

# Pre-operative nasal probe tests with adrenaline and lidocaine ease insertion during flexible bronchoscopy and reduce post-operative bleeding: a randomized controlled trial

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## Abstract

**Background:** Nasal insertion is the preferred method for non-intubated patients in flexible bronchoscopy; however, the relatively narrow nasal cavity results in difficulties related to bronchoscope insertion. This study aimed to investigate whether pre-operative nasal probe tests could reduce the time to pass the glottis, improve the first-pass success rate and patients' tolerance, and reduce postoperative bleeding.

**Methods:** This three-arm prospective randomized controlled trial was conducted in a tertiary hospital between May and October 2020. Three hundred patients requiring diagnosis and treatment using flexible bronchoscopy were randomly allocated to three groups: control group, simple cotton bud detection group (CD group), and adrenaline + lidocaine detection group (AD group). The primary outcome was the time to pass the glottis. Secondary outcomes included the first-pass success rate, the patients' tolerance scores, and post-operative bleeding. One-way analysis of variance, Kruskal-Wallis *H* test, Chi-squared test, Fisher's exact test, and Bonferroni's multiple comparison tests were used in this study.

**Results:** In total, 189 men and 111 women were enrolled in this study, with a mean age of  $55.72 \pm 12.86$  years. The insertion time was significantly shorter in the AD group than in the control group (18.00 s [12.00–26.50 s] *vs.* 24.00 s [14.50–45.50 s],  $P = 0.005$ ). Both the AD (99% *vs.* 83%,  $\chi^2 = 15.62$ ,  $P < 0.001$ ) and CD groups (94% *vs.* 83%,  $\chi^2 = 5.94$ ,  $P = 0.015$ ) had a significantly higher first-pass success rate than the control group. Compared with the control group, post-operative bleeding (1% *vs.* 13%,  $\chi^2 = 11.06$ ,  $P < 0.001$ ) was significantly lower in the AD group. However, no significant difference was found in the patients' tolerance scores.

**Conclusions:** Pre-operative nasal cavity probe tests especially with adrenaline and lidocaine during flexible bronchoscopy can significantly reduce the time to pass the glottis, improve the first-pass success rate, and reduce post-operative nasal bleeding. Pre-operative nasal probe tests are recommended as a time-saving procedure for patients undergoing flexible bronchoscopy.

**Trial registration:** Chinese Clinical Trial Registry (ChiCTR), ChiCTR2000032668; <http://www.chictr.org.cn/showprojen.aspx?proj=53321>.

**Keywords:** Complications; Flexible bronchoscopy; Nasal cavity-glottis time; Nasal probe test

## Introduction

Flexible bronchoscopy is a crucial method widely used in the diagnosis and treatment of pulmonary diseases.<sup>[1-4]</sup> In recent years, the nasal insertion has become the preferred method for non-intubated spontaneously breathing patients in most centers.<sup>[5-7]</sup> However, the relatively narrow nasal cavity and fragile nasal mucosa impede insertion, and a quick and blind removal may be necessary.<sup>[8]</sup> Moreover, the septum is not always located in the middle of the nasal cavity and the nasal passage on both sides is not the same size.<sup>[9]</sup> Thus, a maneuver to help

identify whether or not the bronchoscope can easily pass through the nasal passage is needed.

Bleeding is one of the most concerning complications of bronchoscopy.<sup>[10]</sup> Fiber-optic endobronchial adrenaline instillation was determined as an effective therapy for air bleeding.<sup>[11-13]</sup> Topical anesthesia with lidocaine administered through the bronchoscope is a widespread method

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based on the advantages of better toleration and fewer complications.<sup>[14,15]</sup> However, data evaluating the combined effect of adrenaline and lidocaine in the nasal probe test for flexible bronchoscopy with respect to reducing post-operative bleeding and improving the patients' tolerance are lacking.

Based on these findings, this study aimed to investigate whether pre-operative nasal probe tests could reduce the time to pass the glottis, improve first-pass success rate and the patients' tolerance, and reduce post-operative bleeding.

