ORIGINAL ARTICLE

Allergic Rhinitis and its Impact on Asthma (ARIA) Classes in MASK-air Users

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Abstract

Background: The Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines classify rhinitis as "intermittent" or "persistent" and "mild" or "moderate-severe".
Objectives: To assess ARIA classes in a real-world study in terms of phenotypic differences and their association with asthma.
Methods: We performed a cross-sectional real-world study based on users of the MASK-air® app who reported data for at least 3 different months. We assessed the frequency of users according to the ARIA classes and compared these classes in terms of rhinitis symptoms, use of comedication, frequency of comorbid asthma, and the association between comorbid asthma and rhinitis control.
Results: A total of 2273 users (180 796 days) were assessed. Most users had moderate-severe rhinitis (n=2003; 88.1%) and persistent rhinitis (n=1144; 50.3%). The frequency of patients with probable asthma was 35.7% (95%CI, 34.5%-37.0%) for intermittent rhinitis and 48.5% (95%CI, 47.1%-49.9%) for persistent rhinitis. The maximum values on the visual analog scale (VAS) for rhinitis symptoms and the combined symptom-medication score were lower in patients with mild rhinitis than in those with moderate-severe rhinitis (irrespective of whether they had persistent or intermittent rhinitis). In most ARIA classes, VAS nose and VAS eye and rhinitis comedication were more frequent in patients with rhinitis+asthma than in those with rhinitis alone.
Conclusion: This study suggests that the presence of asthma is more closely related to persistence of rhinitis than to severity and that the presence of comorbid asthma may be associated with poorer control of rhinitis across the different ARIA classes.

Key words: Allergic rhinitis. Asthma. mHealth.

Resumen

Antecedentes: Las guías de Rinitis Alérgica y su Impacto en el Asma (ARIA) clasifican la rinitis como "intermitente" o "persistente" y como "leve" o "moderadamente severa".
Objetivos: Evaluar las clases de ARIA en un estudio en vida real, considerando las diferencias fenotípicas y su asociación con el asma.
Métodos: Realizamos un estudio transversal en vida real basado en usuarios de la aplicación MASK-air® que reportaron datos en al menos tres meses diferentes. Evaluamos la frecuencia de usuarios según las clases ARIA y comparamos estas clases en cuanto a los niveles de síntomas de rinitis, uso de co-medicación, frecuencia de asma como comorbilidad y su asociación con el control de la rinitis.
Resultados: Se evaluaron un total de 2273 usuarios (180.796 días). La mayoría de los usuarios (N=2003; 88,1%) tenían rinitis moderadamente severa y rinitis persistente (N=1144; 50,3%). La frecuencia de pacientes con probable asma fue del 35,7% (IC95%=34,5-37,0%) para rinitis intermitente y del 48,5% (IC95%=47,1-49,9%) para rinitis persistente. Los valores máximos en la escala visual analógica (EVA) para los síntomas de rinitis y del puntaje combinado máximo de síntomas y medicación (CSMS) fueron más bajos en pacientes con rinitis leve en comparación con aquellos con rinitis moderadamente severa (independientemente de si tenían rinitis persistente o intermitente). En la mayoría de las clases de ARIA, la EVA para nariz y ojos y la co-medicación para rinitis aumentaron en pacientes con rinitis+asma en comparación con aquellos con solo rinitis.
Conclusión: Este estudio sugiere que la presencia de asma está más relacionada con la persistencia de la rinitis que con la severidad de la rinitis, y que la presencia de asma como comorbilidad puede estar asociada con un peor control de la rinitis en las diferentes clases de ARIA.

Palabras clave: Rinitis alérgica. Asma. eSalud.

Summary box

- **What do we know about this topic?**
  The Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines classify allergic rhinitis as "intermittent" or "persistent" and as "mild" or "moderate-severe".
- **How does this study impact our current understanding and/or clinical management of this topic?**
  This mHealth study suggests that comorbid asthma may be associated with poorer control of rhinitis in all ARIA classes. However, the presence of asthma is more closely related to whether rhinitis is persistent or intermittent than to rhinitis severity.

