Validation of the Asthma Impairment and Risk Questionnaire in Spain: A Useful Tool for Assessing Asthma Control in Adolescents and Adults

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Asthma is a heterogeneous condition characterized by clinical manifestations ranging from mild symptoms to life-threatening attacks [1,2]. Asthma guidelines underline the need to distinguish between asthma severity and asthma control. Although the concept of asthma control includes both the domain of symptom control and the estimation of future risk, commonly used numerical tools such as the Asthma Control Test (ACT) [3] and Asthma Control Questionnaire (ACQ) [4] only assess symptoms and do not consider history of previous exacerbations, despite the fact that this poses an increased risk of future flare-ups [5]. A composite control measure capable of identifying individuals with uncontrolled asthma based on exacerbation history in addition to symptom impairment may help to more accurately describe the patient's clinical condition. In this context, the Asthma Impairment and Risk Questionnaire (AIRQ) [6] is a 10-item, yes/no, composite asthma control tool for assessment of symptoms over the previous 2 weeks and exacerbations over the previous 12 months. It can predict exacerbations over the following 12 months [7] and, probably, the time to the first exacerbation. The AIRQ has been evaluated in a US population of adult and adolescent asthma patients across all levels of severity,

yielding area under the receiver operating characteristic (AUROC) curve values of 0.94 for discriminating between well-controlled and not well-/very poorly controlled asthma and 0.93 for discriminating between well-/not well-controlled and very poorly controlled asthma. The above observations justify the translation of the instrument to other languages and validation in additional populations. To address this need, we aimed to validate the locally adapted version of the AIRQ in Spain (Figure 1S). Prior to this validation, the questionnaire underwent a rigorous translation-backtranslation and cultural adaptation process.

The AIRQ Study was a cross-sectional, observational, multicenter study conducted in 10 specialized Spanish asthma hospital units. A total of 300 adults and adolescents aged ≥12 years with clinically confirmed asthma were enrolled. Patients were included consecutively over a 4-month period, ensuring an equal number of patients across ACT score groups (well-controlled, ≥20; not well-controlled, 16-19; and very poorly controlled, ≤15) to cover different levels of asthma control and severity. The number of patients receiving biologics was monitored and capped at 10% of the total sample. Patient information was obtained from medical records. Patients completed the AIRQ, the ACT, and the ACQ-6, and the physician's perception of control was collected through ad hoc questions.

The patients' sociodemographic and clinical characteristics are presented in Table 1S; the asthma control levels according to the questionnaire findings and the number of previous exacerbations are summarized in Table 2S and Table 3S.

All analyses were conducted using SAS version 9.4. Categorical variables are expressed as frequencies and percentages. The 95%CIs were presented where appropriate. Continuous variables were expressed as mean (SD), median (IQR), and minimum and maximum. Two logistic regression models were constructed to distinguish (1) well-controlled from not well-controlled/very poorly controlled asthma and (2) well-controlled/not well-controlled from very poorly controlled asthma. We also calculated the following statistics: positive likelihood ratio (LR+), negative likelihood ratio (LR–), sensitivity, specificity, positive predictive value, negative predictive value, Akaike information criterion (AIC), and ROC curve. The same analysis was performed to generate ROC curves, considering, in this case, ACQ-6 as the gold standard (Table 4S). A descriptively analyzed weighted κ statistic was used to assess pairwise agreement between the AIRQ score, the ACT score, the ACQ-6 score, and the physician's perception of asthma control.

