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Validation of the ARIA items to assess allergic rhinitis control (ARIA-C)

To the editor,

Allergic rhinitis (AR) is the chronic disease with the highest global prevalence. Since it has a major impact on patient quality of life (QoL), its severity has usually been evaluated following QoL outcomes. The original Allergic Rhinitis and Its Impact on Asthma Guideline (ARIA) severity classification used 4 items (sleep, daily activities/sport, work/school performance, and troublesome symptoms) and defined AR as mild (no items affected) or moderate/severe (1 to 4 items affected).[1] Since the 'moderate-severe' patient's group has been argued to be too broad and heterogeneous,[2,3] a modified three-level ARIA (mARIA) classification was proposed that discriminated AR severity between moderate (1 to 3 items affected) and severe (all 4 items affected).[3] This mARIA classification has been validated for adults and children.[3-5]

In recent years the concept of 'disease control' for chronic conditions has been introduced to indicate a disease status in which the treatment objectives are reached and symptoms are minimized (i.e., no limitations in activities, minimal use of rescue medications, infrequent exacerbations).[2] Several instruments have been developed for the assessment and quantification of AR control.[6-8]

The objective of the present study was to use the four original ARIA items to validate a three-level assessment of AR control (ARIA-C): controlled, partially controlled, and not controlled (Table

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1). ARIA-C aims to combine estimations of control of daily and nocturnal symptoms, impairments in social and work activities, and respiratory function into a single instrument.

To psychometrically validate ARIA-C, a prospective, observational, cross-sectional, study in real-life conditions was carried out between November 2015 and October 2016 with the participation of 27 allergologists and otolaryngologists working in hospitals throughout Spain. Patients included in the study were adults diagnosed with moderate-to-severe AR using both mARIA severity criteria[3] and a reflective total nasal symptom score (rTNSS) ≥8. Patients diagnosed with obstructive septal deviation, chronic rhinosinusitis or nasal polyposis were excluded. Treatments followed routine medical practice and the most frequent were intranasal corticosteroids plus oral antihistamines (57.9%), intranasal formulation of fluticasone propionate and azelastine (MP-AzeFlu, 29.4%), antihistamines (8.3%) and intranasal corticosteroids in monotherapy (4.4%). Patients were interviewed twice within a month (at baseline and at follow-up visit) and data was collected on demography, concomitant diseases, allergic sensitization, AR severity by mARIA and a visual analogue scale (0-10cm) (VAS), and impact on QoL (ESPRINT-15 questionnaire). Additionally, patient's control was assessed with the validated Spanish version of the Rhinitis Control Assessment Test (RCAT).[9]

AR patients included in this study (N=252) had a mean (±SD) age of 35±12 years and 71% were women. The disease evolution time was 6.3±9.7 years. AR was persistent in 60% of patients and intermittent in 40%; 35.7% had concomitant asthma (34.4% mild, 65.6% moderate) and 60% presented ocular symptoms.

At baseline (n=252), the ARIA-C showed that AR was partially controlled in 51 (20.2%) patients and not controlled in 201 (79.8%). At the follow-up visit (n=223), 66 (29.6%) patients were controlled, 89 (39.9%) partially controlled, and 68 (30.5%) not controlled, suggesting AR control was improved in a significant number of patients. Test-retest reliability of the ARIA-C was assessed by concordance of control in patients reporting the same health status between baseline and follow-up visits. The concordance was of 65.5% (kappa index=0.43, p=0.0043 when estimated by the patients [n=29]; and kappa index=0.57, p=0.006 when estimated by the physicians [n=25]), suggesting a weak test-retest reliability.

Convergent validity was examined by comparison of the scores obtained at the follow-up visit in the validated AR control test (RCAT) for patients in each ARIA-C category, and also in a variety of well-validated scores and questionnaires: total nasal symptom score (rTNSS), total ocular symptom score (rTOSS), total symptom score (rTSS: rTNSS +rTOSS), health-related QoL (ESPRINT-15), and VAS (Figure 1). In all cases the differences in scores for patients in each ARIA-C category were highly significant, suggesting good convergent validity.