Introduction

The Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines have classified "intermittent" allergic rhinitis as a condition involving the presence of symptoms for fewer than 4 days per week or for fewer than 4 consecutive weeks. By contrast, "persistent" allergic rhinitis involves the presence of symptoms on at least 4 days per week and for at least 4 consecutive weeks. Disease severity is classified as mild when patients' sleep is unimpaired and they can perform normal activities (including work and school) and as moderate-severe if symptoms substantially affect sleep or activities of daily living and/or if they are considered bothersome [1].

ARIA was initiated to assess the links between rhinitis and asthma. It was hypothesized that asthma was more often associated with persistent than with intermittent rhinitis [1]. Although several studies displayed results in line with this hypothesis (indicating the persistence of symptoms to be more frequently associated with asthma) [2-7], this was not observed in all studies [8]. The association between the multimorbidity of rhinitis and asthma and severity of rhinitis is largely unclear. However, direct patient data can help address the links between asthma and the different ARIA rhinitis classes in the real world. Mobile health apps comprise a key source of direct patient data. MASK-air® is one such app. MASK-air assesses the daily control of allergic rhinitis and asthma, is freely available, and has been launched in 29 countries [9]. It has been classified as a Good Practice of the Directorate General for Health and Food Safety (European Commission) for digitally enabled, patient-centered care in multimorbid rhinitis and asthma [10]. Furthermore, it is one of the 13 Organisation of Economic Cooperation and Development (OECD) Best Practices in integrated care for chronic diseases [11].

The aim of this study was to analyze the phenotypic characteristics of MASK-air users according to the ARIA classes. In particular, we aimed to compare patients in the different ARIA classes based on their rhinitis symptoms, patterns of rhinitis medication use, and frequency of comorbid asthma. In addition, we aimed to assess, across the different ARIA classes, how the presence of comorbid asthma was associated with control of rhinitis and medication patterns.

Methods

Study design

We performed a cross-sectional study based on direct patient data from MASK-air users who reported data for at least 3 different months [12]. We assessed the frequency of MASK-air users according to the ARIA classification and compared the frequency of asthma, rhinitis symptoms, and rhinitis comedication (use of more than 1 rhinitis medication formulation on the same day) across the 4 ARIA classes. In addition, for the different ARIA classes, we compared users with "no evidence of asthma", "possible asthma", and "probable asthma" [12], assessing whether the presence of comorbid asthma was associated with more severe rhinitis symptoms.

Settings and Participants

We assessed MASK-air data provided between June 2015 and December 2022 by users aged between 13-16 years (age of digital consent depending on the country [13]) and 90 years. We assessed all users with self-reported rhinitis, whose data enabled them to be classified into 1 of the 4 ARIA classes and who reported data for at least 3 different months. This last criterion enabled the classification of patients into those having "no evidence of asthma" (rhinitis alone), "possible asthma", or "probable asthma". The classification is based on self-reported asthma, reported asthma symptoms, and asthma medication use patterns and has been applied elsewhere [14].

Ethics

MASK-air complies with the General Data Protection Regulation [15]. All data are anonymously entered by users. Geolocation-related data are subsequently "blurred" using k-anonymity [16]. Users consented to having their data analyzed in the terms of use of the app. The use of MASK-air data has been approved by an independent review board (Köln-Bonn, Germany) [17]. Consequently, and given that this is an observational noninterventional study, specific ethics committee approval was not necessary.

Data Sources and Variables

MASK-air currently includes a daily monitoring questionnaire to assess the control and impact of allergy

symptoms through 4 mandatory visual analog scales (VAS) scored 0 to 100 (eTable 1). In the daily monitoring questionnaire, MASK-air users also provide their daily medication use via a scroll list customized for each country and regularly updated.

