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ORIGINAL RESEARCH

Proposal and Verification of New Revised Criteria for ABPA/ABPM Diagnosis

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Background: Although several diagnostic criteria for allergic bronchopulmonary aspergillosis (ABPA) have been proposed, the disease remains frequently misdiagnosed and underdiagnosed. In 2021, Asano et al introduced new diagnostic criteria for allergic bronchopulmonary mycosis (ABPM), which were found to improve diagnostic sensitivity compared to existing criteria, but the specificity was lower.

Methods: To develop revised scoring criteria for ABPA/ABPM diagnosis, delphi surveys were conducted with two rounds in 14 experts. The integer value of the mean importance scores for each item was used as the assigning values of revised scoring criteria. We evaluated the performance of existing diagnostic criteria against revised scoring criteria, using both physician diagnosis and latent class analysis (LCA) diagnosis of ABPM as reference standard.

Results: We screened a total of 168 patients as initial suspected ABPM. Using physician diagnosis as the reference, diagnostic sensitivity for the Rosenberg-Patterson criteria, ISHAM criteria, revised ISHAM criteria, Asano criteria and revised scoring criteria were 39.8%, 51.6%, 64.5%, 76.3% and 86.0%, while the diagnostic specificity was 100%, 100%, 100%, 85.3% and 94.7%, respectively. When using LCA as the reference, the sensitivities of these criteria were 45.1%, 48.0%, 56.7%, 71.0%, and 76.4%, the diagnostic specificity was 100%, 100%, 98.4%, 83.8% and 95.2%, respectively.

Conclusion: Revised scoring criteria showed improved diagnostic sensitivity compared to existing criteria while also enhancing specificity compared to the Asano criteria.

Keywords: allergic bronchopulmonary aspergillosis, allergic bronchopulmonary mycosis, revised scoring criteria, sensitivity, specificity, latent class analysis (LCA)

Introduction

Allergic bronchopulmonary aspergillosis (ABPA) is a complex chronic lung disease caused by hypersensitivity reactions to *Aspergillus fumigatus* (*A. fumigatus*). This condition is frequently associated with elevated in serum total IgE levels and positive *A. fumigatus* specific IgE/IgG antibodies. ABPA primarily affects individuals with asthma and cystic fibrosis[1] and may coexist with other pulmonary conditions such as COPD.[2] Conidia or hyphae of *A. fumigatus* can lead to inflammation, bronchiectasis and/or mucus plugs in the airway, manifesting in symptoms such as recurrent wheezing, hemoptysis, lung opacity or lung collapse.[3] In addition to *A. fumigatus*, other molds (such as *A. flavus*) or

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filamentous fungi can also induce similar airway inflammatory changes and symptoms, which are called allergic bronchopulmonary mycosis (ABPM).[4]

India hosts approximately 1.6 million ABPA patients,[5] yet the prevalence in China remains unclear. Delays in diagnosis and treatment often lead to serious complications, including progressive bronchiectasis and declining lung function.[6] Hence, early identification and diagnosis of individuals at a high risk of ABPA/ABPM are of utmost importance.

The first diagnostic criteria for ABPA were proposed by Rosenberg et al in 1977, later refined by Greenberger and Patterson with the inclusion of "specific IgE antibody to A. fumigatus".[7] The International Society for Human and Animal Mycology (ISHAM) proposed new diagnostic criteria in 2013, becoming the most widely used diagnostic criteria for ABPA.[8] Despite these advancements, unified standard for early diagnosis and screening of ABPA/ABPM is still lacking, resulting in a high rate of misdiagnosis and missed diagnosis. Saxena et al proposed lowering the total IgE levels threshold in the ISHAM criteria from 1000 IU/mL to 500 IU/mL, showing superior diagnostic performance for ABPA.[9] In 2024, ISHAM working group reached consensus and proposed the revised ISHAM criteria (S1 Table), recommending separate diagnoses for ABPA and ABPM.[10] The diagnostic efficacy remains unknown. Additionally, new 10-component diagnostic criteria were proposed for the diagnosis of ABPM in Japanese population (S2 Table). The criteria were verified by Asano et al (so-called Asano criteria) and showed great diagnostic performance.[11] Recently, our studies showed that compared with the existing diagnostic criteria, the Asano criteria showed better sensitivity for diagnosing ABPA, but the specificity was slightly lower.[12]

Although Asano criteria includes more diagnostic items and greatly reduces the rate of missed diagnosis, it does not take into account the primary and secondary order and different weights of the diagnostic items. This may be the reason why its diagnostic specificity has not been improved. To address this, we used the Delphi survey to unify and synthesize the opinions of experts in the relevant fields,[13,14] assigning weighted scores based on their evaluations. we have adapted the previous criteria into a weighted scoring system to make the criteria more objective (revised scoring criteria). Revised scoring criteria focus particularly on ABPM, due to the challenge of distinguishing it from ABPA and the lack of criteria available to ABPM diagnosis, especially within the Chinese population.

