

## Postprint: Survey and Analysis of Bronchial Provocation Test Implementation in Guangdong Province

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### Abstract

**Background** The prevalence of bronchial asthma is increasing year by year; however, primary healthcare institutions still face difficulties in early diagnosis and treatment. As an important diagnostic tool, the Bronchial Provocation Test (BPT) is of great significance. Although BPT is widely applied both domestically and internationally, its penetration rate in Guangdong Province remains low with unbalanced development. Understanding the current application status and existing problems of BPT in Guangdong Province can contribute to improving early diagnosis and management of bronchial asthma. **Objective** To investigate the current application status of BPT in Guangdong Province and analyze critical issues requiring urgent improvement during its development. **Methods** This study employed convenience sampling to select 236 medical institutions across 21 prefecture-level cities in Guangdong Province in 2024, encompassing 19 primary, 69 secondary, and 148 tertiary hospitals. Each institution designated one staff member from the respiratory department or pulmonary function laboratory to complete a questionnaire. The questionnaire covered basic hospital information, duration of BPT implementation, equipment usage, provocation reagents, adverse reactions, training needs, quality control measures, and mastery of BPT-related knowledge. **Results** Among the 236 medical institutions, 136 (57.63%) had implemented BPT, comprising 109 tertiary hospitals (80.15%), 27 secondary hospitals (19.85%), with no primary hospitals conducting the test. The median duration of BPT implementation was 6.00 (2.25, 10.00) years. Among the 136 institutions performing BPT, 133 (97.79%) utilized imported provocation equipment, while domestic equipment accounted for 13.97% (19/136). Quantitative aerosol inhalation method was employed by 106 hospitals (77.94%). Methacholine served as the primary reagent in 83.09% (113/136) of institutions. Among the 100 hospitals not implementing BPT, 60.00% (60/100) of respondents identified lack of equipment as the main limiting

factor. Regarding quality control, only 66.18% (90/136) of hospitals performed regular calibration of nebulization equipment. A total of 97.06% (132/136) of respondents reported familiarity with BPT-related knowledge. Common adverse reactions during BPT included cough (95.59%), wheezing (86.03%), and chest tightness (69.12%). Only 16.91% (23/136) of respondents demonstrated correct understanding of evaluation indices, and merely 5.88% (8/136) had clear knowledge of positive criteria. Conclusion The penetration rate of BPT in Guangdong Province remains low with unbalanced implementation, and primary hospitals have yet to adopt it. BPT calibration, methodology, quality control, and result interpretation lack standardization. Pulmonary function practitioners urgently require standardized training.

## Full Text

### Investigation and Analysis of the Current Status of Bronchial Provocation Testing in Guangdong Province

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## Abstract

### Background

The prevalence of bronchial asthma has been rising annually, yet primary health-care institutions still face difficulties in early diagnosis and treatment. Bronchial provocation test (BPT) is an important diagnostic tool with significant clinical value. Although BPT is widely used both domestically and internationally, its prevalence in Guangdong Province remains low and development is uneven. Understanding the current status and challenges of BPT implementation in Guangdong will help improve early diagnosis and management of bronchial asthma.

### Objective

To investigate the current status of bronchial challenge tests in Guangdong Province and analyze the issues requiring improvement during its development.

## Methods

This study used convenience sampling to select 236 medical institutions from 21 cities in Guangdong Province, including 19 primary hospitals, 69 secondary hospitals, and 148 tertiary hospitals. Each institution appointed one staff member from the respiratory department or pulmonary function laboratory to complete a questionnaire. The questionnaire covered hospital information, years of experience performing bronchial challenge tests, equipment used, challenge agents, adverse event management, staff training, quality control measures, and knowledge of bronchial challenge test protocols.

## Results

Among the 236 medical institutions, 136 (57.63%) had implemented BPT, including 109 tertiary hospitals (80.15%) and 27 secondary hospitals (19.85%); no primary hospitals offered this test. The median duration of BPT implementation was 6.00 (2.25, 10.00) years. Of the 136 institutions conducting BPT, 133 (97.79%) used imported equipment, while domestic equipment accounted for 13.97% (19/136); 106 (77.94%) used the quantitative nebulization inhalation method; methacholine was the primary agent in 83.09% (113/136) of cases. Among the 100 hospitals not conducting BPT, 60.00% (60/100) cited lack of equipment as the main limiting factor. Regarding quality control, only 66.18% (90/136) of hospitals performed regular calibration of nebulization devices. 97.06% (132/136) of respondents reported familiarity with BPT-related knowledge. Common adverse reactions during BPT included cough (95.59%), wheezing (86.03%), and chest tightness (69.12%). Only 16.91% (23/136) of respondents had correct understanding of judgment indicators, and merely 5.88% (8/136) clearly understood positive criteria.

