

CLINICAL IMPORTANCE OF EOSINOPHIL COUNT IN NASAL FLUID IN PATIENTS WITH ALLERGIC AND NON-ALLERGIC RHINITIS

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Eosinophil count in nasal fluid (ECNF) was used to differentiate nasal pathologies. Receiver Operating Characteristic (ROC) curve analysis and the area under the curve (AUC) were performed to evaluate the ECNF's accuracy in distinguishing allergic rhinitis (AR) from non-allergic rhinitis (NAR). We also evaluated the accuracy of ECNF in recognizing patients with mild and severe symptoms of rhinitis and patients with ineffective and effective clinical responses to antihistamines. 1,170 consecutive adult patients with a clinical history of rhinitis were studied. ECNF's median in AR was 6.0 and 2.0 in NAR and the best cut-off value was > 3.0 , $AUC = 0.75$. ECNF's median in AR with mild nasal symptoms was 3.0 and 7.0 with severe symptoms, and the best cut-off value was 4.0, $AUC = 0.90$. ECNF's median in NAR with mild nasal symptoms was 2.0 and 8.5 with severe symptoms, and the best cut-off value was > 4.0 , $AUC = 0.86$. ECNF's median in AR with effective clinical response to antihistamines was 4.0 and 8.0 with ineffective response, the best cut-off value was ≤ 5.0 , $AUC = 0.94$. ECNF's median in NAR with an effective clinical response to antihistamines was 1.0 and 2.0 with ineffective response, and the best cut-off value was ≤ 3.0 , $AUC = 0.64$. Our results suggest an interesting practical use of ECNF data as evaluator of the clinical severity both AR and NAR. As predictor of the clinical response to antihistamines, ECNF is accurate only in patients with AR. The ECNF's performance was moderately accurate in distinguish patients with AR and NAR.

The most common diagnostic tests for allergic rhinitis are the Skin Prick Test (SPT) and the determination of serum allergen-specific IgE. A less common diagnostic tool is nasal cytology. Nasal cytology is generally employed by subspecialists or in research, but does not play a role in the routine evaluation of rhinitis (1). The techniques

for obtaining cells for cytology in lavage, or brushings, have not been standardized as the criteria for evaluating cell counts (2). Nasal lavage is the reference method among adult patients (3). Brushing was compared to lavage among adults by Juliusson et al. They found a strong correlation between the two methods regarding the percentage of eosinophils

Key words: eosinophil count in nasal fluid, allergic rhinitis, non-allergic rhinitis, receiver operating characteristic curve

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(4). Therefore, the use of nasal cytology to evaluate mucosal cellular patterns has the potential to distinguish inflammatory from non-inflammatory nasal conditions, to follow the course of an allergic disease and to evaluate the response to the treatment (5-6). Previously, we evaluated the importance of eosinophil count in nasal fluid (ECNF) (7-11), hence, we use ECNF routinely, integrating it in diagnostic tests: i.e. SPT and total and allergen-specific IgE assays.

Other investigators have studied nasal cytology in relationship to various upper respiratory diseases (2, 12-13). However, few prospective studies evaluating the diagnostic utility of nasal cytology in allergic rhinitis have been performed (14-17).

The accuracy of a diagnostic test is characterized by its sensitivity and specificity. However, the sensitivity and specificity of a test depends on the level that has been chosen as the cut-off to distinguish two conditions, i.e. normal or abnormal. Therefore, if the results of a clinical test, i.e. ECNF, are quantitative and provided on a continuous scale, the Receiver Operating Characteristic (ROC) curve is widely accepted as a method for selecting an optimal cut-off point for the test (18-20). The ROC curve is also important because the area under the curve (AUC) is a reflection of how good the test is to distinguish between the presence or the absence of a clinical characteristic. The greater the AUC, the better the test (20-21).

The characteristics of the ROC curve was used to evaluate the discriminating value of ECNF between patients with AR and patients with NAR, between patients with mild and severe nasal symptoms, and between patients with effective and ineffective response to antihistamines.

MATERIALS AND METHODS

Patients

Between March 2001 and October 2005, 1,170 consecutive adult patients with a clinical history of rhinitis were tested at the Outpatient Allergy Unit of the Department of Clinical Medicine and Emerging Diseases, University of Palermo, Italy. At the time of the first visit all the included patients had been symptomatic for rhinitis symptoms for at least two years. Patients with nasal polyps, and/or symptoms of asthma, urticaria, or eczema were excluded from the study. All the study patients had taken

antihistamines in the past. However, no patient had taken any medication for at least 5 days before the first visit.