Both models of the Spanish AIRQ performed well (Figure), exceeding model-fit criteria with AUROC curves of 0.94 for model 1 and 0.92 for model 2. An AIRQ score cut-point of ≥2 for separating well-controlled asthma from all other types yielded a sensitivity of 89.3%, a specificity of 85.9%, and a positive and negative predictive value of 94.1% and 76.0%, respectively (model 1). A cut-point of ≥5 for separating very poorly controlled asthma from all other types yielded a sensitivity of 74.8%, a specificity of 91.2%, and a positive and negative predictive value of 84.8% and 84.6%, respectively

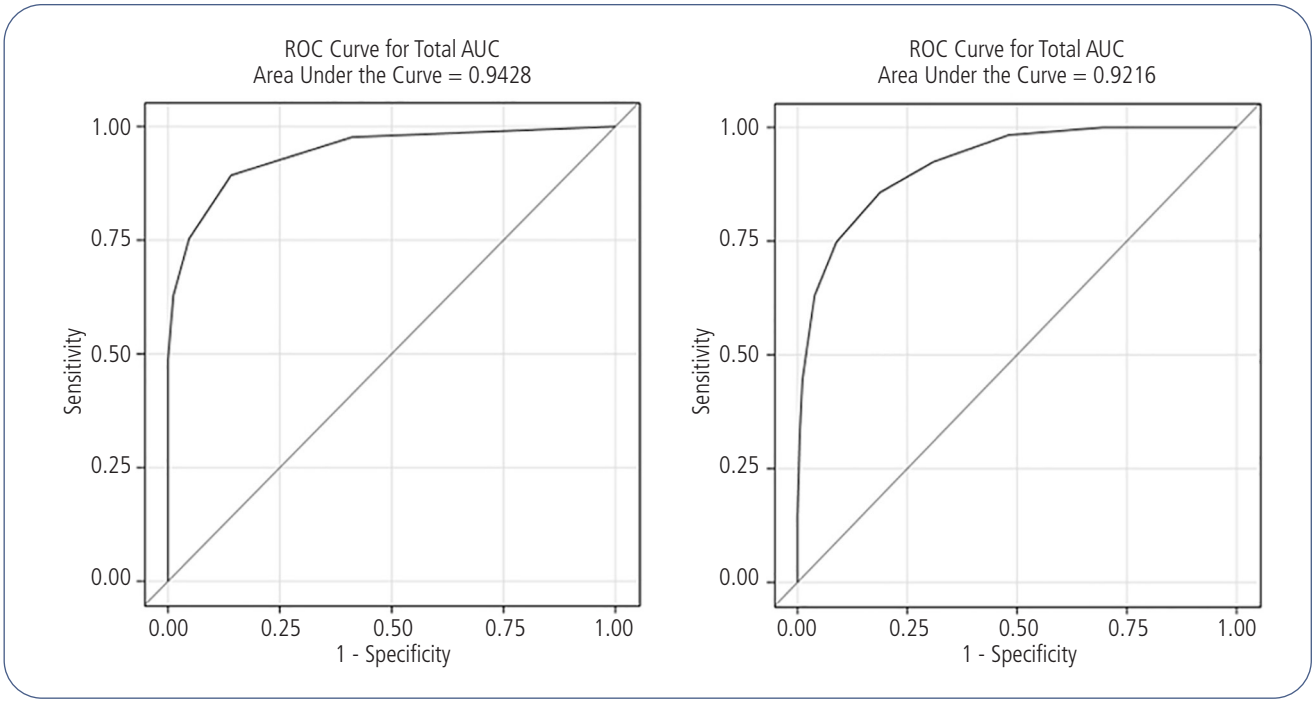

Figure. Receiver operating characteristic (ROC) curves for models 1 and 2. A, ROC curve and performance characteristics of the AIRQ for a Spanish cohort based on the participant's ACT score plus exacerbation history to distinguish well-controlled from not well-controlled/very poorly controlled asthma (model 1). B, ROC curves and performance characteristics of the AIRQ for a Spanish cohort based on the participant's ACT score plus exacerbation history to distinguish well-controlled/not well-controlled from very poorly controlled asthma (model 2). AIRQ indicates Asthma Impairment and Risk Questionnaire; AUC, area under the curve; ACT, Asthma Control Test.

(model 2). Table 3S shows the performance characteristics of the AIRQ in relation to the sum of the ACT and the exacerbation history.