## Conclusion

The prevalence of BPT in Guangdong Province remains low with uneven implementation; primary hospitals have not yet introduced this test. Standardization is lacking in calibration, methodology, quality control, and result interpretation. Pulmonary function practitioners urgently need standardized training.

**Keywords:** Bronchial provocation test; Bronchial asthma; Diagnostic techniques, respiratory system; Surveys and questionnaires; Quality control

## Introduction

Bronchial asthma is a heterogeneous disease characterized by chronic airway inflammation, with progressively worsening and variable respiratory symptoms (including wheezing, shortness of breath, chest tightness, and cough), accompanied by airway hyperreactivity (AHR) and variable expiratory airflow limitation<sup>1</sup>. According to the China Health Statistical Yearbook, the overall prevalence of bronchial asthma in China showed an upward trend from 2011 to 2020,

with significant regional variations<sup>2</sup>. Bronchial asthma typically presents with intermittent and variable symptoms, making it difficult to obtain a reliable diagnosis during time-limited clinical consultations<sup>3</sup>. Studies have shown that many asthma patients fail to receive timely diagnosis and treatment at the community level<sup>4-6</sup>. As the prevalence of bronchial asthma continues to rise annually, early diagnosis and management are crucial for improving patients' quality of life and reducing medical burden.

Bronchial provocation test (BPT) is a valuable diagnostic tool that involves inhaling antigens or non-specific stimuli to induce airway smooth muscle contraction and inflammatory responses, with changes in pulmonary function indicators measured before and after stimulation to assess the degree of airway narrowing<sup>7-10</sup>. BPT holds significant value in the diagnosis of bronchial asthma and evaluation of treatment efficacy. Despite recent advances in asthma diagnostic technologies, the low implementation rate and awareness of BPT have contributed to the underdiagnosis of asthma in China<sup>{11}-12</sup>.

This study employed convenience sampling to investigate 236 medical institutions across 21 prefecture-level cities in Guangdong Province in 2024, including 19 primary hospitals, 69 secondary hospitals, and 148 tertiary hospitals. Each institution selected one staff member from the respiratory department or pulmonary function laboratory for the survey.

## Methods

### Survey Content and Methods

After expert review and revision, the questionnaire was distributed via QR code through the Pulmonary Function Group of the Guangdong Medical Association Respiratory Disease Branch and the Pulmonary Function Committee of the Guangdong Chest Disease Society to the selected medical institutions. One respiratory department or pulmonary function laboratory staff member from each institution completed the questionnaire. The survey covered basic respondent information (such as hospital level and professional title), hospital BPT implementation status (including testing methods, years of implementation, equipment usage, provocation agents, adverse reaction management, staff training, reasons for non-implementation), quality control measures (such as nebulizer flow and volume calibration, compressed air source testing, nebulizer cup output calibration and frequency), and respondents' understanding of BPT (including indications/contraindications, positive interpretation criteria, and AHR severity classification).

### BPT Knowledge Criteria

Survey content covered six major aspects: BPT indications, relative contraindications, absolute contraindications, test judgment indicators, positive criteria, and AHR severity classification. Respondents were considered to have comprehensive knowledge only if they correctly answered all items in each category.

**Indications:** (1) Patients with atypical clinical symptoms suspected of having bronchial asthma; (2) Clinically diagnosed asthma patients requiring evaluation of AHR severity; (3) Allergic rhinitis patients at risk of developing asthma; (4) Patients requiring evaluation of anti-asthma treatment efficacy; (5) Personnel in positions where AHR poses high safety risks; (6) Chronic disease patients with AHR tendency; (7) Others requiring airway reactivity assessment.

**Relative Contraindications:** (1) Forced expiratory volume in one second (FEV1) <70% of predicted value, though methacholine challenge test (MCT) may be considered if FEV1  $\geq$  60% of predicted value with strict observation and adequate preparation; (2) Acute asthma exacerbation; (3) Baseline pulmonary function test not meeting quality control requirements; (4) Recent respiratory infection (<4 weeks); (5) Pregnancy or lactation; (6) Patients currently using cholinesterase inhibitors; (7) Airway spasm already induced by pulmonary function test.

**Absolute Contraindications:** (1) History of severe allergic reaction to methacholine or histamine; (2) History of near-fatal asthma attack or mechanical ventilation due to asthma within the past 3 months; (3) FEV1 <60% of predicted value or FEV1 <1.0 L; (4) Severe urticaria; (5) Myocardial infarction or stroke within the past 3 months; (6) Uncontrolled hypertension; (7) Aortic aneurysm; (8) Recent ophthalmic surgery or increased intracranial pressure; (9) Other conditions unsuitable for forced vital capacity (FVC) measurement.

