

On the Road to Improving Asthma Outcomes in Older Adults: The Phenotyping of Asthma in Older Adults



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There have been 2 National Institutes of Health workshops and a National Institutes of Health publication on the topic of asthma in the elderly.¹⁻³ The consistent message from these comprehensive overviews is that more research is needed for us to truly understand the unique features of asthma in older adults. Clinical investigations of this population are a priority because elderly patients with asthma are at a greater risk for morbidity and mortality when compared with younger patients. Such observations may be attributable in part to numerous comorbidities in older persons. The coexistence of irreversible airway obstruction and asthma (ie, asthma-chronic obstructive pulmonary disease overlap syndrome), for example, is widely recognized to exist in elderly populations.⁴ Thus, it is not surprising that elderly patients with asthma have reduced quality of life.⁵

It is reasonable to hypothesize that asthma phenotypes may exist for elderly patients that are quite distinct from those for their nonelderly adult counterparts and that understanding these better may improve the overall management in this age group. A cross-sectional study published by Baptist et al⁶ in this issue of *Journal of Allergy and Clinical Immunology: In Practice* provides a valuable insight into phenotypes of asthma in older adults to begin sorting out contrasts and comparisons to younger adults with asthma.

Following the initial categorization of the inflammatory phenotypes of asthma,⁷ there has been great interest in identifying clinically relevant phenotypes of asthma. With current therapies such as the anti-IL-5 biologics and others in development

targeting other cytokines, there is great interest in identifying which individuals are most likely to respond to a given therapy. As the authors point out, morbidity and mortality are greater in the older population with asthma. Thus, improved management of asthma in this population is greatly needed. The identification of clinically relevant phenotypes and biomarkers is a clear path to identifying unique therapeutic regimens for older adults with asthma.

In the work by Baptist et al,⁶ cluster analysis of 24 clinical variables identified 4 distinct clusters among 180 patients with asthma aged 55 years and older. The largest cluster (cluster 1), representing 38% of subjects, was characterized by late-onset asthma and the lowest prevalence of atopy (45%); cluster 2 included patients with mild asthma and low burden of comorbidities; cluster 3, representing 26% of the study population, included early onset asthma with a higher prevalence of atopy (74%) and bronchodilator reversibility; and cluster 4 represented 14% of patients, who were predominantly black and appeared to have the most severe asthma, based on greater prevalence of fixed airway obstruction, worse asthma control, and relatively more hospitalizations than observed in other clusters. The Severe Asthma Research Program (SARP) published a cluster analysis of adults with asthma and identified 2 clusters that had older patients, one characterized by late-onset asthma.⁸ Perhaps unique to the Baptist et al⁶ study is the observation that the 2 largest clusters segregated into either of the following: late age of onset and lower prevalence of aeroallergen sensitization; or earlier age of onset with high rate of aeroallergen sensitization. Thus, the authors were able to subdivide the older population with asthma even further than in the SARP study.

Interestingly, lung function measures and duration of asthma could categorize into the clusters with a low rate of misclassification. Similarly, for the SARP clusters, lung function measures and age of asthma onset were able to categorize into the clusters with a low rate of misclassification.⁸ Is it possible that all the comorbidities and inflammatory features ultimately distill into the only clinically relevant features of asthma: airway obstruction and reversibility?

The cross-sectional observational design of this study is a limitation and future longitudinal studies with greater numbers of subjects may be required to replicate these findings and validate these cluster-derived phenotypes. Although cluster 4 was identified with the most severe asthma, the study was underpowered to clearly identify the cluster at the highest risk for asthma exacerbations, a key determinant of asthma morbidity and mortality.⁹ Other factors known to impact asthma control in elderly patients with asthma such as self-management skills, depressive symptoms, adherence, and exposure to traffic pollutants were not evaluated.¹⁰⁻¹² It is unknown what impact, if any,

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such variables might have on these cluster-derived phenotypes but these could be assessed in a future longitudinal study.

This work by Baptist et al⁶ is an important first step in better understanding asthma in older adults. It remains to be determined whether these 4 clusters have relevance for the use of distinct therapies. Future evaluations of biomarkers may assist in defining these phenotypes more precisely in older patients with asthma. Determining clinical responses to existing and future therapies in different subpopulations of older patients with asthma will be a critical step in developing personalized approaches that could ultimately reduce morbidity and mortality in this population.

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