**Supplementary File**

**Protocol**

***Effects of pre-operative nasal probe tests in flexible bronchoscopy: protocol for a single center randomized controlled trial***

**Introduction**

In flexible bronchoscopy, non-intubated patients are inclined to nasal insertion. While the insertion might be impeded by narrow nasal cavity, fragile nasal mucosa, deviated septum location, and non-uniformed size of two nasal passages. Thus, a maneuver to identify whether the bronchoscope can easily pass through the nasal passage is needed.

This study investigates whether pre-operative nasal probe tests can shorten the time of passing the glottis, improve the first-pass success rate, ameliorate patients’ patience, and reduce post-operative bleeding.

**Methods**

***Ethical approval***

Being reviewed and approved by the Institutional Review Board of West China Hospital, Sichuan University (No. 1044), this protocol was registered at chictr.org.cn (Identifier: ChiCTR2000032668). Written informed consent will be obtained from all the patients before enrollment. No personal information of potential or enrolled patients will be shared or published, and no individual will access the final trial dataset except for researchers and members of the ethics committee.

***Study design***

This study is a single center randomized controlled trial with participants undergoing flexible bronchoscopy. Three hundred subjects will be randomized at a 1:1:1 ratio into three groups: CD group, AD group, and control group. To identify a better nasal passage for insertion, participants in the CD group and AD group will receive pre-operative nasal probe tests: using 2 mL of saline (Shijiazhuang No. 4 Pharmaceutical, Shijiazhuang, China) with cotton buds (Chengdu Medical and Sanitary Material Factory, Chengdu, China) for CD group, and 2 mL of a mixture of 0.01% adrenaline (GRANDPHARMA, Wuhan, China) and 2% lidocaine (Shanghai Fosun Zhaohui Pharmaceutical, Shanghai, China) with cotton buds for AD group. Participants in the control group will not receive pre-operative nasal probe tests, and the nasal passage of them will be selected randomly. The primary endpoint is the insertion time. Secondary endpoints include the first-pass success rate, patients’ tolerance scores, and post-operative complications.

***Study participants***

Inclusion criteria:

(1) Having indications of flexible bronchoscopy from respiratory specialists;

(2) Undergoing flexible bronchoscopy for the first time.

Exclusion criteria:

(1) Aged <18 years or aged >85 years;

(2) Having comorbidities such as decompensated heart failure, severe respiratory failure, history of upper airway surgery or radiation, bleeding disorder, or mental illness;

(3) Needing general anesthesia;

(4) Having nasal diseases that require an orotracheal approach.

***Assignment of interventions (for controlled trials)***

A simple randomization method will be applied, in which a statistical profession will use SPSS software (IBM SPSS, version 20, Chicago, IL, USA) to select suitable segment lengths, give a seed number, generate random numbers, and finally list the randomized treatment assignment scheme corresponding to the ordinal numbers 01–300. Subjects will be randomized to AD, CD, and control groups in a 1:1:1 ratio. To ensure the randomization of grouping, the randomization numbers will be placed in airtight and opaque envelopes, and then kept in exclusive custody. The trial will be blinded to patients and the final efficacy evaluator, and the blind will be uncovered only at the end of the trial efficacy evaluation.

***Data collection and management***

All results will be independently recorded and entered twice; any missing values will be verified to ensure data completeness and accuracy; all data will be recorded on the case report form immediately in the Excel database and abnormal data must be clarified by the physician; dropouts and adverse events will be recorded timely; after principal researcher, sponsor, statistical analyst, and data manager have signed the data lock record, the data administrator will lock the database.

The main indicators include insertion time, first-pass success rate, patient tolerance score (including pain, foreign body sensation, and comfort degree), patient vital signs (including HR, SBP, DBP, SpO2, and RR), and post-operative complications (including nasal bleeding and hemostatic agents application).