Latent class analysis (LCA) is a statistical method for categorization based on probability estimation and has been employed in diagnostic tests for many diseases lacking gold standards.[9,15–17] In this study, we compared the diagnostic efficiency of revised scoring criteria and existing criteria for discriminating ABPM and non-ABPM including related diseases (chronic eosinophilic pneumonia (CEP), eosinophilic granulomatosis with polyangiitis (EGPA), severe asthma with fungal sensitization (SAFS) and chronic pulmonary aspergillosis (CPA)) using physician and LCA diagnosis of ABPM as reference standard.

Methods

Delphi Survey

We used Delphi survey and selected 14 experts from different top-tier (Grade 3, Class A) hospitals in 14 provinces across China. Each expert met predefined inclusion criteria: 1. Over ten years of experience in the diagnosis, treatment, teaching, and research of related diseases (asthma or ABPA/ABPM), with most being leading figures in the field and holding a doctoral degree or higher. 2. Voluntary participation with informed consent.[18] The specific implementation method for the Delphi survey can be found in Supplementary Material.

Collection of Patient Data

This study included patients (from 4 cohorts) assessed as suspected ABPA/ABPM during their initial consultation from January 2018 to December 2023. Detailed demographic information, including the age and sex of the patients, was collected. The diagnosis of asthma was according to the guidelines of the Global Initiative for asthma (GINA) of 2023. The data of laboratory, radiology, spirometry and bronchoscopy in the diagnosis of ABPM were collected. SIgE was analysed using the fluorescent enzyme immunoassay technology (m3, gold domain medical test laboratory). A value more than 0.35 KUA/L was considered positive. sIgG was assayed using the automated fluorescent enzyme

immunoassay method (gold domain medical test laboratory), sIgG values >120 AU/mL were considered positive results. The computed tomography (CT) images were evaluated by two radiologists to determine whether there was obvious bronchiectasis, pulmonary radiographic infiltrates and bronchial high-density mucus. Additionally, fungal species from bronchoalveolar lavage fluid or sputum cultures were also recorded.

Control Population

Four kinds of confusing differential diseases were screened out among the suspected ABPA/ABPM patients. The first group included patients with CEP. These patients had peripheral blood eosinophil count ≥500 cells/mm^3, typical chest CT showing bilateral peripheral opacities, mainly in the upper lobe, and lung biopsy showing eosinophil infiltration into pulmonary interstitium or alveoli.[19,20] The second group included patients with EGPA. The criteria (proposed by the American College of Rheumatology in 1990) for diagnosis included (1) asthma, (2) eosinophilia >10% or absolute value >1500 cells/mm^3, (3) mononeuropathy or polyneuropathy, (4) nonfixed pulmonary infiltration, (5) sinusitis, and (6) extravascular eosinophil infiltration; any four of these items were sufficient for diagnosis.[21] The third group included patients with SAFS. Patients with severe asthma, *Aspergillus* specific IgE positive, but total IgE level <1000 IU/mL, and did not meet the diagnostic criteria of ABPA (ISHAM criteria) were classified as SAFS.[22] The fourth is CPA, which is diagnosed by positive culture of mold/filamentous fungi in airway secretions or immunological response to *Aspergillus* species (elevated serum *Aspergillus* IgE or IgG), combined with typical radiological findings including one or more cavities with or without fungal ball or nodules, additionally, duration of the symptoms or radiological changes for at least three months.[23]

Latent Class Analysis (LCA)

We performed LCA using the poLCA package in R version 4.3.2 (https://www.r-project.org/) to estimate the accuracy of five sets of diagnostic criteria. Each individual test of the criteria was applied to every patient. Compliance or non-compliance with each of the diagnostic test was reported in a binary fashion (0 or 1). The latent class for each patient was determined, starting from zero and progressively increased the categories. The conditional independence hypothesis was tested by goodness-of-fit test, based on the Bayesian information criterion (BIC), with their lowest values predicting the optimal model. The residual correlation between the tests was deduced by the method of lo-Mendell-Rubin likelihood ratio test (LMR), P value >0.05 indicates that there is no significant difference in the fit between k categories and k+1 categories, so the model of current categories has a good fit.[24]