**Judgment Indicators:** FEV1, peak expiratory flow (PEF), specific airway conductance (sGaw).

**Positive Criteria:** FEV1 decrease  $\geq$  20% from baseline; PEF decrease  $\geq$  20% from baseline; Respiratory resistance (Rrs) increase  $\geq$  2 times initial value with Astograph method; Resistance at 5 Hz (R5) increase  $\geq$  50% from baseline; sGaw decrease  $\geq$  35% from baseline.

**Airway Reactivity Severity Classification:** (1) Normal: Methacholine >2.500 mg (>12.80 mol) or Histamine >2.400 mg (>7.8 mol); (2) Extremely mild: Methacholine 1.076-2.500 mg (5.50-12.80 mol) or Histamine 1.013-2.400 mg (3.3-7.8 mol); (3) Mild: Methacholine 0.294-1.075 mg (1.50-5.40 mol) or Histamine 0.276-1.012 mg (0.9-3.2 mol); (4) Moderate: Methacholine 0.035-0.293 mg (0.18-1.40 mol) or Histamine 0.031-0.275 mg (0.1-0.8 mol); (5) Severe: Methacholine <0.035 mg (<0.18 mol) or Histamine <0.031 mg (<0.1 mol).

## Statistical Methods

SPSS 25.0 software was used for data analysis. Non-normally distributed continuous data were expressed as M (P25, P75), and categorical data as number of institutions (%).  $P < 0.05$  was considered statistically significant.

## Results

### Overall Situation

A total of 236 valid questionnaires were collected from medical institutions, covering respiratory physicians and pulmonary function technicians, including 43 senior-level (18.22%), 137 intermediate-level (58.05%), and 56 junior-level (23.73%) professionals. BPT was implemented in 136 (57.63%) institutions, comprising 109 tertiary hospitals (80.15%) and 27 secondary hospitals (19.85%); no primary hospitals conducted this test. The median duration of BPT implementation was 6.00 (2.25, 10.00) years, with tertiary hospitals at 8.00 (3.00, 12.00) years and secondary hospitals at 3.00 (2.00, 6.00) years.

### BPT Implementation by Hospital Level

Among the 136 hospitals conducting BPT, 133 (97.79%) used imported equipment, while domestic equipment accounted for 13.97% (19/136); 106 (77.94%) used the quantitative nebulization inhalation method (APS method); methacholine was the primary agent in 83.09% (113/136) of cases. Among the 100 hospitals not conducting BPT, 60 (60.00%) cited lack of equipment as the main limiting factor. and show the detailed breakdown.

### BPT Quality Control

Regarding quality control, 90 (66.18%) of the 136 BPT-implementing hospitals regularly calibrated nebulizer flow and volume. The calibration rates for compressed air source and nebulizer cup output were both 38.97% (53/136), with calibration frequencies primarily once daily and once weekly. provides detailed quality control data.

### BPT Safety

Common adverse reactions during BPT included cough (95.59%), wheezing (86.03%), and chest tightness (69.12%). The incidence of severe adverse reactions (acute laryngeal edema, anaphylactic shock, and loss of consciousness) was extremely low. shows the detailed adverse reaction profile.

### Knowledge of BPT-Related Information

Among the 136 hospitals conducting BPT, 132 (97.06%) respondents reported familiarity with BPT-related knowledge. However, only 23 (16.91%) correctly understood judgment indicators, and merely 8 (5.88%) clearly understood positive criteria, indicating that result interpretation needs improvement. presents the detailed knowledge assessment.

## Discussion

### Current Status of BPT Application

In recent years, with the release of the “Technical Specifications for Methacholine (Methacholine Chloride) Bronchial Provocation Test (2023 Edition)”<sup>{13}</sup> and the “Chinese Expert Consensus on Clinical Application of Bronchial Provocation Test (2024 Edition)”<sup>{{{14}}}</sup>, BPT has gradually gained attention in clinical practice. These guidelines emphasize the test’s important role in diagnosing typical and atypical asthma and its key significance in differential diagnosis and treatment evaluation for chronic cough, recurrent chest tightness, and dyspnea. However, this study shows that BPT prevalence in Guangdong Province is only 57.63%, concentrated primarily in tertiary and some secondary hospitals, while primary hospitals show almost zero implementation. This uneven distribution severely limits early diagnosis and intervention for bronchial asthma, particularly affecting screening capabilities for high-risk patients in primary care settings.

Among institutions conducting BPT, 97.79% still use imported equipment, while domestic equipment accounts for only 13.97%, representing a significant increase from the 2013 survey<sup>{15}</sup> (13.97% vs. 5.60%). This indicates that while some hospitals have begun using domestic equipment, overall dependence on imported devices remains strong. Future promotion of domestic equipment will help reduce medical costs and further facilitate BPT implementation in primary healthcare institutions.