Diagnostic process

A detailed questionnaire, concerning the history of rhinitis and the severity of nasal symptoms, was filled out by the patients, under the supervision of the authors (GDL and PM). The questionnaire used in this study was the same used for the selection of the patients in a randomized control trial study that compared placebo, an intranasal H1-antihistamine and an intranasal steroid in patients with AR (8). Nasal symptoms were judged mild if they did not interfere with work and sleep, and severe if they did (1). Nasal appearance was examined by anterior rhinoscopy. Special attention was directed to the occurrence of nasal secretion and changes in the mucosa of the *conchae* (3). We performed the SPT and nasal cytology, using nasal lavage. All these tests were performed at the first visit. During the diagnostic process, patients were also asked to state if the rhinitis symptoms were controlled by antihistamines, indicating 'Yes' or 'No' (22).

The Institutional Review Board approved the study, which was conducted according to the Declaration of Helsinki. Authorization of the study was not required according to our institutional policy and the ethical committee of our institution because ECNF was used routinely among the diagnostic tests. However, written informed consent to the study was obtained from each patient in compliance with our institutional policy.

Skin Prick Test

Patients performed the SPT using standard aeroallergens panels (Alk Abellò, Milan, Italy) that are present in our geographical area. The SPT was performed and evaluated on the volar aspect of the forearm. The panel included the following extracts: grass (*Phleum pratense*, *Dactyla glomerata*, *Festuca elator*, *Lolium perenne*, *Poe pratensis*); weeds [mugwort (*Artemisia vulgaris*), pellitory-of-the-wall or sticky weed [(*Parietaria judaica*) and *Salsola kali*]; trees [birch (*Olea europea* and *Cupressus*)]; house dust mite (HDM, *Dermatophagoides pteronyssinus* and *farinae*); moulds (*Alternaria alternata*, *Cladosporium erbarium* and *Aspergillus fumigatus*); animal dander (cat and dog), plus a negative (glycerinated saline) and a positive control (histamine, 10 mg/mL). Positive responses were defined as any wheal with a diameter 3 mm greater than the negative control, 15 min after application. The wheal diameters were reported for each patient (23-24).

Eosinophil Count in Nasal Fluid

Nasal lavage was performed using a disposable metered-dose nasal inhaler (Markos, Monza, Italy) filled with sterile, room-temperature, normal saline solution. The

device consists of a plastic cup with two compartments. The central compartment was filled with sterile saline solution while the external compartment collected the liquid after washing. Total input of saline solution was approximately 8 mL (4 mL in each nostril for 5 min). To collect the nasal washings, the subjects were instructed to actively breathe during a Valsalva maneuver in order to harvest nasal fluid in the cup. The samples obtained were stored on ice and centrifuged at 400 g for 10 min at 4°C. The individual variation in the recovered vs. introduced volume was $86\% \pm 8\%$. Nasal eosinophil counts were performed on nasal lavage. One cytopspin slide for each sample (1×10^4 cells in 170 mL per slide) was centrifuged at 10 g for 10 min in a Shandon cytocentrifuge (Shandon Southern Ltd, Runcorn, Cheshire, UK). The slides were immediately fixed in 95% ethyl alcohol, dipped in Wright-Giemsa stain, and examined under oil immersion by light microscopy at a magnification of 400x. Eosinophils were expressed as a percentage of 300 cells counted (7, 10-11).

All specimens were examined by the same blinded microscopist (VD), without knowing the clinical histories, the results of the SPT, the severity of the rhinitis symptoms, or the subjects' clinical responses to antihistamines.

Statistical analysis

In order to distribute the data, the results are presented as an arithmetic mean (normally distributed) and a confidence interval of 95% (95%CI) and analyzed using Student's *t* test. If the normal distribution of data was rejected, the results are presented as median and 25th and 75th percentiles (P25th and P75th), and analyzed using the Mann-Whitney U-test. For statistical analyses a value of $P = 0.05$ was considered statistically significant. To define sensitivity, specificity, positive likelihood ratio (LR+), and negative likelihood ratio (LR-) of ECNF we analyzed the ROC curve analysis.

The ROC curve is a graphical technique for assessing the ability of the ECNF to discriminate between subjects with AR and subjects with NAR. ROC curves allow visual analyses of the trade-offs between the sensitivity and the specificity of a test with regard to the various cut-off values that may be used. The curve is obtained by calculating the sensitivity and specificity of the test at every possible cut-off point, and plotting sensitivity against 100-specificity.