Statistical Analysis

Data were analyzed using SPSS Version 22.0 software (IBM SPSS Inc, Armonk NY). Numerical data are expressed as average ± standard deviation or median ± quartile spacing and categorical data as counts and percentages. The differences between continuous variables were analyzed using t-test (for normally distributed data) or Mann–Whitney U-test (for skewed data), chi-square, likelihood ratio chi-square, and Fisher's exact test for categorical data. Receiver operating characteristic (ROC) curve analysis and area under the curve (AUC) analysis were used to compare the accuracy of different diagnostic criteria. GraphPad Prism (version 8.0; GraphPad Software Inc, La Jolla, California) was used to generate statistical charts. The statistical difference of AUC was analyzed by Z test. $P < 0.05$ was considered to indicate statistical significance.

Results

Clinical Diagnostic Criteria for ABPM

The response rate for two rounds of Delphi survey was 92.3% and 100%, respectively. The coefficient of variation (CV) indicates the degree of consensus among the experts, while a larger CV indicates a lower level of consensus.[25] The coefficient of variation for the expert scores of each diagnostic item was less than 0.3, with specific results shown in Tables S3 and S4. The integer values of the mean expert scores for each item were assigned as the scores in revised scoring criteria. Our revised scoring criteria primarily assign higher weights to "Elevated total serum IgE levels" and

"positive specific IgE for *Aspergillus*/filamentous fungi", with either criterion being worth two points, while the remaining items are assigned 1 point. To determine the minimum scores required for diagnosing ABPM of the revised scoring criteria, we calculated the sensitivity and specificity for diagnosing ABPM when total scores reached ≥5, ≥6, ≥7, and ≥8 points among the 168 patients we collected, (using the physician's diagnosis ABPA/ABPM as the reference standard). The highest diagnostic accuracy was achieved with total scores of ≥6 and ≥7 points, with diagnostic accuracies of 89.9% and 88.6%, respectively (S5 Table). Therefore, definitive diagnosis of ABPM was established at a total score of ≥7 points, while a score of 6 points suggested probable diagnosis of ABPM (Table 1).

The Rosenberg and ISHAM criteria have also been adapted for the diagnosis of ABPM, primarily changing the specific testing from *A. fumigatus* to a broader range of mold mix and filamentous fungi (S6 and S7 Tables).

Clinical and Demographic Characteristics

Our study included 168 cases initially identified with suspected ABPM at their first consultation. After thorough evaluation of medical records by more than three pulmonologists with expertise in allergy and ABPA/ABPM research,[12] 93 patients were confirmed with ABPM, while 75 were classified as non-ABPM. Table 2 summarizes differences between the physician-diagnosed ABPM and the non-ABPM groups with regard to demographics and diagnostic clinical characteristics (Table 2). Detailed patient characteristics from cohort 1 to 4 are listed in S8 Table.

Performance of Various Diagnostic Criteria Towards Physician-Diagnosed ABPM

Among the 93 cases of physician-diagnosed ABPM, 32 fulfilled all items of the Rosenberg-Patterson criteria, while five met all items except bronchiectasis. Using physician-diagnosed ABPM as the reference standard, the Asano criteria identified 55 cases as definite ABPM and 27 as probable, achieving a sensitivity of 76.3%. The revised scoring criteria diagnosed 67 cases as definite ABPM and 17 cases as probable ABPM, yielding the highest sensitivity at 86.0% (Figure 1A). For diagnostic specificity, the Rosenberg, ISHAM, and revised ISHAM criteria were all 100%, with the revised scoring criteria showing a slight reduction to 94.7% but still surpassing the Asano criteria's specificity of 85.3% (Figure 1B) (Table 3).

We evaluated the diagnostic performance of five sets of criteria in 168 cases of physician-diagnosed ABPM and non-ABPM. ROC analysis indicated the superior performance of the revised scoring criteria (AUC of 0.944), significantly outperforming the others (AUC for Rosenberg-Patterson, ISHAM, revised ISHAM and Asano criteria was 0.852, 0.855, 0.903 and 0.902, respectively). (Figure 2). The optimal cutoff value for the revised scoring criteria was determined as 5.5, closely aligning with our defined threshold for probable ABPM, leading to the best balance of diagnostic sensitivity (84.8%) and specificity (92.0%), with the most favorable Youden index.