Symptom and medication data provided daily by patients enable the calculation of the daily combined symptom-medication score (CSMS), which assesses daily control of rhinitis [18], as follows:

[(0.037 × VAS global symptoms) + (0.033 × VAS eyes) + (0.020 × VAS nose) + (0.027 × VAS asthma) + (0.450 if azelastine-fluticasone is used) + (0.424 if nasal corticosteroids are used) + (0.243 if asthma medication is used) + (0.380 if other rhinitis relief medication is used)] × 7.577

In addition to the daily monitoring of symptoms and medication, MASK-air users provide clinical and demographic information when setting up their profile [19-22]. This information enables the classification of patients according to that of ARIA [19].

Sample Size

We analyzed all valid data from users meeting the eligibility criteria. No sample size calculation was performed.

Statistical Analysis

When responding to the MASK-air daily monitoring questionnaire, it is not possible to skip any of the questions, and data are saved to the dataset only after the final answer. This precludes missing data for each questionnaire.

We compared the frequency of self-reported asthma across the 4 ARIA classes. In addition, we compared median values of the symptoms VAS and of the CSMS. These values were compared both across the aforementioned groups and in patients classified as having "no evidence of asthma" (rhinitis alone), "possible asthma", or "probable asthma". This classification was developed according to a previously reported clustering methodology (based on self-reported asthma, reported asthma symptoms, and asthma medication use patterns). It aims to overcome the limitations associated with classifying patients based solely on the presence of self-reported asthma [12,14].

Categorical variables were described using absolute and relative frequencies, while continuous variables were described using median (IQR) or mean (SD). With a large sample such as that of MASK-air, statistical tests of hypotheses will almost always result in *P* values indicating significance, even in the case of small differences. We therefore used Cohen effect sizes to quantify the differences [23]. Values >0.2 were considered to represent clinically meaningful differences (ie, large enough to be potentially relevant from a clinical standpoint). Values of 0.2-0.5 were considered to represent small clinically relevant effect sizes, 0.5-0.8 medium effect sizes, and >0.8 large effect sizes [23].

Results

Demographic Characteristics of the Users

We classified 2273 users (28.0% of all MASK-air users) who provided data over at least 3 different months, reporting a total of 180 796 days (Table 1; eFigure 1). Most participants (n=1302; 57.3%) were female, and the mean age was 39.8 (14.4) years. Table 1 shows the demographic and clinical characteristics of the participants by ARIA class; eTable 2 shows the participants' distribution by country.

Distribution of ARIA Classes

Most users (n=2003; 88.1%) had moderate-severe rhinitis. The remainder (n=270; 11.9%) had mild rhinitis. A similar percentage of patients had persistent rhinitis (50.3%) and intermittent rhinitis (49.7%). The average number of days

Table 1. Demographic and Clinical Characteristics of Assessed Participants According to ARIA Class.

	Moderate-severe persistent rhinitis	Moderate-severe intermittent rhinitis	Mild persistent rhinitis	Mild intermittent rhinitis	Maximal effect size
Patients, No. (%)	1013 (44.6)	990 (43.6)	131 (5.8)	139 (6.1)	-
No. of days (mean no. of days per user)	88 934 (87.8)	71 955 (72.7)	10 865 (82.9)	9042 (65.1)	-
Females, No. (%)	601 (59.3)	555 (56.1)	75 (57.3)	71 (51.1)	0.17
Mean (SD) age, y	40.1 (14.3)	38.5 (14.4)	43.3 (14.6)	42.4 (14.8)	0.33[a]
Self-reported conjunctivitis, No. (%) [95%CI]	859 (84.8) [84.0-85.6]	791 (79.9) [78.9-80.9]	83 (63.3) [59.3-67.3]	79 (56.8) [52.7-60.9]	0.63[b]
No evidence of asthma, No. (%) [95%CI]	284 (28.0) [26.8-29.2]	356 (36.0) [34.6-37.4]	50 (38.2) [34.2-42.2]	47 (33.8) [30.1-37.5]	0.22[a]
Possible asthma, No. (%) [95%CI]	234 (23.1) [22.0-24.2]	274 (27.7) [26.4-28.9]	21 (16.0) [13.7-18.3]	49 (35.3) [31.5-39.1]	0.45[a]
Probable asthma, No. (%) [95%CI]	495 (48.9) [47.4-50.4]	360 (36.4) [35.0-37.8]	60 (45.8) [41.5-50.1]	43 (30.9) [27.4-34.4]	0.37[a]