***Intervention***

Patients in CD and AD groups will undergo nasal probe tests before flexible bronchoscopy to identify a better nasal passage for insertion. Patients in the control group will not receive nasal probe tests and the nasal passage of them will be selected randomly. In detail, operators will perform the nasal probe tests, using 2 mL of saline with cotton buds for CD group, and 2 mL of a mixture of 0.01% adrenaline and 2% lidocaine with cotton buds for AD group. The cotton buds will be inserted through both sides of the nasal cavity and will remain at the nasopharynx for at least 2 s. The nasal passage resisting less during the probe tests will be selected to insert the bronchoscope.

***Flexible bronchoscopy procedure***

The procedure of flexible bronchoscopy is based on the British Thoracic Society guidelines. Briefly, all patients will be required to fast for 4–6 h and be initiated on 2% lidocaine by nebulized inhalation 30 min before the procedure. Intravenous lines will be established after entering the endoscopy room. Vital signs, including BP, HR, RR, and SpO2, will be continuously monitored by the anesthesiologist and nurse during the flexible bronchoscopy (iPM patient monitor, Shenzhen Mindray Bio-Medical Electronics Co, Ltd, Shenzhen, China). Alarms will be set to sound if the SpO2 dropped to <90%, the BP <90 mmHg, the HR <40 beats/min, or the RR <8 breaths/min. Bronchoscopy will be performed with a flexible bronchoscope (model BF-1TQ290; Olympus; Tokyo, Japan) with the patient in the supine position. The procedure will be performed by two experienced bronchoscopists with relevant professional qualifications and >10 years of practice. During the bronchoscopy, all patients will receive supplemental oxygen.

***Monitoring***

Subjects will be included in this study strictly according to the inclusion and exclusion criteria and they can withdraw in the event of serious adverse events or complications against continuing the trial. The investigator will inform patients to report any adverse events throughout the trial, record the reported events, and perform treatment accordingly.

***Study endpoints***

The primary endpoint is the bronchoscope insertion time, meaning the duration from touching the nasal ostium to touching the glottis. The secondary endpoints include the first-pass success rate, patients’ tolerance scores (including pain, foreign body sensation, and comfort degree), and post-operative complications. An independent investigator will record the insertion time with a stopwatch (measurement accuracy of 0.01 s), and note whether the first insertion succeeds (recording yes or no). Patients’ tolerance scores will be assessed and recorded within 30 min after the operation, using the VAS score, including pain (0 = non-existent; 100 = unbearable), foreign body sensation (0 = non-existent; 100 = unbearable), and comfort degree (0 = satisfied, feeling nothing; 100 = too uncomfortable to tolerate). In addition, the operators will be asked to report the smoothness of the flexible bronchoscopy operation (5 = smoothest; 0 = unbearable) using the VAS score within 30 min after the procedure. The post-operative complications, including nasal bleeding, and the application of hemostatic agents within 24 h after the procedure will be recorded.

***Sample size calculation***

The sample size will be calculated with PASS 11 (NCSS, Kaysville, UT, USA). The primary endpoint of this study is the insertion time. A pilot study showed that the hypothesized means ± SDs of the CD, AD, and control groups were 25 ± 19 s, 24 ± 17 s, and 33 ± 25 s, respectively. At an alpha error of 0.05, a sample of 231 patients (77 patients per group) can detect the differences among groups to 90%, thus we will enroll 300 patients, considering the dropouts.

***Statistical analysis***

All statistical analyses will be performed with SPSS software (IBM SPSS, version 20, Chicago, IL) and SAS version 9.4 (SAS Institute Inc.). Continuous variables in normal and non-normal distribution will be presented as mean ± SD or median (IQR), respectively. Categorical variables will be presented as frequencies and proportions. To analyze the insertion time, tolerance and smoothness scores, and post-operative complications among three groups, one-way analysis of variance (ANOVA) or Kruskal–Wallis *H* test will be used for continuous variables and Chi-squared test or Fisher’s exact test for categorical variables. Bonferroni’s multiple comparison tests will be used for multiple group comparisons. Reported two-sided *P*-values <0.05 will be considered statistically significant.



**Supplementary Figure 1**: A 62-year-old man was performed with nasal probe test before flexible bronchoscopy.