Subgroup Analyses

Subgroup analysis was conducted among 93 physician-diagnosed ABPM patients. Among them, 73 patients had coexisting asthma, with 67 (91.8%) meeting revised scoring criteria and 61 (83.6%) meeting the Asano criteria. The diagnostic sensitivity

Table 1 Revised Scoring Criteria for ABPM

Tests	Score
1.Elevated total serum IgE levels(≥ 417 IU/mL)	2
2.Positive specific IgE for *Aspergillus*/ filamentous fungi	2
3.Current or previous history of asthma or asthmatic symptoms	1
4.Peripheral blood eosinophilia (≥ 500 /mm^3)	1
5.Positive specific IgG for *Aspergillus*/ filamentous fungi	1
6.*Aspergillus*/ filamentous fungi growth in sputum cultures or bronchial lavage fluid	1
7.History of pulmonary infiltrates (variable or multifocal)	1
8.Central bronchiectasis on CT	1
9.Presence of high-attenuation mucus plugs in central bronchi based on CT or removal of mucus plug via bronchoscopy (presence or absence of fungal hyphae), or mucus plug expectoration history	1

Notes: *Aspergillus*/ filamentous fungi in items 2, 5 and 6 should be identical. Patients with total score seven or more are diagnosed with definite ABPM and total score six for probable ABPM.

Table 2 Comparisons of Demographic Data Between Physician-Diagnosed ABPM and Non-ABPM

	Physician-Diagnosed ABPM	Non-ABPM	*P* value
No. of subjects	93	75	
Age (y)	54.01±14.24	60.14±17.42	0.005
Female	51(54.84%)	30(40.00%)	0.056
History of asthma	73(78.49%)	41(54.67%)	0.002
Peripheral blood eosinophil counts (cells/mm^3)	800.00 (1040.00)	225.00 (1190.00)	0.006
Total serum IgE concentrations (IU/mL)	1421.80 (848.78)	343.30 (855.45)	<0.001
Aspergillus/filamentous fungi-specific hypersensitivity			
Aspergillus/filamentous fungi-specific IgE	3.14 (11.04)	0.15 (0.82)	<0.001
Aspergillus/filamentous fungi-specific IgG	96.01 (203.81)	79.29 (70.76)	0.152
Sputum or bronchial samples culture			
Any Aspergillus spp., n *(%)*	29(31.18%)	24(32.00%)	0.910
A. fumigatus, n *(%)*	22(23.66%)	23(30.67%)	0.308
Spirometry			
FEV1, % predicted	65.34±23.79	64.12±23.35	0.875
FVC, % predicted	85.82±19.73	81.63±15.12	0.519
FEV1/FVC, %	68.49±14.75	56.82±23.86	0.103
FeNO	54.94±39.40	35.00±11.40	0.338
Thoracic CT			
Lung opacities	43(46.24%)	42(59.15%)	0.208
Central bronchiectasis	70(75.27%)	33(46.48%)	<0.001
High attenuation mucus	37(39.78%)	14(18.67%)	0.003
Mucus in tracheoscope	37(39.78%)	17(22.67%)	0.018

Notes: All values are represented as mean ±SD (standard deviation), median (interquartile range) or number (percentage).

of Rosenberg-Patterson, ISHAM, and revised ISHAM criteria for asthmatic ABPM was 43.9%, 54.8%, and 79.5%, respectively (S1A Figure). There were 30 cases with positive culture for *Aspergillus*/filamentous fungi, and in this subgroup, the sensitivity of the revised scoring criteria remained the highest (73.3%), higher than that of the Asano criteria (70.0%). The trend was consistent across subgroup lacking microbiological evidence (S1B Figure). In 70 cases with bronchiectasis and 23 cases without bronchiectasis, the diagnostic sensitivity of the revised scoring criteria was the highest (S1C Figure).

Control Group Analysis

Among the control group, none of the patients with Chronic Eosinophilic Pneumonia (CEP) were misclassified as ABPM according to five sets of criteria. Twelve patients meeting the diagnostic criteria for EGPA were identified, with one diagnosed as probable ABPM based on the Asano criteria (Table 4). The detailed information of these patients can be found in S9 Table.