Abbreviation: ARIA, Allergic Rhinitis and its Impact on Asthma.
[a]Small effect size.
[b]Medium meaningful effect.

reported per user was higher among those with persistent rhinitis than among those with intermittent rhinitis, based on both moderate-severe rhinitis (87.8 vs 72.7 days per user) and mild rhinitis (82.9 vs 65.1 days per user).

ARIA Classes and Comorbidities

No evidence of asthma ("rhinitis alone") was detected in 737 users (32.4%), possible asthma was recorded in 578 (25.4%), and probable asthma in 958 (42.1%) (Table 1). Probable asthma was more common in persistent rhinitis (moderate-severe, 48.9% [95%CI, 47.4%-50.4%]; and mild, 45.8% [95%CI, 41.5%-50.1%]) than in intermittent rhinitis (moderate-severe, 36.4% [95%CI, 35.0-37.8%]; mild, 30.9% [95%CI, 27.4%-34.4%]) (Table 1). This ranking order was not found for possible asthma. On the other hand, an increased prevalence of conjunctivitis was observed from mild intermittent rhinitis to mild persistent rhinitis, moderate-severe intermittent rhinitis, and moderate-severe persistent rhinitis (mild intermittent rhinitis, 56.8% [95%CI, 52.7%-60.9%]; moderate-severe persistent rhinitis, 84.8% [95%CI, 84.0%-85.6%]).

Rhinitis Symptoms and Medication Use Patterns

Patients with moderate-severe rhinitis tended to have higher maximal nose and eye VAS and CSMS values than those with mild rhinitis (effect sizes, 0.24-0.36). For median values, patients with persistent rhinitis tended to have higher nose/eye VAS and CSMS values than those with intermittent rhinitis (effect sizes, 0.61-0.76). Comedication was more common in patients with persistent rhinitis than in those with intermittent rhinitis (maximal effect size, 0.45) (Table 2).

Differences in VAS and in Allergens Depending on Asthma in the Different ARIA Classes

In most ARIA classes, VAS global, VAS nose, and VAS eye values were higher in patients with probable asthma than in those with no evidence of asthma (Table 3; Figure). Probable or possible asthma (vs no evidence of asthma) was associated with a larger difference in maximal VAS values for mild than for moderate-severe rhinitis (Figure). For median VAS nose values, the smallest difference was for mild intermittent rhinitis. The presence of "possible asthma" or "probable asthma" was also associated with a higher percentage of days using comedication (eFigure 2).

Overall, across the different ARIA classes, patients with probable asthma tended to have a higher frequency of allergy to indoor allergens than patients with no evidence of asthma (eTable 3). No such differences were observed for pollen allergy. In addition, patients with probable asthma displayed higher across–ARIA class differences in the frequency of pollen and house dust mite allergy.

Discussion

The present study is the first to assess ARIA classes in the MASK-air database and provides important, novel information.

Table 2. Demographic and Clinical Characteristics of Assessed Participants According to ARIA Class.