One way of interpreting the area under the ROC curve is that an AUC ≥ 0.90 indicates high accuracy, while between 0.89 to 0.70 indicates moderate accuracy, between 0.69 to 0.51 low accuracy, and ≤ 0.50 a chance result (20-21, 25-26).

RESULTS

The study population comprised 1,170 adult

patients, 651 females and 519 male, aged 18 to 81 years [mean age 34.6 years (95%CI 33.8-35.3)] (Fig. 1). All 1,170 patients referred symptoms of rhinitis going back at least two years. The mean of the years of the onset of nasal symptoms was 7.08 (95%CI 6.68-7.48). Patients reported at least two of the following symptoms of rhinitis: sneezing, watery and/or mucous rhinorrhea, nasal itch, and nasal obstruction. All the patients had previously taken antihistamines for their nasal symptoms and 163 also decongestants, 115 anti-cholinergics, 88 nasal corticosteroids, 53 oral corticosteroids, and 47 systemic corticosteroids. The SPT was positive in 827 patients (70.7%) and negative in 343 patients (29.3%). The SPT was positive to pollens in 348 patients (grass and/or *Artemisia vulgaris* and/or *Parietaria judaica* and/or *Olea Europea* and/or *Cupressus*), in 108 patients to perennial allergens (HDM and/or cat and/or dog dander), and in 371 patients to both pollen and perennial allergens. The frequency of the distributions of the ECNF in AR and in NAR patients are reported in Fig. 2 and it show an important overlap between AR and NAR.

ECNF and AR and NAR

The medians of ECNF were significantly different between patients with AR [6.0 (P25th and P75th 4.0-8.0)] and patients with NAR [2.0 (P25th and P75th 1.0-4.7)] ($P < 0.0001$). The ECNF was not significantly different among patients with SPT positive only to pollens [6.0 (P25th and P75th 4.0-8.0)], only to HDM and/or cat and/or dog dander [5.0 (P25th and P75th 4.0-8.0)], and both to pollens and to HDM and/or cat and/or dog dander [6.0 (P25th and P75th 4.0-8.0)] ($P = 0.7$).

The ROC curve is shown in Fig. 3a. The best cut-off point between patients with AR and NAR was > 3.0 [sensitivity 0.79 (95%CI 0.76-0.82) and specificity 0.66 (95%CI 0.61-0.71), LR+ 2.37 (95%CI 2.20-2.60) and LR- 0.31 (95%CI 0.30-0.40)], and the AUC was 0.75 (95%CI 0.72-0.77). Fig. 3b shows the number of patients with positive and negative SPT in respect to the best cut-off (> 3.0) of ECNF. Considering that the ECNF was moderately accurate for distinguishing AR from NAR patients, we examined ECNF in respect to the severity of nasal symptoms (mild vs severe) and the clinical response to antihistamines (effective vs

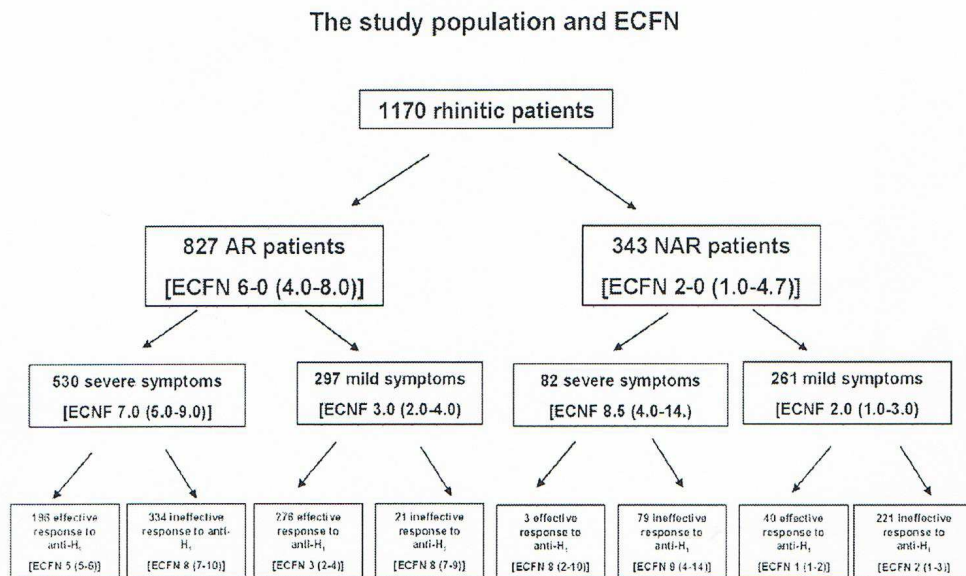


Fig. 1. Diagram flow chart of schematic characteristics of the patients and medians (25th and 75th percentiles) of ECFN.

ineffective) separately, in patients with AR and with NAR.

