Validation of the Asthma Impairment and Risk Questionnaire (AIRQ) in Spain: a useful tool to assess asthma control in adolescent and adult patients

Pérez de Llano L1, Martínez Moragón E2, Entrenas LM3, Martínez Rivera C4, Cisneros C5, Blanco-Aparicio M6, Trisán A7, Plaza V8, Ramos J9, Funenga Fitas E10, Sanchez-Covisa J10, Dominguez-Ortega J11

1Hospital Universitario Lucus Augusti (HULA EOXI), Lugo, Monforte, Cervo
2Hospital Universitario Doctor Peset, Valencia
3Hospital Quirónsalud Córdoba, Córdoba
4Hospital Universitari Germans Trias i Pujol, IGTP, UAB, Badalona, Barcelona
5Hospital Universitari de La Princesa, Madrid
6Hospital Universitario de A Coruña (CHUAC), A Coruña
7Hospital Universitario Puerta de Hierro Majadahonda, Madrid
8Hospital de la Santa Creu i Sant Pau, Barcelona
9Hospital Universitario de Salamanca, Salamanca
10Departamento Médico AstraZeneca, Madrid
11Department of Allergy. Hospital Universitario La Paz, Institute for Health Research (IdiPAZ), Madrid

Corresponding author:
Joaquín Sanchez-Covisa
Departamento Médico AstraZeneca, Madrid
Email: joaquin.sanchez-covisa@astrazeneca.com

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.18176/jiaci.0881
Asthma is a heterogeneous condition, and clinical manifestations range from mild symptoms to life-threatening attacks [1,2]. Asthma guidelines have underlined 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 they do not take into account the 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 patients’ clinical condition. In this context, the Asthma Impairment and Risk Questionnaire (AIRQ) [6] is a 10-item, yes/no, composite asthma control tool that has been developed in order to assess symptoms over the prior 2 weeks and exacerbations over the prior 12 months, being predictive of future 12-month exacerbations [7] and probably of time to first exacerbation. It has been evaluated in a US population of adult and adolescent patients with asthma across all levels of severity, yielding receiver operating characteristic area under the curve (ROC AUC) values of 0.94 to identify well-controlled vs not well-/very poorly controlled asthma and 0.93 to identify well-/not well-controlled vs very poorly controlled asthma. All the above justifies the translation to other languages and validation in additional populations. To address this need, this study aims to validate the locally adapted version of the AIRQ in Spain (Figure 1S). Prior to this validation, a rigorous translation-retro-translation and cultural adaptation of the questionnaire into Spanish were carried out.

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

Patient’s sociodemographic and clinical characteristics are presented in Table 1S; whereas the asthma control levels according to questionnaires’ results and the number of prior exacerbations are summarized in Table 2S and Table 3S.
All analyses were conducted using SAS version 9.4. Frequencies and percentages were used to describe categorical variables. 95% confidence intervals (CIs) were presented where appropriate. Continuous variables were described by means and standard deviations and medians and interquartile ranges, minimum and maximum. Two logistic models were conducted 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. The following statistics were also calculated: likelihood ratio for a positive test (LR+), likelihood ratio for a negative test (LR-), sensitivity, specificity, positive predictive value, negative predictive values, Akaike information criterion (AIC), and ROC curve. The same analysis was done to generate ROC curves, considering in this case ACQ-6 as the gold standard method (table 4S). In order to assess the pairwise degree of agreement between the AIRQ score, the ACT score, the ACQ-6 score, and the physician’s perception of asthma control, a descriptively analyzed weighted kappa was used.

As for the performance of the Spanish AIRQ, both models performed well (Figure 1), exceeding model-fit criteria with ROC curves of 0.94 for model 1 and 0.92 for model 2. An AIRQ score cut point of ≥2 for separating well-controlled vs all others yielded a sensitivity of 89.3%, a specificity of 85.9%, and positive and negative predictive values of 94.1% and 76.0%, respectively (model 1). A cut point of ≥5 showed a sensitivity of 74.8%, a specificity of 91.2%, and positive and negative predictive values of 84.8% and 84.6%, respectively, for separating very poorly controlled from all others (model 2). Table 3S shows the performance characteristics of AIRQ in relation to the sum of ACT and exacerbation history.