	Moderate-severe persistent rhinitis	Moderate-severe intermittent rhinitis	Mild persistent rhinitis	Mild intermittent rhinitis	Maximal effect size
Maximum values					
VAS global	72 (38)	71 (36)	63 (38)	63 (47)	0.30[a]
VAS nose	74 (41)	75 (40)	68 (37)	68 (53)	0.24[a]
VAS eye	59 (41)	58 (40)	52 (37)	49 (53)	0.32[a]
CSMS	49.2 (28.8)	48.2 (28.8)	41.7 (27.2)	42.6 (29.9)	0.36[a]
Median values					
VAS global	13 (24)	9 (22)	15 (25)	6 (16)	0.64[b]
VAS nose	13 (26)	9 (23)	16 (24)	6 (18)	0.76[b]
VAS eye	5 (26)	2 (23)	11 (24)	3 (18)	0.61[b]
CSMS	11.4 (16.7)	7.5 (14.8)	13.9 (21.0)	5.5 (11.8)	0.76[b]
Medication – No. of days (%) [95%CI]					
No medication	29 459 (33.1) [33.0-33.2]	42 535 (59.1) [58.9-59.3]	2969 (27.3) [26.9-27.7]	5469 (60.5) [60.0-61.0]	0.68[b]
Single medication	32 550 (36.6) [36.4-36.8]	18 693 (26.0) [25.9-26.1]	4754 (43.8) [43.3-44.3]	2465 (27.3) [26.9-27.7]	0.38[a]
Comedication	26 925 (30.3) [30.2-30.4]	10 727 (14.9) [14.8-15.0]	3142 (28.9) [28.5-29.3]	1108 (12.3) [12.1-12.5]	0.45[a]

Abbreviations: ARIA, Allergic Rhinitis and its Impact on Asthma; CSMS, combined symptom-medication score; VAS, visual analog scale.
[a]Small meaningful effect.
[b]Medium meaningful effect.

Table 3. VAS Values and Comedication Frequency per ARIA Class and According to the Presence of Asthma.

	Moderate-severe persistent	Moderate-severe intermittent	Mild persistent	Mild intermittent	Maximal effect size
A. No evidence of asthma					
Maximum values					
Median (IQR) VAS global –	66 (38)	64 (39)	56 (36)	61 (46)	0.36″
Median (IQR) VAS nose	67 (47)	69 (43)	56 (34)	60 (49)	0.42[a]
Median (IQR) VAS eye	47 (47)	48 (43)	49 (34)	45 (49)	0.12
Median (IQR) CSMS	38.4 (26.4)	38.6 (27.1)	35.1 (22.8)	37.0 (27.3)	0.18
Median values					
Median (IQR) VAS global	8 (23)	6 (16)	11 (20)	6 (15)	0.44[a]
Median (IQR) VAS nose	8 (24)	6 (17)	11 (21)	6 (16)	0.41[a]
Median (IQR) VAS eye	0 (24)	0 (17)	4 (21)	0 (16)	0.33[a]
Median (IQR) CSMS	5.9 (14.2)	4.2 (9.9)	8.2 (12.7)	3.4 (10.0)	0.70[b]
Medication – No. of days (%) [95%CI]					
No medication	8755 (43.0) [42.7-43.3]	14 640 (64.3) [64.0-64.6]	726 (27.1) [26.4-27.8]	2270 (67.6) [66.9-68.3]	0.84[c]
Single medication	6510 (31.9) [31.6-32.2]	5350 (23.5) [23.3-23.7]	1163 (43.4) [42.5-44.3]	833 (24.8) [24.2-25.4]	0.43[a]
Comedication	5116 (25.1) [24.8-25.4]	2784 (12.2) [12.1-12.3]	792 (29.5) [28.7-30.3]	253 (7.5) [7.3-7.7]	0.59[b]
B. Possible asthma					
Maximum values					
Median (IQR) VAS global	76 (39)	78 (34)	68 (44)	62 (46)	0.52[b]
Median (IQR) VAS nose	81 (41)	80 (36)	69 (50)	68 (58)	0.35[a]
Median (IQR) VAS eye	67 (41)	70 (36)	64 (50)	43 (58)	0.96[c]
Median (IQR) CSMS	52.3 (28.2)	55.1 (27.3)	47.6 (34.9)	42.2 (30.2)	0.58[b]
Median values					
Median (IQR) VAS global	13 (24)	11 (22)	26 (39)	5 (14)	1.02[c]
Median (IQR) VAS nose	12 (24)	12 (23)	19 (28)	6 (15)	0.87[c]
Median (IQR) VAS eye	5 (24)	6 (23)	17 (28)	4 (15)	0.87[c]
Median (IQR) CSMS	9.7 (15.0)	8.8 (14.7)	18.4 (25.2)	5.0 (9.8)	0.98[c]
Medication – No. of days (%) [95%CI]					
No medication	6069 (33.8) [33.4-34.1]	10,660 (57.1) [56.7-57.5]	599 (38.4) [37.2-39.6]	1714 (60.1) [59.2-61.0]	0.53[b]
Single medication	6895 (38.4) [38.1-38.7]	4866 (26.1) [25.8-26.4]	403 (25.8) [24.9-26.8]	834 (29.2) [59.2-61.0]	0.27[a]
Comedication	4970 (27.7) [27.4-28.0]	3151 (16.9) [16.7-17.1]	557 (35.7) [34.6-36.8]	304 (10.7) [10.3-11.1]	0.61[b]
C. Probable asthma					
Maximum values					
Median (IQR) VAS global	72 (35)	73 (33)	69 (35)	72 (37)	0.15
Median (IQR) VAS nose	75 (36)	73 (41)	77 (37)	80 (43)	0.25[a]
Median (IQR) VAS eye	62 (36)	63 (37)	51 (41)	66 (43)	0.50[a]
Median (IQR) CSMS	55.0 (27.5)	53.3 (26.2)	45.4 (29.0)	51.6 (30.8)	0.45[a]