## Methods

### Ethical approval

This single-center randomized controlled trial was designed in accordance with the ethics principles expressed in the *Declaration of Helsinki* and *International Conference on Harmonisation Guidelines for Good Clinical Practice*. This study was approved by the Institutional Review Board of West China Hospital, Sichuan University (ethical approval No. 1044). Detailed study protocol could be found in the Supplementary File, <http://links.lww.com/CM9/A942>. This study was registered at [chictr.org.cn](http://chictr.org.cn) (Identifier: ChiCTR2000032668) and was conducted between May and October 2020. Written informed consent was obtained from all the patients before enrolment.

### Participants

A total of 300 patients from the Department of Pulmonary and Critical Care Medicine, West China Hospital undergoing flexible bronchoscopy participated in this prospective randomized controlled trial between May and October 2020. Both inpatients and outpatients requiring diagnosis and treatment using flexible bronchoscopy were enrolled.

The inclusion criteria were as follows: (1) having indications of flexible bronchoscopy from respiratory specialists; (2) undergoing flexible bronchoscopy for the first time. The exclusion criteria were: (1) aged < 18 years or > 85 years; (2) having comorbidities such as decompensated heart failure, severe respiratory failure, a history of upper airway surgery or radiation, a bleeding disorder, or mental illness; (3) needing general anesthesia; (4) having nasal diseases that require an orotracheal approach.

### Randomization and masking

Eligible patients were simply randomized into the simple cotton bud detection group (CD group), adrenaline + lidocaine detection group (AD group), and control group in a 1:1:1 ratio. A random number was generated via SPSS software (IBM SPSS, version 20, Chicago, IL, USA) by an independent investigator who was not involved in the operation procedure and outcome measurement process. Randomization results were concealed in opaque envelopes and were not revealed until the beginning of the operation. The patient was blinded to the allocation.

### Procedures and patient management

Patients in the CD and AD groups underwent nasal probe tests before flexible bronchoscopy to help identify a better nasal passage for inserting the bronchoscope [Supplementary Figure 1, <http://links.lww.com/CM9/A942>]. Participants in the CD group and the AD group received 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 the CD group, and 2 mL of a mixture of 0.01% adrenaline (GRAND-PHARMA, Wuhan, China) and 2% lidocaine (Shanghai Fosun Zhaohui Pharmaceutical, Shanghai, China) with cotton buds for the AD group. The cotton buds were inserted successively through both sides of the nasal cavity to the nasopharynx (using a twisting motion) and kept at the site for at least 2 s. The nasal passage with the least resistance during the probe tests was chosen to perform the flexible bronchoscopy. Pre-operative nasal probe tests were not performed on the control group, and the nasal passage of them was selected randomly.

The procedure of the flexible bronchoscopy was based on the British Thoracic Society guidelines.<sup>[16]</sup> Briefly, all patients were required to fast for 4–6 h and were initially given 2% lidocaine by nebulized inhalation 30 min before the procedure. Intravenous lines were established after entering the endoscopy room. Vital signs, including blood pressure (BP), heart rate (HR), respiratory rate (RR), and pulse oxygen saturation (SpO<sub>2</sub>), were continuously monitored by the anesthesiologist and nurse during the flexible bronchoscopy (iPM patient monitor, Shenzhen Mindray Bio-Medical Electronics Co., Ltd, Shenzhen, China). Alarms were set to sound if the SpO<sub>2</sub> dropped to <90%, the BP dropped to <90 mmHg, the HR dropped to <40 beats/min, or the RR dropped to <8 breaths/min. Bronchoscopy was performed with a flexible bronchoscope (model BF-1TQ290, Olympus, Tokyo, Japan) with the patient in the supine position. The procedure was performed by two experienced bronchoscopists with relevant professional qualifications and >10 years of practice. During the bronchoscopy, all patients received supplemental oxygen.

### Data collection and outcome measurement

Demographics (including age, sex, and body mass index [BMI]) and patients' disease types were collected at enrolment.