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

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

The locally adapted Spanish version of the AIRQ has demonstrated that it is a valid tool with similar measurement properties as the original instrument, which was developed in a US population. This tool 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 the disease severity. In consequence, the resulting therapeutic intervention will not only focus on current symptoms, but also on preventing future exacerbations, which are the main goals of asthma treatment. Although this questionnaire was validated using exacerbation risk items with a 12-month recall period, it has been recently shown that a 3-month recall period is valid for classifying current asthma control and 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 AIRQ on assessment of asthma control and changes to treatment management.
Funding sources
Astrazeneca

Conflict of Interest
LPL reports grants, personal fees and non-financial support from AstraZeneca, personal fees and non-financial support from GSK, grants and personal fees from TEVA, personal fees and non-financial support from Novartis, personal fees and non-financial 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 non-financial support from FAES, personal fees from Leo-Pharma, personal fees from GEBRO, personal fees from GILEAD, outside the submitted work.

EMM in the last three years received honoraria for speaking at sponsored meetings from Astrazeneca, Chiesi, Gebro, GSK, ALK, Novartis, Sanofi and Teva. Act as a consultant for AstraZeneca and GSK
LM Entrenas in the last three years received honoraria for speaking at sponsored meetings from Amgen, AstraZeneca, Boehringer-Ingelheim, Chiesi, Gebro, GSK, Menarini, Novartis, Pfizer, Rovi, Sanofi and Teva. Act as a consultant for AstraZeneca, GSK, and Sanofi.
CMR report payment or honoraria from Astra Zeneca, Chiesi, GSK, Gebro, Mundipharma, Novartis, TEVA, and Sanofi for lectures, presentations, speakers bureaus, manuscript writing or educational events, payment for participation on a Data Safety Monitoring Board or Advisory Board from Astra Zeneca, GSK, and grants from AstraZeneca, GSK and TEVA.
CCS states that she has received financial aid in the last 3 years from: Astra Zeneca, Chiesi, Novartis, Sanofi, GSK, Pfizer, Gebro Pharma for: advisory services, papers, research studies, attendance at congresses or training courses.
MBA in the last three years received honoraria for speaking at sponsored meetings from Astrazeneca, Chiesi, GSK and Sanofi. Received help assistance to meeting travel from Astrazeneca, Faes, Teva. Act as a consultant for AstraZeneca, GSK, Sanofi and Teva.
ATA in the last three years received honoraria for speaking at sponsored meetings from Astrazeneca, Chiesi, GSK, Mundipharma, Novartis and Sanofi. Received help assistance to meeting travel from AstraZeneca and Sanofi. Payment for participation on a Data Safety Monitoring Board or Advisory Board from Astra Zeneca, GSK and Novartis. And received grants from AstraZeneca, GSK, Novartis and Sanofi.
VP in the last three years received honoraria for speaking at sponsored meetings from Astrazeneca, Boehringer-Ingelheim, Chiesi, Gebro, GSK and Sanofi. Received help assistance to meeting travel from AstraZeneca and Chiesi. Act as a consultant for AstraZeneca, GSK, and Sanofi. And received funding/grant support for research projects from a variety of Government agencies and not-for-profit foundations, as well as AstraZeneca, Chiesi and Menarini.
JR in the last three years received honoraria for speaking at sponsored meetings from Astrazeneca, Chiesi, Gebro, GSK, Menarini, Novartis, Sanofi and Teva. Act as a consultant for Sanofi.
JDO has received funding for research, honoraria for consultancy and conferences from AstraZeneca, Chiesi y GSK; honoraria for consultancy and conferences from Bial, Novartis, Sanofi and Teva; and speaker fees from ALK, LETI Pharma and Mundipharma.
References

Figure 1. Receiver operating characteristic (ROC) curves for models 1 and 2. 1a) ROC curve and performance characteristics of the AIRQ for the Spanish cohort based on the participant’s ACT score plus exacerbation history to distinguish 1a) well-controlled vs not well-controlled/very poorly controlled asthma (model 1). 1b) ROC curves and performance characteristics of the AIRQ for the Spanish cohort based on the participant’s ACT score plus exacerbation history to distinguish well-controlled/not well-controlled vs very poorly controlled asthma (model 2).

Abbreviations: AIRQ, Asthma Impairment and Risk Questionnaire; AUC, area under the curve; ROC, receiver operating characteristic