The secondary objective was to determine the performance of the Spanish AIRQ relative to the sum of the ACQ-6 score plus exacerbations. Both models performed well. An AIRQ score cut-point of ≥2 for separating well-controlled from all other types yielded a sensitivity of 89.0%, a specificity of 80.2%, and a positive and negative predictive value of 91.2% and 76.0%, respectively. A cut-point of ≥5 for separating very poorly controlled asthma from all other types of asthma yielded a sensitivity of 69.6%, a specificity of 94.4%, and a positive and negative predictive value of 91.4% and 78.5%, respectively, (Figure 2S, Figure 3S, and Table 4S).

The exploratory objective was to assess agreement between the degree of asthma control perceived by physicians and the degree of asthma control determined by the AIRQ score, ACT score plus exacerbations, and ACQ-6 score plus exacerbations (Table 5S).

The locally adapted Spanish version of the AIRQ has proven to be a valid tool with measurement properties similar to those of the original instrument, which was developed in a US population. The AIRQ offers the advantage of incorporating both symptom control and future risk domains, thus providing the clinician with a more holistic view of the patient's clinical situation, regardless of disease severity. Therefore, the resulting therapeutic intervention will focus not only on current symptoms, but also on preventing future exacerbations, which is the main goal of asthma treatment. Although this questionnaire was validated using exacerbation risk items with a 12-month recall period, it was recently shown that a 3-month recall period is valid for classifying current asthma control and that the questionnaire can be administered between annual AIRQ assessments [8]. Future studies in large, real-life populations will inform us about the impact of the use of the AIRQ on assessment of asthma control and changes to treatment management.

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Conflicts of Interest

LPL reports grants, personal fees, and nonfinancial support from AstraZeneca, personal fees and nonfinancial support from GSK, grants and personal fees from TEVA, personal fees and nonfinancial support from Novartis, personal fees and nonfinancial support from Chiesi, personal fees from Sanofi, personal fees from Menarini, grants and personal fees from Esteve, personal fees from MSD, personal fees from TECHDOW PHARMA, grants and nonfinancial support from FAES, personal fees from Leo-Pharma, personal fees from GEBRO, and personal fees from GILEAD outside the submitted work.

In the last 3 years, EMM has received honoraria for speaking at sponsored meetings from AstraZeneca, Chiesi, Gebro, GSK, ALK, Novartis, Sanofi, and Teva. EMM has acted as a consultant for Astra Zeneca and GSK.

In the last 3 years, LME has received honoraria for speaking at sponsored meetings from Amgen, AstraZeneca, Boehringer-Ingelheim, Chiesi, Gebro, GSK, Menarini, Novartis, Pfizer, Rovi, Sanofi, and Teva. LME has acted as a consultant for AstraZeneca, GSK, and Sanofi.

CMR reports the following: payment or honoraria from Astra Zeneca, Chiesi, GSK, Gebro, Mundipharma, Novartis, TEVA, and Sanofi for lectures, presentations, speakers bureaus, manuscript writing, and educational events; payment for participation on data safety monitoring boards and advisory boards from Astra Zeneca and GSK; and grants from AstraZeneca, GSK, and TEVA.

In the last 3 years, CCS has received financial aid from Astra Zeneca, Chiesi, Novartis, Sanofi, GSK, Pfizer, and Gebro Pharma for advisory services, papers, research studies, attendance at congresses, and training courses.

In the last 3 years, MBA has received honoraria for speaking at sponsored meetings from AstraZeneca, Chiesi, GSK, and Sanofi and assistance for travel to meetings from AstraZeneca, Faes, and Teva. MBA has also acted as a consultant for AstraZeneca, GSK, Sanofi, and Teva.

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In the last 3 years, JR has received honoraria for speaking at sponsored meetings from AstraZeneca, Chiesi, Gebro, GSK, Menarini, Novartis, Sanofi, and Teva and has acted as a consultant for Sanofi.

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