Performance of Various Diagnostic Criteria Using LCA

Considering the subjectivity in physician-diagnosed ABPM, we re-evaluated the diagnostic criteria using LCA in 168 patients. In each set of criteria, we selected the optimal model based on the BIC. For Rosenberg-Patterson, ISHAM, revised ISHAM, Asano and the revised scoring criteria, the selected model of categories were 2, 2, 2, 2, and 4, respectively. As for p-value of the LMR, only the model of ISHAM criteria had a p-value of 0.07 (>0.05), indicating a good goodness-of-fit, while the p-values for the other criteria were less than 0.05, suggesting a lack of fit according to LMR. The revised scoring criteria demonstrated improved diagnostic sensitivity (76.4% vs 71.0%) and specificity (95.2% vs 83.8%) compared to the Asano criteria (Figure 1C and D) (S10 Table).

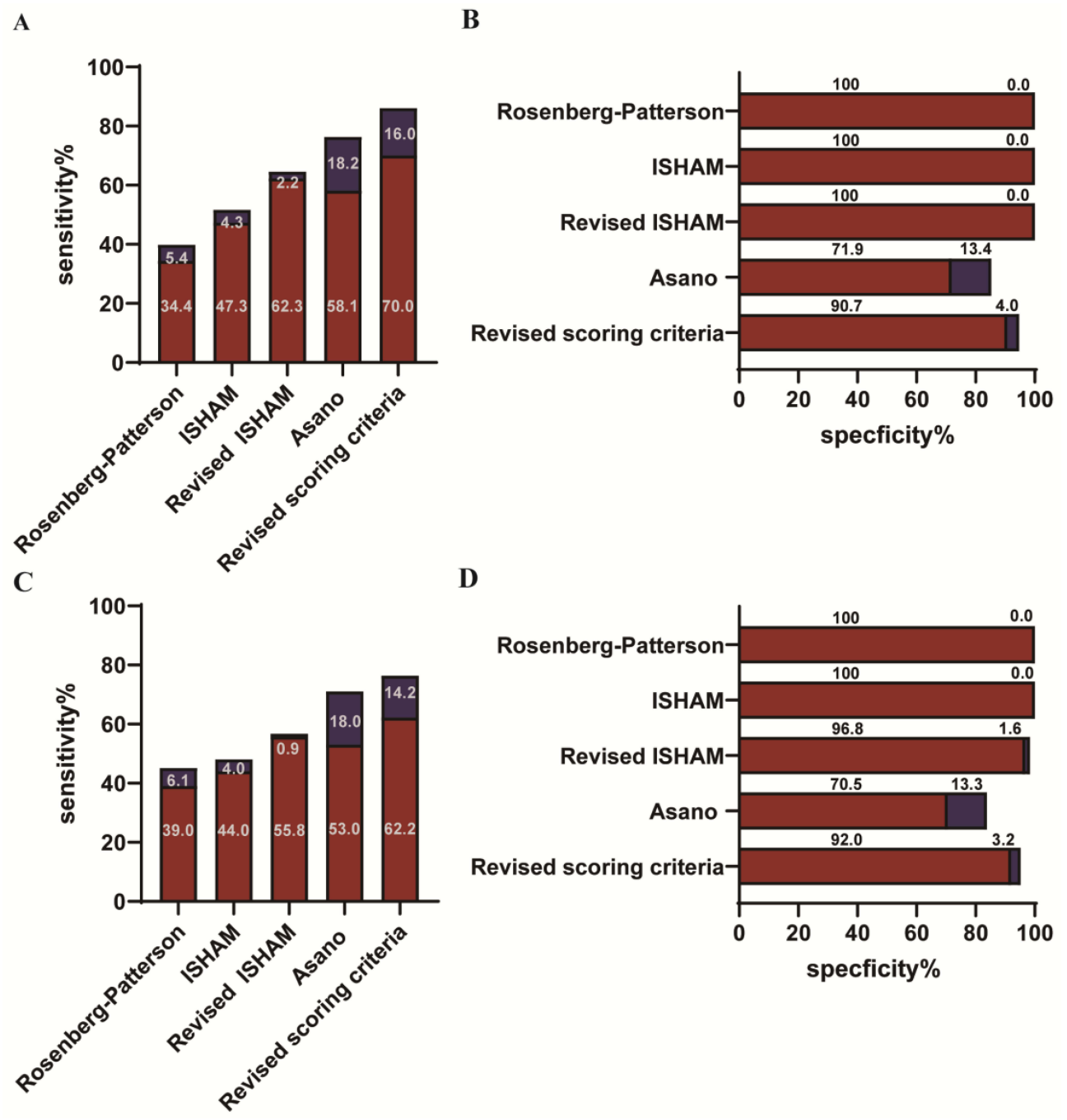

Figure 1 Sensitivity of five sets of diagnostic criteria using physician (**A**) and LCA (**C**) diagnosis of ABPM as reference standard. Specificity of five sets of diagnostic criteria using physician (**B**) and LCA (**D**) diagnosis of ABPM as reference standard. Red bars represent definite ABPM, and blue bars indicate probable cases.