(continued)

Table 3. VAS Values and Comedication Frequency per ARIA Class and According to the Presence of Asthma (*continuation*).

	Moderate-severe persistent	Moderate-severe intermittent	Mild persistent	Mild intermittent	Maximal effect size
Median values					
Median (IQR) VAS global	15 (25)	10 (23)	16 (22)	6 (17)	0.76[b]
Median (IQR) VAS nose	16 (26)	11 (26)	17 (25)	8 (20)	0.62[b]
Median (IQR) VAS eye	6 (26)	4 (26)	14 (25)	4 (20)	0.69[b]
Median (IQR) CSMS	14.2 (17.5)	10.1 (17.0)	16.6 (22.0)	8.8 (17.9)	0.60[b]
Medication – No. of days (%) [95%CI]					
No medication	14 635 (28.9) [28.7-29.1]	17 235 (56.5) [56.2-56.8]	1644 (24.8) [24.4-25.2]	1485 (52.4) [51.5-53.3]	0.66[b]
Single medication	19 145 (37.8) [37.6-38.0]	8477 (27.8) [27.6-28.0]	3188 (48.1) [47.5-48.7]	798 (28.2) [27.5-28.9]	0.42[a]
Comedication	16 839 (33.3) [33.1-33.5]	4792 (15.7) [15.6-15.8]	1793 (27.1) [26.6-27.6]	551 (19.4) [18.8-20.0]	0.42[a]

Abbreviations: CSMS, combined symptom-medication score; VAS, visual analog scale.
[a]Small meaningful effect.
[b]Medium meaningful effect.
[c]Large meaningful effect.

Our findings indicate the following: (*i*) persistence of rhinitis is more strongly associated with asthma than severity of rhinitis, as users with persistent rhinitis more often have asthma than those with intermittent disease; and (*ii*) the presence of asthma is associated with more severe nasal and ocular symptoms.

Strengths and Weaknesses

Selection bias is inherent to any study reporting app-generated data, and the participants assessed are not representative of the general population. This is demonstrated by the fact that, in a general population study in France (Constances cohort), 60% of patients were classified as having mild rhinitis [24], compared with 11% in our study. There may also be a selection bias within the MASK-air sample, as we only assessed participants who could be placed in an ARIA class and who reported data in at least 3 different months. These selection biases may result in an overrepresentation of patients with severe rhinitis or patients who are more concerned or aware of their disease and of days where control of rhinitis was poorer. While these selection biases warrant caution in terms of generalizability, they are unlikely to substantially alter the results of the study for the association between ARIA class and asthma. Importantly, we are not able to generalize our results on the frequency of participants in the different ARIA classes to the general population. However, such was not the aim of this study. In addition, patients were enrolled using different methods, ie, by physicians or by downloading the app spontaneously.