ECNF and the severity of nasal symptoms

Among AR patients, 530 (64.0%) indicated their rhinitis as severe and 297 (36.0%) as mild, while among NAR patients 261 (76.0%) defined their rhinitis as mild and 82 (24%) as severe ($P < 0.0001$). We found a significant difference in the ECFN between patients with nasal symptoms indicated as severe [7.0 (P25th and P75th 5.0-9.0)] and as mild [3.0 (P25th and P75th 2.0-4.0)] in patients with AR ($P < 0.0001$). Fig. 4a shows the ROC curve obtained from patients with AR. The best cut-off point of ECFN was > 4.0 [sensitivity 0.90 (95%CI 0.88-0.93) and specificity 0.84 (95%CI 0.79-0.88), LR+ 5.73 (95%CI 5.40-6.10) and LR- 0.11 (95%CI 0.08-0.20)]; the AUC was 0.90 (95%CI 0.88-0.92). Fig. 4b shows the number of patients with mild and severe symptoms in respect to the best ECFN cut-off (> 4.0).

Similarly, we found a significant difference in the ECFN between patients with nasal symptoms indicated as severe [8.5 (P25th and P75th 4.0-14.0)] and as mild [2.0 (P25th and P75th 1.0-3.0)] in patients with NAR ($P < 0.0001$). The ROC curve obtained

from patients with NAR is shown in Fig. 5a. The best cut-off point of ECFN was > 4.0 [sensitivity 0.74 (95%CI 0.63-0.83) and specificity 0.90 (95%CI 0.86-0.93), LR+ 7.77 (95%CI 6.80-8.90) and LR- 0.28 (95%CI 0.20-0.50)]; the AUC was 0.86 (95%CI 0.82-0.90). Fig. 5b shows the number of patients with mild and severe symptoms in respect to the best ECFN cut-off (> 4.0).

We did not find statistical differences between the ECFN in severe AR [7.0 (P25th and P75th 5.0-9.0)] and in severe NAR [8.5 (P25th and P75th 4.0-14.0)] ($P = 0.2$). On the contrary, we found statistical differences between mild AR [3.0 (P25th and P75th 2.0-4.0)] and mild NAR [2.0 (P25th and P75th 1.0-3.0)] ($P < 0.0001$).

ECNF and the clinical response to antihistamines

Of the 472 (57.0%) patients with AR, 196 (37%) with severe symptoms and 276 (97%) with mild symptoms, judged the clinical response to antihistamines as effective, and 355 (43.0%) as ineffective, of whom 334 (63%) with severe symptoms and 21 (3%) with mild symptoms. While among patients with NAR only 43 (12.5%), 3 (3.7%) with severe symptoms and 40 (15.3%) with mild symptoms, judged the clinical response to