Discussion

This study proposed revised scoring diagnostic system on the basis of Asano criteria to differentiate the weights of various diagnostic items for ABPA/ABPM. The suspected ABPM cases from four regions and centers in China were incorporated and the diagnostic performance of revised scoring criteria and existing criteria for ABPM was validated. By employing physician-diagnosed ABPM and LCA diagnosis of ABPM as reference standards, our findings reveal that revised scoring criteria not only improve diagnostic sensitivity compared to all existing criteria but also enhanced

Table 3 Performance of Various Diagnostic Criteria Towards Physician-Diagnosed ABPM

Diagnostic Criteria	Definite /Probable ABPM	Sensitivity%	Specificity%	PPV	NPV
Rosenberg-Patterson criteria	32/5	39.8 (29.9%~50.5%)	100 (93.9%~100%)	100 (88.3%~100%)	57.3 (48.3%~65.8%)
ISHAM criteria	44/4	51.6 (41.1%~62.0%)	100 (93.9%~100%)	100 (90.8%~100%)	62.5 (53.2%~71.0%)
Revised ISHAM criteria	58/2	64.5 (53.8%~74.0%)	100 (93.9%~100%)	100 (92.5%~100%)	69.4 (59.7%~77.8%)
Asano criteria	55/27	76.3 (66.2%~84.3%)	85.3 (74.8%~92.1%)	86.6 (76.8%~92.8%)	74.4 (63.7%~82.9%)
Revised scoring criteria	67/17	86.0 (76.9%~92.1%)	94.7 (86.2%~98.3%)	95.2 (87.6%~98.5%)	84.5 (74.6%~91.2%)

Note: The figures in parentheses correspond to 2.5%-97.5% bootstrap Cis.
Abbreviations: PPV, Positive predictive value; NPV, Negative predictive value.

diagnostic specificity compared to Asano criteria. The revised scoring criteria consistently demonstrate the highest diagnostic sensitivity across various subgroups. Moreover, compared to the Asano criteria, the revised scoring criteria significantly reduced the misdiagnosis rate of cases that are easily confused with ABPM.

The Rosenberg-Patterson criteria are the earliest widely used diagnostic criteria for ABPA, but due to their stringent diagnostic conditions, the sensitivity has always been low.[16] The revised ISHAM-ABPM criteria proposed in 2024 lowered the cutoff value for total IgE and included microbiological findings as crucial diagnostic criteria.[10] In our study, this modification led to an increased diagnostic sensitivity in the overall population and various subgroups.

Compared with previous criteria, Asano criteria incorporatenew components including high attenuation mucus, sputum culture, and fungal hyphae in mucus.[11] In early studies, it was found that 18.7% of patients diagnosed with ABPA exhibited high attenuation mucus on CT.[8] The specificity of positive *Aspergillus* culturing in diagnosing ABPA is noted to be relatively low.[26,27] Despite this, sputum culture holds particular significance in ABPM diagnosis. As Kuwa et al suggest a significant cross-reactivity between specific IgE and IgG antibodies for various mold species,[28] the identification of *Aspergillus* species from culture may serve as the primary microbiological evidence.