The primary endpoint was the insertion time, defined as the time from touching the nasal ostium to touching the glottis, which was noted with a stopwatch. An independent investigator recorded the insertion time with a stopwatch (measurement accuracy of 0.01 s) and noted whether the first insertion succeeded (recording yes or no). Secondary endpoints included the first-pass success rate, patients' tolerance scores (including pain, foreign body sensation, and comfort degree), and post-operative complications (including nasal bleeding and the application of hemostatic agents). 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) were assessed according to the visual analog scale (VAS) within 30 min after the bronchoscopy. A VAS score of the smoothness of the operation of the flexible bronchoscopy was assessed within 30 min after the procedure (5 = smoothest; 0 = unbearable). Moreover, post-operative complications, including nasal bleeding, and the application of hemostatic agents within 24 h after the procedure were recorded.

**Sample size calculation**

The primary endpoint of this study was the insertion time. A pilot study showed that the hypothesized means ± standard deviations (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, we estimated that a sample size of 231 patients (77 patients per group) would provide the trial with 90% power to detect the differences between groups, calculated using PASS 11 (NCSS, Kaysville, UT, USA). In consideration of potential dropouts, 300 patients were enrolled.

**Statistical analyses**

All statistical analyses were performed using SPSS software (IBM SPSS, version 20, Chicago, IL, USA). Continuous variables with normal and non-normal distribution were presented as means ± SDs or medians (interquartile ranges), respectively. Categorical variables were presented as frequencies and proportions. To analyze the insertion time, tolerance and smoothness scores, and post-operative complications among the three groups, one-way analysis of variance (ANOVA) or Kruskal-Wallis *H* test was used for continuous variables and Chi-squared test or Fisher’s exact test was used for categorical

variables. Bonferroni’s multiple comparison tests were used for multiple group comparisons. Two-tailed *P* values <0.05 were considered statistically significant.

**Results**

**Demographic and clinical characteristics of participants**

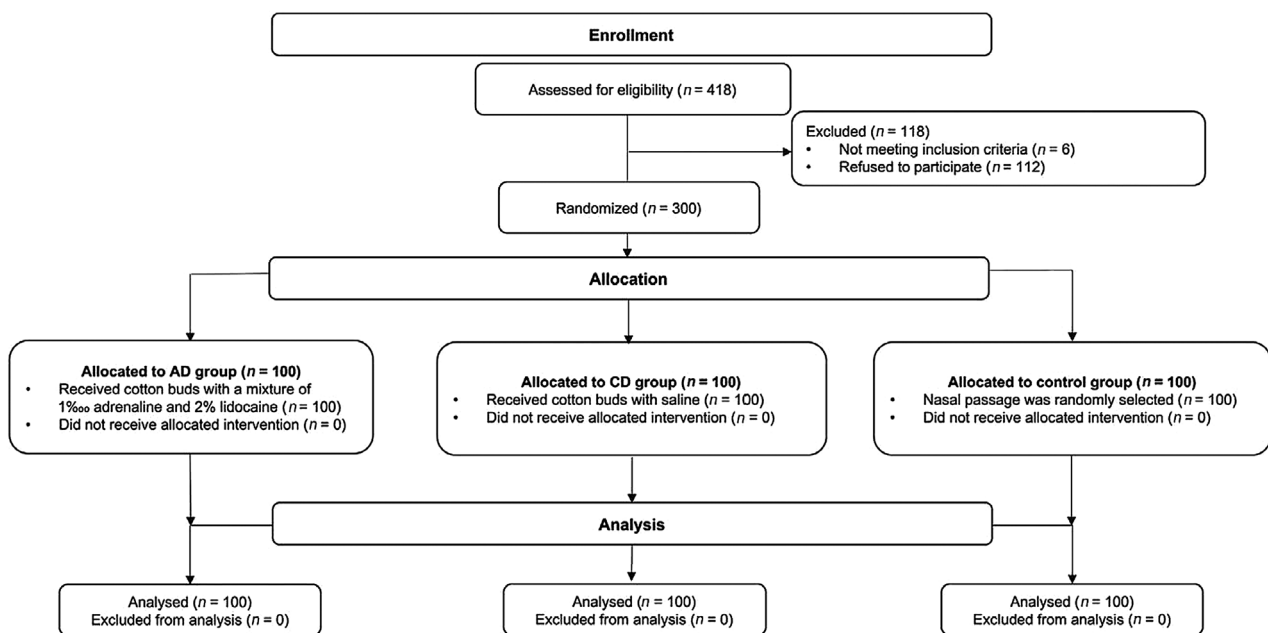
Three hundred patients undergoing routine flexible bronchoscopy between May and October 2020 were enrolled after screening for eligibility and were randomly allocated into three groups (each group *n* = 100) [Figure 1]. In total, 189 men and 111 women were enrolled with a mean age of 55.72 ± 12.86 years. There were no significant differences in age, sex, and BMI among the three groups (all *P* > 0.05). The distribution of the disease types in the three groups was approximately balanced and did not affect the observation of the outcomes [Table 1].