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The responsiveness was assessed by comparisons of the magnitude of the RCAT score changes between initial and final visit for patients who improved or worsened their AR control according to ARIA-C. Patients who improved from ARIA-C not controlled to controlled obtained the maximum change in RCAT score (N=54; median=9.5; interquartile range [IQR]=5.0-13.0) versus the ones who kept the same control, whose change was significantly smaller (N=30; median=2.0; IQR=0.0-7.0) ($p<0.0001$).

Discriminant validity was investigated by testing the ability of ARIA-C to discriminate among groups of patients with controlled, partially controlled or not controlled according to RCAT criteria and among groups of patients who differed on disease severity as determined in the mARIA (mild, moderate, severe) and by VAS. The results show a highly significant discriminant validity of ARIA-C (Supplementary Table 1).

Current questionnaires for the measurement of control (CARAT, RCAT, and ARCT)[6-8] are efficient patient-reported metrics with good psychometric properties. However, because of their relative complexity they are unlikely to be widely adopted. The ARIA-C described here is simple and quick to perform and can readily categorize patients in three distinct levels of control. This approach could be useful both for clinical practice and for clinical trials to obtain more homogeneous populations of patients, or to define and optimize strategies for therapy and follow-up. The results of this study also suggest that the ARIA-C could be used to obtain a fast screening of patients with inadequate AR control, or to help patient's communication with primary care physicians. Measurements of severity with mARIA could be done in parallel with control by ARIA-C, as it has been suggested that methods for measuring severity and control in allergic diseases should be uniform.

This is the first time that the ARIA items are used to evaluate disease control. The three categories of ARIA-C can effectively discriminate between controlled, partially controlled, and not controlled patients. Its validation shows favorable and statistically significant results for test-retest reliability, convergent validity, discrimination among groups, and responsiveness to change. Further studies should be made to establish a correlation between control categories and therapeutic approaches.

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Conflict of interests

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Table 1. Criteria of ARIA-C to assess allergic rhinitis control categories.

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	CONTROLLED	PARTIALLY CONTROLLED	NOT CONTROLLED
Troublesome symptoms	No items affected	1-2 items affected (if two items are affected, sleep cannot be one of the affected items)	2-4 items affected (if only 2 items are affected, one must be sleep)
Daily activities/sport/leisure			
Work productivity/school performance			
Sleep			

