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Clustering analysis in asthmatic outpatients: an experience in clinical practice.

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Abstract

The present real-life study collected medical data from 186 asthmatics with a median age of 40 years. It gathered information on the asthma onset age, allergic rhinitis, comorbidities, smoking, BMI, and severity of respiratory symptoms. Afterwards, ascending hierarchical clustering analysis was performed and outcomes allowed to characterize three different asthma phenotypes. Interestingly, in clustering of asthma patients the most important factor was GINA asthma control scoring corresponding to the asthma control GINA grading.

In conclusion, the current study confirms to clinicians that asthma control grading, used routinely in their daily work, is important and has a clear justification.

Keywords

asthma, asthma control, cluster analysis, phenotype, real-life.

To the Editor,

Asthma control is currently the cornerstone strategy in the management of asthmatics (1). Actually, uncontrolled and severe asthma significantly affect patients and society (2). Uncontrolled asthma represents a relevant risk factor for severe asthma (3,4). Moreover, the common experience confirms that a relevant

proportion of uncontrolled asthmatics may remain uncontrolled over time. So, defining the reasons of uncontrolled asthma may improve the management of asthmatics and may allow a tailored therapy. We previously tested this hypothesis in a real-life retrospective study (5). So, we experienced that proportion (about 70%) of uncontrolled asthmatics still remained uncontrolled despite best practice. Pet allergy associated with domestic exposure to the sensitizing pet, co-morbidities, high BMI, low adherence to treatment, and low FEV₁ are the main predictors for persistent uncontrolled asthma. On the contrary, successful allergen immunotherapy improved asthma control. These outcomes were consistent with another study evidencing that environmental factors, such as obesity and wheeze frequency (as reported symptom) were relevant issues involved in uncontrolled asthma (3). In this regard, Lee and colleagues have recently pointed out that uncontrolled asthma is frequent in common practice: over half (54.4%) of the evaluated patients had poorly or not well-controlled asthma (6). In particular, this study suggested that poor treatment adherence or unmet needs in current treatment may be involved in uncontrolled asthma.

However, a new way of managing asthmatic patients—is the identification of peculiar phenotypes and endotypes (7-9). Cluster analysis is a statistical approach to define asthma endo/phenotypes (10). This methodology defines sub-groups that are characterized by having common features. So, we would contribute to the debate about this relevant issue reporting our experience. One-hundred and eighty-six asthmatic patients (78 males, 41.9%) aged 18 to 84 years (median: 40 years) were evaluated. The visits included the following: history (onset age, allergic rhinitis comorbidity, smoking), clinical examination, BMI calculation, respiratory symptom perception assessed by visual analogue scale (VAS), lung function testing, hospital anxiety depression scale (HADS), asthma control test (ACT) questionnaire, asthma control level according to Global Initiative for Asthma (GINA) criteria, and reported nasal and bronchial symptoms in the past month). Each subject signed a written informed consent according to the procedure for guaranteeing data privacy.

Categorical data were reported as absolute frequencies and percentages, and compared by the Chi-square or the Fisher's Exact test, as appropriate. Quantitative variables were summarized as medians with minimum and maximum values and first and third quartiles (1st -3rd q) and compared by the non-parametric Analysis of

Variance (Kruskal-Wallis test), followed by post-hoc tests (Bonferroni's correction). All the tests were two-sided and a p value <0.05 was considered as statistically significant. Statistica software 9.0 (StatSoft Corp., Tulsa, OK, USA) was used for all the analyses and XLStat 2.0.1 (Addinsoft Co., New-York, USA) for the Clustering.

To better depict the relationships among different socio-demographical and clinical variables, Ascending Hierarchical Clustering analysis was performed: this is a method of cluster analysis which seeks to build a hierarchy of clusters according to the pattern of similarity among different variables.