### Factors Limiting BPT Implementation

This study also identified major factors constraining BPT implementation, including equipment shortage, insufficient trained personnel, and safety concerns. Among hospitals not conducting BPT, 60.00% cited lack of equipment as the primary limiting factor, and 41.00% mentioned insufficient reagents. These issues are particularly prominent in primary hospitals, reflecting not only uneven distribution of medical resources but also inadequate awareness of this test in primary care settings. Although 20.00% of hospitals expressed concerns about test safety, in reality, adverse reactions are mostly mild symptoms such as cough and wheezing, with severe reactions (laryngeal edema and anaphylactic shock) being rare. Enhanced safety education and technical training are expected to alleviate these concerns.

### Current Status and Challenges of Quality Control

Regarding BPT quality control, this study found that despite established protocols, many hospitals fail to follow standardized quality control procedures, particularly in nebulizer cup output calibration and compressed air source testing (both only 38.97%). Failure to perform equipment calibration as required may lead to test result errors, thereby affecting diagnostic accuracy. Quality

control is a critical link ensuring reliability and consistency of BPT results; however, many hospitals currently invest insufficient resources in quality control, indicating gaps in standardization.

Additionally, this survey revealed that some hospital operators have inadequate mastery of test-related knowledge, particularly in result interpretation. Only 16.91% of respondents could correctly identify positive indicators, meaning many healthcare workers may be unable to accurately assess AHR and its severity, increasing risks of misdiagnosis and missed diagnosis. Therefore, future efforts should focus on strengthening healthcare worker training, particularly regarding in-depth understanding of positive criteria and airway reactivity severity classification.

### International Comparison

Compared with studies from countries like Malaysia, BPT implementation in Guangdong Province is somewhat representative. NG et al.<sup>{16}</sup> showed that BPT prevalence in Malaysia is low, with limited physician awareness of the technology, as only 39.28% of surveyed doctors understood BPT applications. In contrast, Guangdong Province demonstrates significantly better implementation in tertiary and some secondary hospitals, though primary hospital situations resemble Malaysia with almost no promotion. Survey results from other Chinese provinces also show uneven BPT prevalence, particularly in economically underdeveloped regions, reflecting that BPT promotion is closely related to medical resource distribution<sup>{{17}}{.}}</sup>

### Future Development Directions

To promote BPT application, future efforts should focus on: (1) Enhancing equipment allocation and technical support in primary hospitals: As domestic equipment matures, promoting cost-effective domestic devices will facilitate BPT implementation in more primary hospitals, thereby improving early screening rates for asthma patients. (2) Strengthening personnel training: BPT operation is complex with high quality control requirements; medical personnel must master standardized procedures and result interpretation. Regular pulmonary function operation training, particularly specialized training on positive criteria, will substantially improve test accuracy and reliability. (3) Improving quality control: Establishing a standardized BPT quality control system is recommended to ensure all implementing hospitals regularly calibrate and maintain equipment and follow standardized protocols. Simultaneously, strengthen monitoring of adverse reactions during testing to ensure patient safety. (4) Enhancing policy support and public education: Government should increase policy support for BPT, including financial assistance and equipment purchase subsidies. Simultaneously, conduct extensive public education to raise BPT awareness and encourage more high-risk populations to participate.

This study primarily covered secondary and tertiary medical institutions, with

limited sample sizes from primary hospitals and community health centers, mainly due to lack of dedicated staff and specialized equipment in these facilities. Preliminary surveys found zero BPT implementation rates in primary hospitals, with many not even conducting routine spirometry, let alone BPT. Future research should expand sample sizes to include more primary care institution surveys. Additionally, the questionnaire logic was complex, potentially causing response bias; subsequent studies could optimize questionnaire design to further improve data accuracy and reliability.

In summary, BPT is a key technology for comprehensive prevention and treatment of respiratory diseases such as bronchial asthma. Quality control levels for BPT in Guangdong Province still need improvement. This investigation studied BPT from perspectives of overall implementation, methodology, and quality control. Through this survey and analysis, we can provide data support for standardization and popularization of BPT in Guangdong Province and nationwide, promote relevant policy and technical improvements, thereby effectively enhancing diagnosis and treatment levels for bronchial asthma and other diseases and improving patient health outcomes. This also provides practical basis for better BPT application in clinical practice.

## Author Contributions

Wu Zhongping was responsible for research design, data collection, statistical analysis, and manuscript writing; Zheng Jingping and Gao Yi contributed to research implementation, evaluation, and revision; Chen Xiaoliang was responsible for quality control and revision.

## Conflict of Interest

The authors declare no conflict of interest.

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