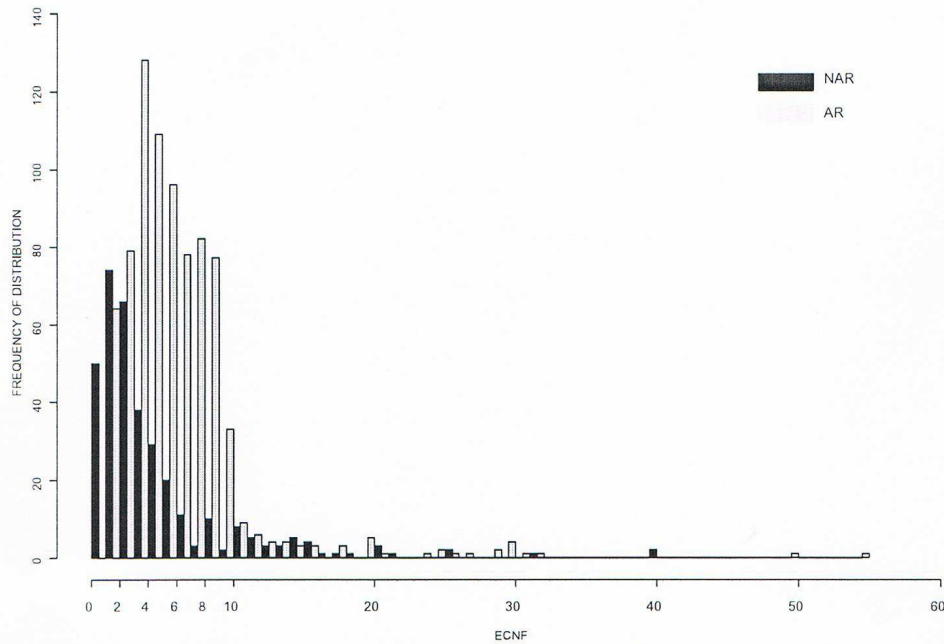
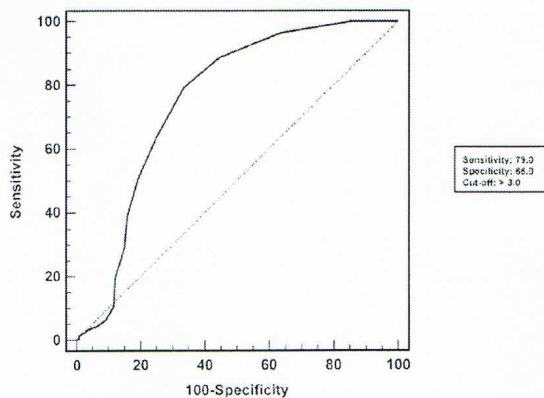


Fig. 2. Distribution of ECNF values in patients with AR and in patients with NAR. In patients with AR the lower value was 1.0 and the higher value was 55.0, the coefficient of Skewness and the coefficient of Kurtosis were 4.1 and 28.1, respectively. In patients with NAR the lower value was 0.0 and the higher value was 40.0, the coefficient of Skewness and the coefficient of Kurtosis were 3.2 and 14.6, respectively.

ROC curve of ECNF in patients with AR and NAR



Patients with NAR and AR respect to the best cut-off (> 3.0) of ECNF

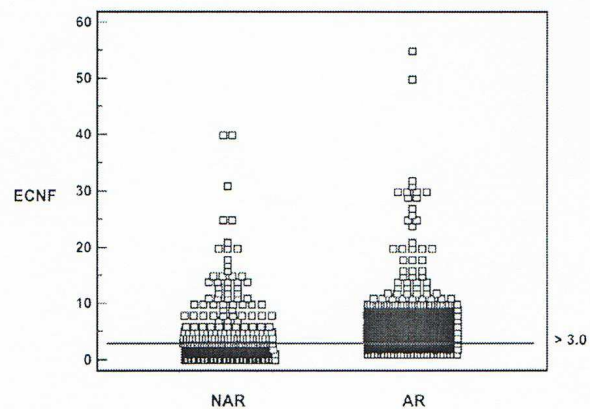
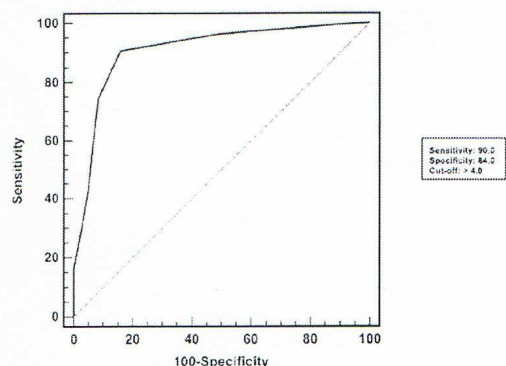


Fig. 3. a) The ROC curve obtained in patients with AR and NAR (N° patients = 1170). The best cut-off point of ECNF between patients with AR and NAR was > 3.0 [sensitivity 0.79 (95%CI 0.76-0.82) and specificity 0.66 (95%CI 0.61-0.71), LR^+ 2.37 (95%CI 2.20-2.60) and LR^- 0.31 (95%CI 0.30-0.40)], and the AUC was 0.75 (95%CI 0.72-0.77). **b)** Number of patients with positive and negative SPT in respect to the best cut-off (> 3.0) of ECNF.