**Efficiency of nasal probe tests in flexible bronchoscopy**

To estimate the efficiency of nasal probe tests, the insertion time and first-pass success rate were assessed by a bronchoscopy specialist. Compared with the control group, the AD group had a significantly shorter time of insertion (18.00 s [12.00–26.50 s] *vs.* 24.00 s [14.50–45.50 s], *P* = 0.005). Both the AD (99% *vs.* 83%,  $\chi^2 = 15.62$ , *P* < 0.001) and CD groups (94% *vs.* 83%,  $\chi^2 = 5.94$ , *P* = 0.015) had a higher first-pass success rate than the control group [Table 2].

**Post-operative complications**

Compared with patients in the control group, postoperative complications such as bleeding (1% *vs.* 13%,



**Figure 1:** Flowchart of patients’ enrolment, allocation, and analysis procedure. AD group: Adrenaline + lidocaine detection group; CD group: Simple cotton bud detection group.

**Table 1: Demographic and clinical characteristics of participants in the three groups.**

Variables	Control group (n = 100)	CD group (n = 100)	AD group (n = 100)	F/ $\chi^2$	P values
Age (years)	53.33 ± 14.21	56.54 ± 11.29	57.30 ± 12.70	2.71	0.068
Sex (female/male)	35/65	35/65	41/59	1.03	0.598
BMI (kg/m <sup>2</sup> )	22.54 ± 3.29	22.43 ± 2.93	22.64 ± 2.99	0.12	0.890
Diseases				21.08*	0.275
COPD	0 (0)	2 (2)	0 (0)		
Space-occupying lesion	55 (55)	65 (65)	58 (58)		
Lung collapse	4 (4)	2 (2)	1 (1)		
Pneumonia	27 (27)	19 (19)	31 (31)		
Lung transplantation	0 (0)	1 (1)	0 (0)		
ILD	1 (1)	2 (2)	1 (1)		
Hemoptysis	7 (7)	2 (2)	1 (1)		
Pleural effusion	1 (1)	2 (2)	4 (4)		
Disease of the trachea	4 (4)	4 (4)	3 (3)		
Others <sup>†</sup>	1 (1)	1 (1)	1 (1)		

Data are presented as mean ± standard deviation, n/n or n (%). \* Likelihood ratio used. † Including mediastinum space-occupying lesion. AD group: Adrenaline + lidocaine detection group; BMI: Body mass index; CD group: Simple cotton bud detection group; COPD: Chronic obstructive pulmonary disease; ILD: Interstitial lung disease.

**Table 2: Efficiency, post-operative complications and tolerance and smoothness scores of nasal probe tests in flexible bronchoscopy.**

Variables	Control group (n = 100)	CD group (n = 100)	AD group (n = 100)	H/ $\chi^2$	P values
Efficiency					
Insertion time (s)	24.00 (14.50–45.50)	19.50 (12.50–32.50)	18.00 (12.00–26.50)*	10.25	0.006
First-pass success rate	83 (83)	94 (94)*	99 (99)*	18.21	<0.001
Post-operative bleeding and the application of hemostatic agents					
Bleeding	13 (13)	10 (10)	1 (1)*,†	10.60	0.005
Hemostatic agents	5 (5)	3 (3)	0 (0)*	7.12	0.028‡
Tolerance and smoothness scores					
Pain	2 (0–5)	1 (0–4)	2 (0–4)	1.98	0.372
Foreign body sensation	4 (2–6)	3 (2–5)	4 (2–5)	2.27	0.321
Comfort degree	4 (2–5)	3 (2–5)	3 (2–5)	1.74	0.419
Smoothness	5 (4–5)	5 (4–5)	5 (4–5)	3.19	0.203