One-hundred and sixty-five patients (88.7%) referred early onset of asthma, 161 (86.6%) had a concomitant diagnosis of allergic rhinitis with actual symptoms in 36% (n = 67) of the cases. Ascending hierarchical clustering analysis, produced three clusters of patients. As shown in Figure 1, the largest cluster (Cluster 1, N = 81) was characterized by controlled asthma, younger age (median = 35; 1st-3rd q = 24--44 years) and more frequent association with concomitant allergic rhinitis. The smallest cluster (Cluster 3, N = 33) was characterized by partially controlled asthma and significantly higher FEF₂₅₋₇₅ (median = 114; 1st-3rd q = 111-133 % pred.) and FEV₁ (median = 117; 1st-3rd q = 112-122 % pred.) values. Cluster 2 (N = 72) was characterized by uncontrolled asthma, older age (median = 46.5 years) and lower pulmonary function tests (median FEV₁ = 83; 1st-3rd q = 73-89.5 % pred.; median FEF₂₅₋₇₅ = 51; 1st-3rd q = 42-59 % pred.), and more frequent asthma symptoms (43; 59.7%). The three clusters were similar in terms of gender distribution, early onset of asthma, rhinitis symptoms, and HADS-A/HADS-D scores.

The current study demonstrates that the GINA asthma control score is also able to well define three different clusters: each cluster is characterized by peculiar clinical and functional factors that are consistent with the GINA asthma control scoring. In addition, the current study confirms Lee's findings underlying the relevance of some issues seem to be important in characterizing the uncontrolled asthma group: frequent respiratory symptoms, older age, poor lung function, and perception of more severe symptoms.

In conclusion, the current real-world study suggests that cluster analysis confirms the GINA asthma control scoring as it defines three different asthma phenotypes corresponding to the asthma control GINA grading.

This issue may have also a relevant impact in the context of Precision Medicine, that is the grounds for Personalized Medicine. So, asthma control assessment should be considered in all asthmatics in clinical practice.

Conflict of interest

all co-authors have nothing to declare.

Declaration of interest:

All the authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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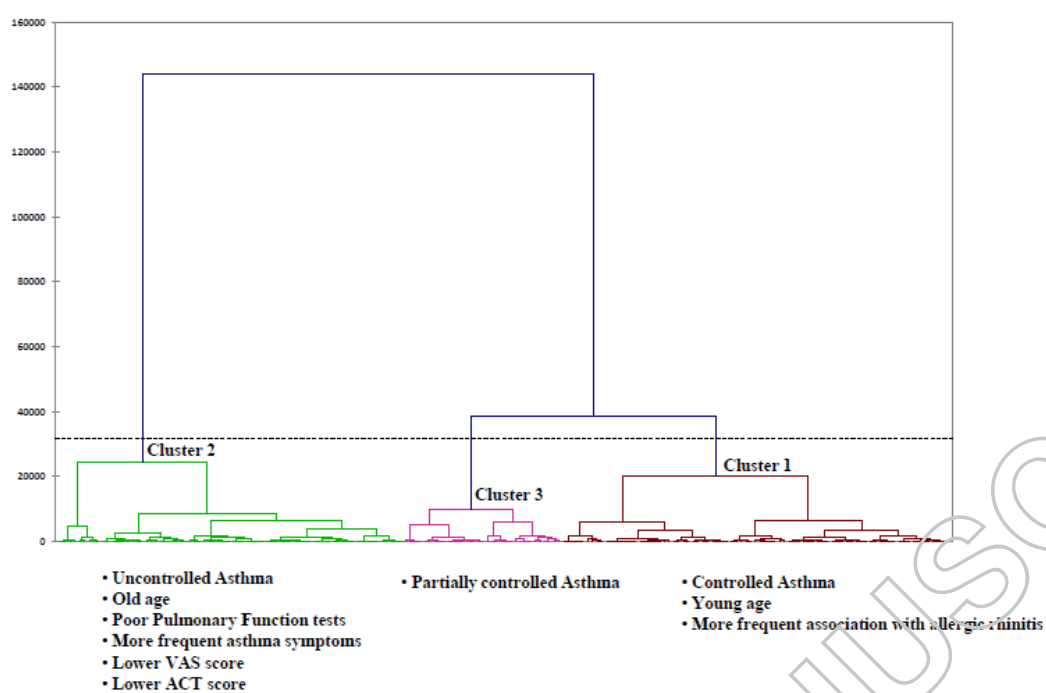


Figure 1. Ascending hierarchical clustering analysis of 186 asthmatic patients.