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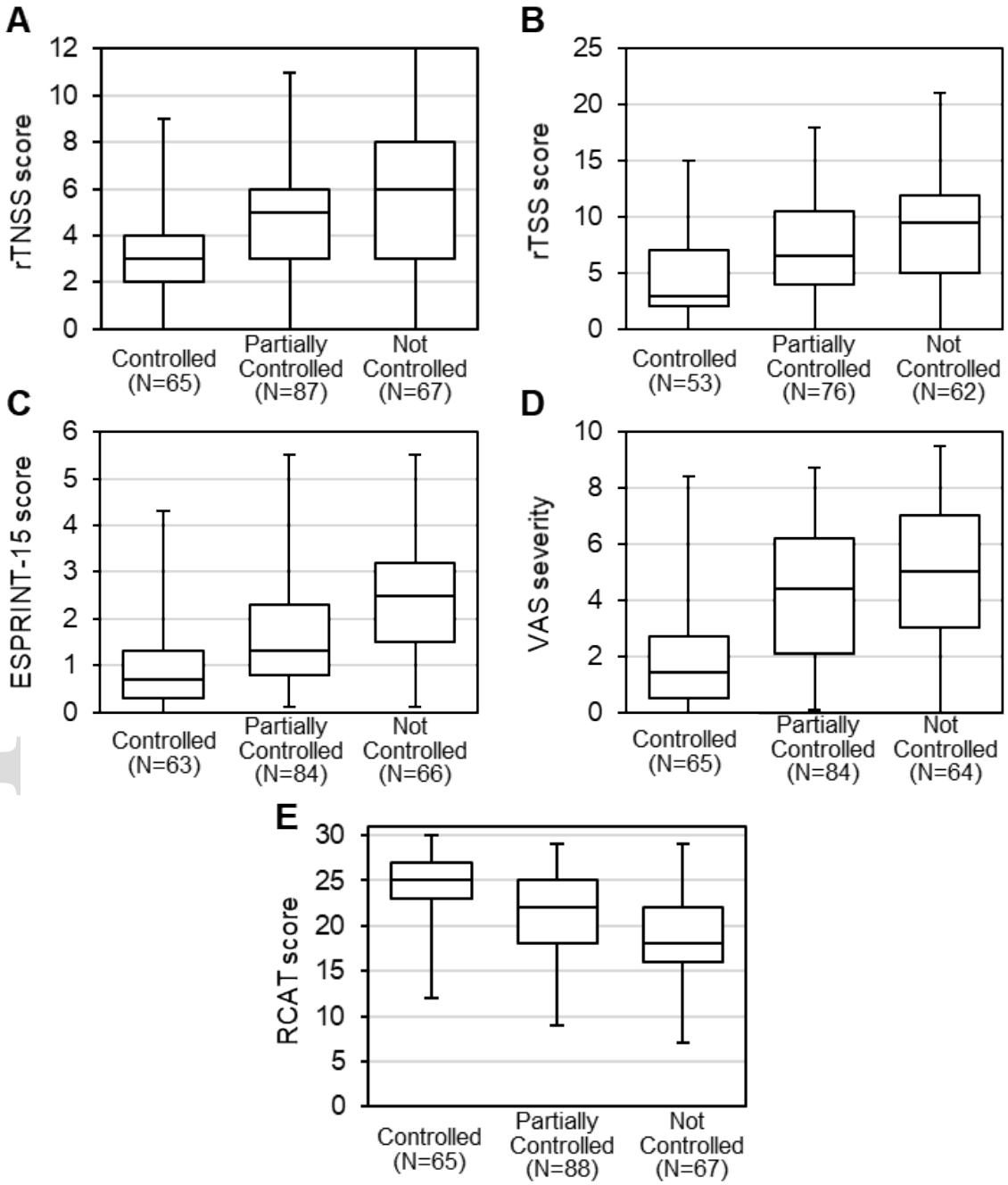
Figure 1. Convergent validity analysis of ARIA-C categories to assess allergic rhinitis control. Boxplots show the scores (median, 25th and 75th interquartile values, minimal and maximal values) of rTNSS (A), rTSS (rTNSS + rTOSS) (B), ESPRINT-15 (C), disease severity by VAS (D), and RCAT (E) as a function of ARIA-C categories. The differences are statistically significant in all cases ($p<0.0001$). Abbreviations: ARIA, Allergic Rhinitis and its Impact on Asthma; RCAT, rhinitis control assessment test; rTNSS, reflective total nasal symptom score; rTSS, reflective total symptom score; VAS, visual analogue scale.



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Supplementary Materials

Supplementary Table 1. Discriminant validity analysis of ARIA-C categories to assess allergic rhinitis (AR) control.

		CONTROLLED N (%)	PARTIALLY CONTROLLED N (%)	NOT CONTROLLED N (%)	Total N (%)	p
mARIA	Mild	66 (100)	0 (0)	0 (0)	66 (29.6)	<0.0001
	Moderate (1-3 items affected)	0 (0)	89 (100)	45 (66.2)	134 (60.1)	
	Severe (4 items affected)	0 (0)	0 (0)	23 (33.8)	23 (10.3)	
VAS	Mild (0-4cm)	56 (86.2)	38 (45.2)	26 (40.6)	120 (56.3)	<0.0001
	Moderate (>4-7cm)	7 (10.8)	33 (39.3)	23 (35.9)	63 (29.6)	
	Severe (>7-10cm)	2 (3.1)	13 (15.5)	15 (23.4)	30 (14.1)	

ARIA-C, allergic rhinitis control criteria according to Allergic Rhinitis and Its Impact on Asthma Guideline items
mARIA, modified severity ARIA classification of allergic rhinitis
VAS, Visual Analogue Scale for severity classification of allergic rhinitis