ROC curve of ECNF in patients with mild and severe AR



Patients with mild and severe symptoms of AR respect to the best cut-off (> 4.0) of ECNF

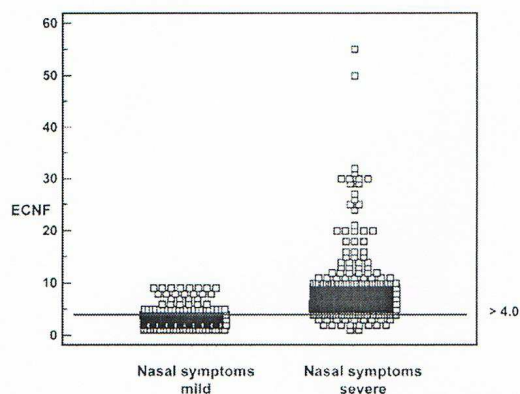
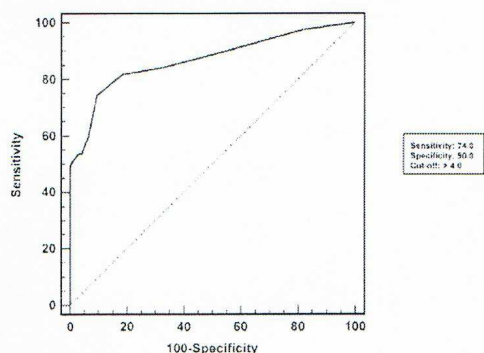


Fig. 4. a) The ROC curve obtained in patients with AR and mild and severe nasal symptoms (N° patients with AR = 827). The best cut-off point of ECNF between patient with mild and severe nasal symptoms was > 4.0 [sensitivity 0.90 (95%CI 0.88-0.93) and specificity 0.84 (95%CI 0.79-0.88), LR+ 5.73 (95%CI 5.40-6.10) and LR- 0.11 (95%CI 0.08-0.20)]; the AUC was 0.90 (95%CI 0.88-0.92). **b)** Number of patients with mild and severe symptoms in respect to the best ECNF cut-off (> 4.0).

ROC curve of ECNF in patients with mild and severe NAR



Patients with mild and severe symptoms of NAR respect to the best cut-off (> 4.0) of ECNF

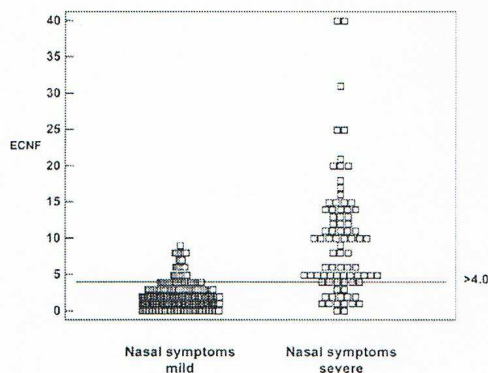


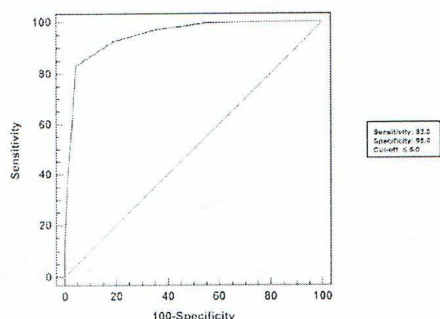
Fig. 5. a) The ROC curve obtained in patients with NAR and mild and severe nasal symptoms (N° patients with NAR = 343). The best cut-off point of ECNF between patient with mild and severe nasal symptoms was > 4.0 [sensitivity 0.74 (95%CI 0.63-0.83) and specificity 0.90 (95%CI 0.86-0.93), LR+ 7.77 (95%CI 6.80-8.90) and LR- 0.28 (95%CI 0.20-0.50)]; the AUC was 0.86 (95%CI 0.82-0.90). **b)** Number of patients with mild and severe symptoms in respect to the best ECNF cut-off (> 4.0).

antihistamines as effective compared to 300 (87.5%) as ineffective, of whom 79 (96.3%) with severe symptoms and 221 (84.7%) with mild symptoms ($P < 0.0001$).

There was a significant difference in the ECNF between patients with an effective [4.0 (P25th and P75th 3.0-5.0)] and an ineffective response

to antihistamines [8.0 (P25th and P75th 7.0-9.0)] in patients with AR ($P < 0.0001$). Fig. 6a shows the ROC curve obtained in patients with AR and effective and ineffective clinical response to antihistamines. The best cut-off point of ECNF was ≤ 5.0 [sensitivity 0.83 (95%CI 0.79-0.86) and specificity 0.95 (95%CI 0.92-0.97), LR+ 18.43

ROC curve of ECNF in patients with AR and ineffective and effective clinical response to antihistamines, respect to the best cut-off (≤ 5.0) of ECNF



Patients with AR and ineffective and effective clinical response to antihistamin respect to the best cut-off (≤ 5.0) of ECNF