Data are presented as medians (interquartile ranges) or n (%). \* P < 0.017 compared with CD group with Bonferroni's correction. † P < 0.017 compared with CD group with Bonferroni's correction. ‡ Likelihood ratio Chi-square value was used. AD group: Adrenaline+lidocaine detection group; CD group: Simple cotton bud detection group.

$\chi^2 = 11.06$ ,  $P < 0.001$ ) and the application of hemostatic agents (0 vs. 5%,  $\chi^2 = 7.06$ ,  $P = 0.008$ ) were significantly less common among those in the AD group. When compared with patients in the CD group, those in the AD group were significantly less likely to bleed after the operation (1% vs. 10%,  $\chi^2 = 7.79$ ,  $P = 0.005$ ) [Table 2].

**Tolerance and smoothness scores**

There were no differences in the VAS scores for pain, foreign body sensation, comfort degree toward flexible bronchoscopy, and the smoothness of the operation among the three groups (all  $P > 0.05$ ) [Table 2].

**Safety of nasal probe tests**

To estimate the safety of nasal probe tests, patients' vital signs (including HR, systolic BP, diastolic BP, SpO<sub>2</sub>, and RR) at three time-points (beginning of the operation, glottis-pass, and at the end of the operation) were

collected. There were no significant differences among the groups [Table 3].

**Discussion**

To our knowledge, this is the first three-arm prospective randomized controlled trial to investigate the effect of nasal probe tests used in flexible bronchoscopy with respect to shortening the insertion time, reducing post-operative complications, and improving the patients' tolerance. For the first time, we identified that probing the nasal cavity with cotton buds before flexible bronchoscopy significantly reduced the time to reach the glottis, improved the first-pass success rate, and reduced post-operative bleeding and the application of hemostatic agents.

In relation to the efficiency of this method, we found that performing nasal probe tests using cotton buds with a

**Table 3: Safety estimation of nasal probe tests in patients undergoing flexible bronchoscopy.**

Variables	Control group (n = 100)	CD group (n = 100)	AD group (n = 100)	H	P values
Beginning of the operation					
HR (beats/min)	81.50 (69.50–94.00)	78.50 (68.50–91.50)	80.00 (68.50–92.00)	0.51	0.775
SBP (mm Hg)	132.00 (118.00–146.00)	131.50 (121.00–145.50)	130.00 (116.00–145.00)	0.04	0.980
DBP (mm Hg)	82.00 (76.00–89.00)	82.00 (74.00–88.50)	78.00 (71.00–85.50)	5.83	0.054
SpO <sub>2</sub> (%)	98.00 (96.00–99.00)	99.00 (97.00–100.00)	99.00 (96.50–100.00)	3.90	0.142
RR (breaths/min)	20.00 (20.00–20.00)	20.00 (20.00–21.00)	20.00 (20.00–21.00)	3.68	0.159
Glottis-pass					
HR (beats/min)	90.00 (79.00–103.50)	96.00 (80.50–107.50)	95.00 (78.50–106.50)	0.99	0.610
SBP (mm Hg)	142.00 (124.00–155.50)	143.50 (122.50–161.50)	138.50 (120.50–158.00)	1.11	0.575
DBP (mm Hg)	90.50 (81.50–99.00)	92.00 (83.00–102.00)	88.00 (77.50–98.50)	2.46	0.293
SpO <sub>2</sub> (%)	99.00 (96.00–100.00)	99.00 (97.00–100.00)	99.00 (97.00–100.00)	1.99	0.370
RR (breaths/min)	21.00 (20.00–21.50)	21.00 (20.00–22.00)	21.00 (20.00–22.00)	0.08	0.960
At the end of the operation					
HR (beats/min)	94.50 (81.50–108.50)	92.00 (83.50–104.00)	91.50 (80.50–102.00)	0.57	0.751
SBP (mm Hg)	137.00 (124.00–148.50)	136.50 (126.50–153.00)	133.50 (120.00–148.50)	1.57	0.456
DBP (mm Hg)	85.00 (77.50–94.50)	84.00 (76.50–93.00)	82.00 (73.00–89.00)	5.43	0.066
SpO <sub>2</sub> (%)	96.50 (95.00–99.00)	97.00 (95.00–99.00)	97.00 (95.00–99.00)	2.81	0.245
RR (breaths/min)	21.00 (20.00–21.00)	21.00 (20.00–21.00)	21.00 (20.00–21.00)	0.11	0.948