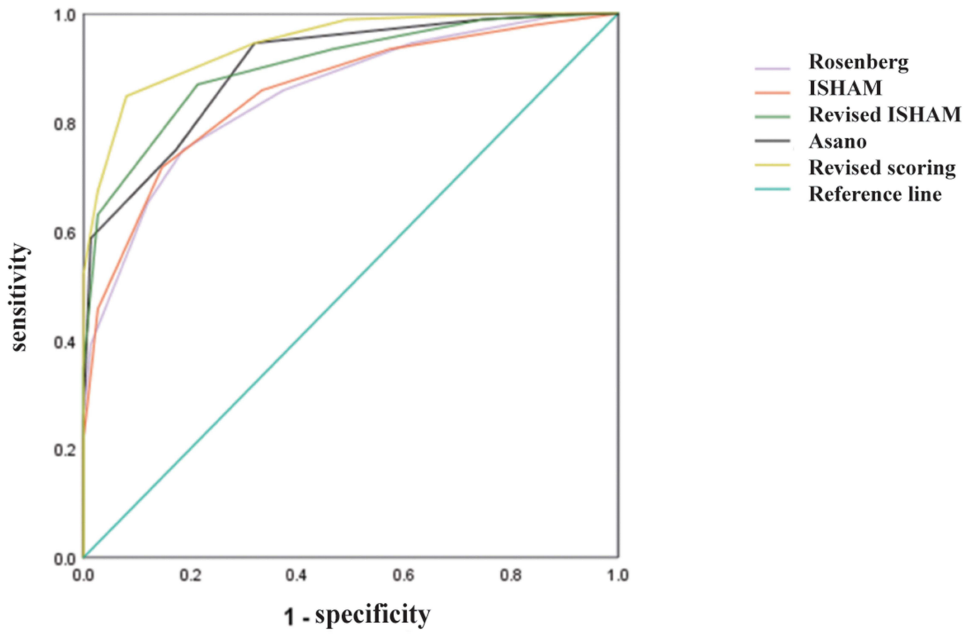

Figure 2 ROC curve analysis for the diagnosis of physician-diagnosed ABPM with Rosenberg-Patterson criteria (purple line), ISHAM criteria (red line), revised ISHAM criteria (green line), Asano criteria (black line) and revised scoring criteria (yellow line). The difference in AUC between the revised scoring criteria and other criteria was statistically significant (vs Rosenberg-Patterson, P<0.001; vs ISHAM criteria, P<0.001; vs revised ISHAM criteria, P<0.001; vs Asano criteria, P=0.001).

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Table 4 Definite/Probable Cases According to Criteria in Related Diseases

	No	Rosenberg-Patterson	ISHAM	Revised ISHAM	Asano	Revised Scoring
		Definite /Probable	Definite /Probable	Definite/ Probable	Definite /Probable	Definite /Probable
Chronic eosinophilic pneumonia	9	0	0	0	0	0
Eosinophilic granulomatosis with polyangiitis	12	0	0	0	1(probable)	0
Severe asthma with fungal sensitization	8	0	0	0	4(probable)	2(probable)
Chronic pulmonary aspergillosis	9	0	0	0	2(probable)	0

Previously, pathology diagnoses based on the presence of fungal hyphae in allergic mucin have been widely accepted for diagnosing allergic fungal sinusitis.[29] The adoption of complex pathological examinations for ABPM diagnosis is not widespread, with only two patients meeting this criterion in our study. To address underdiagnosis caused by technical limitations in obtaining viable biopsy specimens, we consolidated fungal hyphae identification with characteristic mucoid impaction features into unified diagnostic item.However, the latest technology that permits direct visualization of the fungus, MAI DI-TOF, can rapidly and efficiently identify microbial species and hyphae in purulent secretions and mucus plugs. It has been used in the diagnosis of chronic rhinosinusitis (CRS) and is expected to address complexity of pathological examinations and provide convenience for the rapid clinical diagnosis, particularly for pulmonary fungal diseases.[30]

Revised scoring criteria are similar to the Asano criteria in terms of components but differ in weighting. Previous studies have shown that sIgE is the most accurate indicator for diagnosing ABPA, followed by total IgE.[9,16] According to the revised scoring criteria, in cases where both elevated sIgE and total IgE are satisfied, a diagnosis of probable ABPA can be made by meeting any two of the remaining components. In comparison with the Asano criteria, we observed that some patients who met four components of Asano criteria were included in the probable ABPM according to revised scoring criteria, while some who met five were excluded. In fact, compared to those diagnosed by Asano criteria, patients diagnosed under revised scoring criteria demonstrated a significantly higher proportion of confirmed cases with both elevated sIgE and total IgE, leading to an improvement in diagnostic specificity.

In recent years, it has been observed that a considerable portion of patients with ABPA do not have accompanying asthma.[31,32] Additionally, the ISHAM classifies ABPA into serological ABPA (ABPA-S) and ABPA-CB based on the presence of bronchiectasis.[33,34] The differences in symptoms and prognosis revealed by these studies among various subgroups may influence the assessment of diagnostic performance. Our research found that the revised scoring criteria can improve the sensitivity of ABPA/ABPM diagnosis across subgroups based on the presence or absence of asthma, positive or negative culture results, and the presence or absence of bronchiectasis.