Given the smaller number of patients and their more restricted geographical distribution, we did not solely assess patients with asthma recruited by physicians. That is, patients were classified as having asthma based on self-reported information, thus leading to information biases, which could potentially affect our conclusions. To decrease the risk of misclassification, we did not rely solely on self-reported asthma either, but rather on an asthma-related classification, which was found to overcome some of the limitations of self-reporting [12]. This classification was tested in a small sample of patients diagnosed by physicians, with 92% of the "probable asthma" patients diagnosed by a physician as having current or past asthma and 90% of the "no evidence of asthma" patients diagnosed by a physician as having no current asthma [12]. Nevertheless, future studies should include patients enrolled in a clinical setting and assessed by a physician with respect to the severity of their rhinitis and presence of asthma.

Finally, as ours is a cross-sectional observational study, we were unable to establish a causal relationship between asthma and rhinitis symptoms.

A major strength of this study is that we used the exact wording of ARIA, as proposed in 1999. Moreover, the patients were selected in different countries. Finally, we included patients reporting data for at least 3 different months, with an average app adherence higher than other users (79.5 vs 4.4 days).

Interpretation of Results

This study should be compared with a recent study of ARIA classes in Constances, a French general population cohort [24], where the percentage of participants with mild rhinitis was far higher than that of the present study. However, the same phenotypic trends were found (*i*) for participants with comorbid rhinitis and asthma and in those with rhinitis alone and (*ii*) when the 4 ARIA classes were compared. For all 4 ARIA classes, the VAS nose values were higher in patients with rhinitis+asthma than in those with rhinitis alone. The results of these 2 studies are in line with the ARIA-MeDALL hypothesis, which proposes that rhinitis+asthma and rhinitis alone are 2 distinct diseases [25]. Interestingly, in the present study, for mild rhinitis, there is a clear difference between the 2 diseases for maximal nose VAS values only. For