Data are presented as medians (interquartile ranges). AD group: Adrenaline + lidocaine detection group; BP: Blood pressure; CD group: Simple cotton bud detection group; DBP: Diastolic blood pressure; HR: Heart rate; RR: Respiratory rate; SBP: Systolic blood pressure; SpO<sub>2</sub>: Pulse oxygen saturation.

mixture of 0.01% adrenaline and 2% lidocaine before flexible bronchoscopy significantly reduced the insertion time and increased the first-pass success rate compared with the conventional approach. Several potential factors can be attributed to these results. First, probing with cotton buds allowed the initial detection of the nasal cavity anatomy. Second, moist cotton buds could lubricate the nasal mucous membranes, which allowed the work channel to easily pass through the nasal passages. Previous studies have confirmed that the median time to reach the glottis with nasal insertion was around 50 s,<sup>[17,18]</sup> which was much higher than that in our study. The findings of this study confirm the practical value of this method and indicate that the pre-operative detection is of great importance during the process.

Moreover, we determined that the pre-operative nasal probe tests with cotton buds immersed in a mixture of 0.01% adrenaline and 2% lidocaine could reduce postoperative bleeding and the application of hemostatic agents compared with the conventional approach. In general, flexible bronchoscopy is a relatively safe operation, and the incidence of nasal bleeding after flexible bronchoscopy is currently reported in the literature to be about 0.5%,<sup>[19]</sup> which is usually small and can be stopped on its own, with the application of 1:10,000 adrenaline to stop the bleeding locally if necessary.<sup>[20]</sup> Apart from biopsy-related bleeding, the bleeding caused by mechanical friction could cause anxiety and affect the patients' quality of life.<sup>[21]</sup> In this study, we found that prior probing was associated with less nasal bleeding and that adrenaline, which reduced the insertion attempts, protected the nasal mucosa, shrunk the capillaries, and reduced the bleeding.<sup>[1]</sup> However, no significant difference was identified in terms of the patients' tolerance as well as the smoothness of the procedure reported by the bronchoscopist. This may be due to the size of the bronchoscope used in this study. The outer diameter

at the distal tip of the bronchoscope was 6.0 mm, which is relatively larger than the standard size of 4.8 mm. This difference may have resulted in increased discomfort experienced by the patients.<sup>[22]</sup>

To estimate the safety of pre-operative nasal probe tests, we collected several parameters of vital signs at three time-points during the procedure. No significant difference was found among the groups, indicating the relatively safe quality of this method, which could enable its wider application in the future.

In relation to the strengths of this study, this is the first prospective randomized controlled trial to assess the efficiency of pre-operative nasal cavity probe tests. This test is easy to master, economically efficient, and can be applied in other medical procedures, including trans-nasal gastroscopy and nasotracheal intubation. However, this study has some limitations. First, a 6.0 mm bronchoscope was used in this study. Using a bronchoscope with a higher diameter could increase discomfort. There is a need for future studies on a 4.8 mm bronchoscope. Second, since this was a single-center study, these findings may have limited generalizability. Multicenter studies should be conducted to confirm the reliability of these findings in the future.

In conclusion, we recommend nasal probe tests as a timesaving procedure for patients undergoing flexible bronchoscopy as the tests could shorten the time required to reach the glottis and reduce post-operative bleeding.

**Availability of data and materials**

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

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### Conflicts of interest

None.

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