We selected potentially confounding control cases from the suspected ABPM cohort to assess the likelihood of misdiagnosis with various criteria. Among seven confusing cases diagnosed as probable ABPM according to Asano criteria, only two diagnosed as probable ABPM with the revised scoring criteria. In the opinions of some experts, SAFS is considered an intermediate stage between asthma and ABPA.[5] According to the revised scoring criteria, the number of SAFS cases diagnosed as ABPA/ABPM also decreased (from 4 cases to 2 cases). The revised scoring criteria may be more suitable for early disease screening while reducing the misdiagnosis rate, and also helps in the differentiation between ABPA/ABPM and SAFS.

Previous studies have recommended the Asano criteria for early disease screening.[12] In outpatient disease screening, revised scoring criteria will be more sensitive than the Asano criteria and reduce the misdiagnosis rate. Additionally, compared to other three sets of criteria, revised scoring criteria can simultaneously identify suspected ABPA and ABPM cases to improve screening efficiency. Therefore, revised scoring criteria can be used for community and outpatient disease screening, while the recently proposed revised ISHAM criteria are more inclined to be applied in clinical guidelines and treatment practices.

This study also has certain limitations. First, we included a total of four cohorts; however, some of the cohorts had relatively fewer participants, and regional differences in the cohorts may have influenced the overall results. Additionally, a prerequisite for applying LCA is meeting the assumption of conditional independence. However, since the five sets of diagnostic criteria share some of the same diagnostic items, they may not fully meet the assumption of conditional independence. In the goodness-of-fit test of LCA, we selected the optimal model based on the principle of minimum BIC. However, according to LMR, for Rosenberg-Patterson, revised ISHAM, Asano and revised scoring criteria, $p < 0.05$, indicates that adding categories to current model may improve the goodness-of-fit. Yet, when we increased to five categories, the p value of LMR still suggested adding more categories. Too many categories do not align well with the actual situation (individual's confirmed/non-confirmed disease status). Conflicting results between BIC and LMR are also commonly encountered in other studies, and typically, both BIC and LMR results are considered.[35] The simplicity and interpretability of the model should also be considered,[36] as BIC generally favors simpler models,[37] we still selected the model based on the principle of minimum BIC. Considering these limitations, our study utilized both LCA and physician diagnosis as reference standards, thereby complementing the limitations of both techniques and subjective judgment, and obtain more persuasive results.

In conclusion, we proposed revised scoring criteria for diagnosing ABPM/ABPA, which showed improved diagnostic sensitivity compared to existing criteria while also enhancing specificity based on the Asano criteria. The revised scoring criteria are expected to be used in the future for widespread screening of ABPA/ABPM in primary healthcare institutions, thereby reducing the missed diagnosis rate. Of course, further validation of the new criteria on a wider group of patients is necessary.

Abbreviations

ABPA, Allergic bronchopulmonary aspergillosis; ABPM, Allergic bronchopulmonary mycosis; LCA, Latent class analysis; ROC, Receiver operating characteristic; A. fumigatus, Aspergillus fumigatus; COPD, chronic obstructive pulmonary disease; ISHAM, International Society for Human and Animal Mycology; CEP, Chronic eosinophilic pneumonia; EGPA, Eosinophilic granulomatosis with polyangiitis; SAFS, Severe asthma with fungal sensitization; CPA, chronic pulmonary aspergillosis; HAM, High-attenuation mucus; sIgG, molds (including A. fumigatus)/filamentous fungi specific IgG; sIgE, molds (including A. fumigatus)/filamentous fungi specific IgE; CT, computed tomography; AUC, Area under the curve.

Data Sharing Statement

The participants of this study did not give written consent for their data to be shared publicly, so due to the sensitive nature of the research supporting data is not available.

Ethics Approval and Informed Consent

This retrospective study received approval from the Institutional Review Board of Xiangya Hospital of Central South University (No. 2023121128), and was conducted in accordance with the Declaration of Helsinki. The retrospective, observational nature of this study led to the exemption of patient informed consent by the ethics review committee.

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Author Contributions

Runjin Cai, Huan Ge, Bin Liu, Yuling Tang and Jun Wang are co-first authors. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of

the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The author(s) report no conflicts of interest in this work.

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