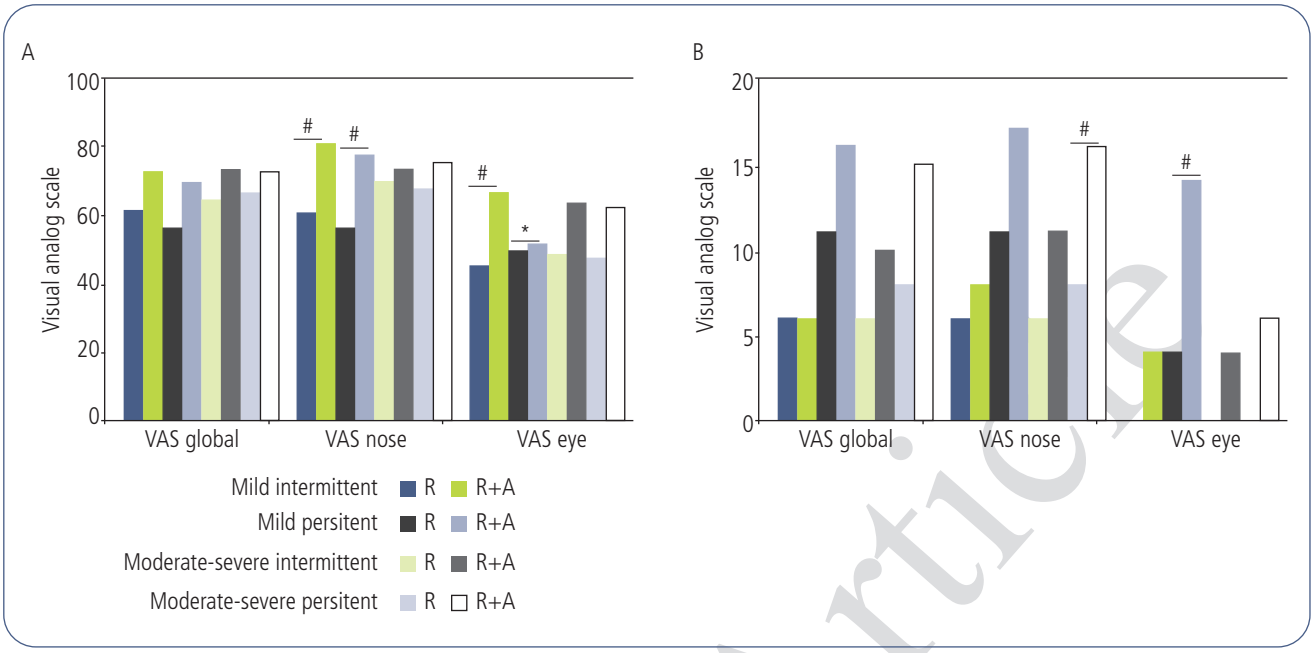

Figure. Maximum (A) and median (B) values of rhinitis visual analog scales (VAS) in patients with no evidence of asthma (R) and in patients with probable asthma (R+A) across the different Allergic Rhinitis and its Impact on Asthma (ARIA) classes. Unless otherwise specified, there are small clinically relevant differences in VAS values for each ARIA class. #Clinically relevant moderate difference in VAS values (Cohen d between 0.5 and 0.8); *Difference not clinically relevant in VAS values (Cohen d <0.2)

conjunctivitis, on the other hand, the presence of asthma was, in most cases, associated with increased maximal and median VAS values. Most of our results are in line with those of the Constances study (except for asthma, since the definitions differed between the studies [24]) and with a recent study on MASK-air using the CSMS [14].

In addition, both studies suggest that the ARIA-MeDALL hypothesis might be extended to conjunctivitis. In Constances, the frequency of conjunctivitis ranged from 47% (mild intermittent) to 57% (moderate/severe persistent) in patients with rhinitis alone and from 65% (mild intermittent) to 75% (moderate/severe persistent) in patients with asthma+rhinitis. In the present study, VAS eye values were higher in patients with rhinitis+asthma than in those with rhinitis alone. The involvement of conjunctivitis in allergic multimorbidity patterns had also been proposed elsewhere [26,27]. However, further studies are needed to understand the role of conjunctivitis in the complex multimorbid patterns of allergic diseases.

For most outcomes, there is a trend in the results obtained when no asthma is compared with possible and probable asthma. For example, in most classes of rhinitis, the frequency of comedication increases when patients with no evidence of asthma are compared with those with possible asthma and probable asthma (eFigure 1). The only class for which this was not observed was that of mild persistent rhinitis, although the finding may reflect variability in sampling.

The MASK-air population is similar to patients seen in primary care [28] and specialist care [3] and differs from patients in general population cohorts [24]. This study is therefore important, given that it improves identification of the population of MASK-air users reporting data for at least 3 months. We previously found that, in patients with asthma, there are differences between this selected population and the general population [12].

Conclusions

Our person-centered study assessed the ARIA classification in the real world. Moreover, it explored the association between asthma and the severity and persistence of rhinitis, suggesting that persistence of rhinitis is more strongly associated with the presence of asthma than its severity and that the presence of asthma is associated with increased severity of nasal and ocular symptoms. In addition, our study provides information on the co-occurrence of conjunctivitis, indicating that ocular comorbidity should be considered more carefully in future randomized controlled trials and observational studies. The results of this study will impact the revision of the ARIA 2024 guidelines.

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Conflicts of Interest

Dr J. Bousquet reports personal fees from Cipla, Menarini, Mylan, Novartis, Purina, Sanofi-Aventis, Teva, Noucor, KYomed-Innov, and Mask-air-SAS, outside the submitted work.

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