprobe | 31 | 17/54.8% |
| Without cryoprobe | 192 | 43/22.3% |
| Diagnostic interventions with or without cryoprobe | TBC only | 109 | 34/31.2% | .019* |
| | TBB | 25 | 14/56.0% |

\*Significant, In NIIB group, 60/223 (26.9%) patients presented intraprocedural desaturation.

Diagnostic interventions include ROSE, EBUS, TBNA, TBC, TBB.

Interventional treatments include electrosurgical snare tumor resection and cryoprobe airway re-cannulation.

ASA=American Society of Anesthesiologists, BMI=body mass index, EBUS=endobronchial ultrasound, NIIB=nonintubated interventional bronchoscopy, ROSE=rapid on-site examinations, TBB=transbronchial biopsy, TBC=transbronchial cryobiopsy, TBNA=transbronchial needle aspiration.

Hospitalized 38 13/34.2% Normal BMI = ref. group

\*Significant, In NIIB group, 60/223 (26.9%) patients presented intraprocedural desaturation.
from the working channel, and the bronchoscope was removed with the cryoprobe for the obtained specimen. Temporally loss of the upper airway might contribute to the intraprocedure desaturation. Complications were associated with procedure-related bleeding but not with patient’s or anesthetic factors. Cryobiopsy increases the risk of iatrogenic bleeding, which might also be associated with desaturation by lower airway obstruction. Most minor bleeding events were managed using an epinephrine spray or balloon compression in a nonintubated anesthetic setting. However, considering the procedure-related complications, cryoprobe-related bleeding and the following desaturation may force the anesthesiologists to choose more advanced airway management, such as endotracheal intubation. As the main factors of complications, the risk of bleeding should be carefully evaluated before using a cryoprobe for biopsy or recannulation. The limitations of this study were the retrospective design, which impeded satisfactory investigation of patients and pulmonologists.

5. Conclusion
For NIB under intravenous general anesthesia with BIS levels between 40 and 60, HFNO is feasible to maintain oxygenation but only if with patent upper airway management. Except the difficulty on upper airway management for patients with higher BMI, use of cryoprobe may bear higher risks of intra procedural desaturation as well as iatrogenic bleeding and severe complications.

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