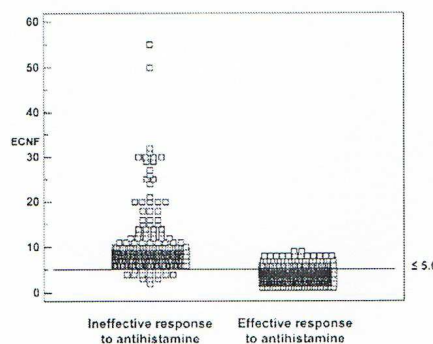
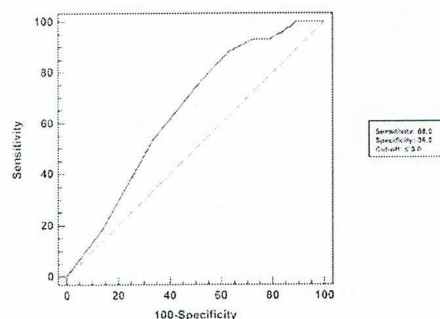


Fig. 6. a) The ROC curve obtained in patients with AR and ineffective and effective clinical response to antihistamines (N° patients with AR = 827). The best cut-off point of ECNF was ≤ 5.0 [sensitivity 0.83 (95%CI 0.79-0.86) and specificity 0.95 (95%CI 0.92-0.97), LR+ 18.43 (95%CI 17.60-19.30) and LR- 0.18 (95%CI 0.10-0.30)]; the AUC was 0.94 (95%CI 0.93-0.96). **b)** Number of patients with effective and ineffective clinical response to antihistamine in respect to the best cut-off (≤ 5).

ROC curve of ECNF in patients with NAR and ineffective and effective clinical response to antihistamines, respect to the best cut-off (≤ 3.0) of ECNF



Patients with NAR and ineffective and effective clinical response to antihistamin respect to the best cut-off (≤ 3.0) of ECNF

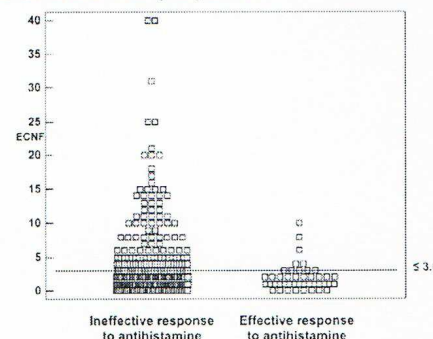


Fig. 7. a) The ROC curve obtained in patients with AR and ineffective and effective clinical response to antihistamines (N° patients with NAR = 343). The best cut-off point was ≤ 3.0 [sensitivity 0.88 (95%CI 0.74-0.96) and specificity 0.36 (95%CI 0.31-0.42), LR+ 1.40 (95%CI 1.20-1.70) and LR- 0.32 (95%CI 0.10-0.70)]; the AUC was 0.64 (95%CI 0.59-0.69). **b)** the number of patients with effective and ineffective clinical response to antihistamine in respect to the best cut-off (≤ 3).

(95%CI 17.60-19.30) and LR- 0.18 (95%CI 0.10-0.30)]; the AUC was 0.94 (95%CI 0.93-0.96). Fig. 6b shows the number of patients with ineffective and effective clinical response regarding the best ECNF cut-off (≤ 5.0).

With regard to patients with NAR, we found a significant difference of ECNF between patients

with an effective [1.0 (P25th and P75th 1.0-2.0)] and an ineffective response to antihistamines [2.0 (P25th and P75th 1.0-5.0)] ($P = 0.001$). The ROC curve obtained in the patients with NAR and effective and ineffective clinical response to antihistamines is shown in Fig. 7a. The best cut-off point was ≤ 3.0 [sensitivity 0.88 (95%CI 0.74-0.96) and specificity

0.36 (95%CI 0.31-0.42), LR+ 1.40 (95%CI 1.20-1.70) and LR- 0.32 (95%CI 0.10-0.70)]; the AUC was 0.64 (95%CI 0.59-0.69). Fig. 7b shows the number of patients with ineffective and effective clinical response in respect to the best ECNF cut-off (≤ 3.0).

DISCUSSION

Our results demonstrate that the ECNF's performance was moderately accurate in distinguishing patients with AR and NAR. However, ECNF showed high accuracy in distinguishing patients with mild rhinitis from patients with severe rhinitis, both in patients with AR and with NAR. Finally, the ECNF had high accuracy in identifying patients with an effective clinical response to antihistamines from patients with an ineffective response, only in patients with AR. The low accuracy of the ECNF in patients with NAR can be traced to several factors. NAR is a heterogeneous disease, and the diagnosis is more problematic than AR because it is made after the exclusion of the IgE-mediated causes. Basically, NAR presents both with and without eosinophilia of nasal mucosa. NAR without the eosinophilia syndrome include vasomotor rhinitis, hormonal rhinitis, occupational rhinitis (irritant subtype), gustatory rhinitis, rhinitis *medicamentosa*, and drug-induced rhinitis. NAR with eosinophilia syndrome (NARES) presents with signs and symptoms that mimic allergic disease, but the patients do not have an identifiable allergen and have negative skin test results. When these patients are symptomatic, a nasal smear with 5-25% of eosinophils confirms the diagnosis.

These considerations might explain why the ECNF present a moderate accuracy (AUC = 0.75) in discriminating AR patients from NAR patients, and a low accuracy (AUC = 0.64) in identifying NAR patients with an effective clinical response to antihistamines.

In AR the tissue recruitment of eosinophils is a hallmark of the natural history of the disease and of untreated allergic inflammation with nasal steroids (7, 27-28). In NARES the cause of eosinophilia is unclear. However, both AR and NAR with eosinophilia have more severe symptoms, particularly nasal obstruction and rhinorrhea (7-11).

Eosinophilia, both in patients with AR and with NAR, may contribute to nasal mucosal dysfunction, through the granules released from eosinophil (i.e. the major basic protein and eosinophil cationic protein) that are capable of damaging the nasal epithelium and prolonging mucociliary clearance (9-11). Intranasal steroid therapy has been employed to reduce the recovery of eosinophils in nasal lavage, when used on a regular basis (27) or on an as-needed basis (28). Some studies have shown that intranasal corticosteroids are particularly effective in the treatment of NAR when nasal eosinophilia is present (29). The options in the treatment of NAR patients who have few or no eosinophilia in nasal smears include either non-specific, broad-based therapy aimed at multiple symptoms or, alternatively, therapy tailored to treat specific symptoms (30-31). The effectiveness of intranasal corticosteroid therapy in NAR without eosinophils has not been clearly demonstrated (12, 29, 31-33). Nonetheless, there is a clinical impression that intranasal corticosteroids are not as effective in NAR without eosinophils, as in NARES (29, 34). With regard to the treatment with antihistamines, currently there are only few studies that have evaluated the effectiveness of these drugs in patients with NAR, with and without eosinophilia. Our results showed that the antihistamines were judged less effective by patients suffering from NAR in respect to those with AR, and that the ECNF have a low predictive power of effective clinical response to antihistamines, in respect to that of ECNF in AR patients.

The monitoring of nasal airway inflammation and cell recruitment, in clinical trials and in real-life medical practice, might provide insight into the mechanism of action of the therapeutic intervention, and in monitoring clinical severity of the disease and/or the response to the prescribed therapy (1).

Nasal lavage is relatively non-invasive, is easy and rapid to perform, is well tolerated, and is repeatable over relatively short periods. Nasal brushing is easy to perform and is well tolerated in general, although some find that the procedure causes a transient unpleasant sensation. However, nasal lavage offers the advantage of providing considerably greater information from the sample. Finally, nasal biopsy is a considerably more invasive procedure and requires expertise, not only in tissue

sampling but also in biopsy processing. Therefore, it is applicable only in specialist centers (1-3, 5-6). Although these approaches have been widely used in the limited research setting, they have been less widely applied as a means of objectively monitoring nasal disease in the clinical trial and/or in real-life clinical practice setting (14-17).

Our study demonstrates that ECNF might be of practical utility in real-life clinical allergology and found that the areas under the ROC curves of the ECNF presented a high accuracy as regards the severity of nasal symptoms (mild *vs.* severe) and the response to antihistamines (effective *vs.* ineffective), 0.90 and 0.94, respectively, in patients with AR, while in patients with NAR only the AUC of the severity of the nasal symptoms was of moderate accuracy (AUC = 0.86). This result seems to be due to the fact that patients with NAR may or may not have eosinophilia in their nasal fluid (35).

In conclusion, our results suggest an interesting practical use of ECNF data as an evaluator of the clinical severity of rhinitis, both allergic and non-allergic. As predictor of the clinical response to antihistamines, ECNF is accurate only in patients with positive SPT and, finally, the ECNF's performance was moderately accurate in distinguishing patients with AR and NAR.

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