Allergy Asthma Immunol Res. 2023 Jan;15(1):8-18
https://doi.org/10.4168/aair.2023.15.1.8
pISSN 2092-7355·eISSN 2092-7363

Allergy, Asthma & Immunology Research AAIR

Review

Check for updates

Management of Elderly Asthma: Key Questions and Tentative Answers

Heung-Woo Park [1,2] **Sang Heon Cho** [1,2*]

[1]Divison of Allergy and Clinical Immunology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea
[2]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea

OPEN ACCESS

Received: Nov 10, 2022
Revised: Dec 21, 2022
Accepted: Dec 22, 2022
Published online: Jan 9, 2023

Correspondence to
Sang Heon Cho, MD, PhD
Department of Internal Medicine, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Korea.
Tel: +82-2-2072-2971
Fax: +82-2-472-3291
Email: shcho@snu.ac.kr

ORCID iDs
Heung-Woo Park
https://orcid.org/0000-0002-6970-3228
Sang Heon Cho
https://orcid.org/0000-0002-7644-6469

Disclosure
There are no financial or other issues that might lead to a conflict of interest.

ABSTRACT

The aging lung undergoes structural changes, immunosenescence, and inflammation, rendering the elderly more susceptible to developing obstructive airway disease. Thus, asthma in those of chronological age ≥ 65 years is not rare. Elderly asthma (EA) imposes considerable burdens in terms of mortality and morbidity, and expenditure. However, clinicians lack knowledge of EA and thus often prescribe inappropriate management. In this review, we ask 3 key questions frequently encountered during EA diagnosis and treatment: 1) Is EA different?; 2) How can we appropriately diagnose EA?; 3) Are there management strategies specific to EA? Based on recent studies, we provide tentative answers as follows: 1) late-onset EA differs in clinical features and pathogenetic mechanisms from non-EA, and thus further phenotypic and endotypic characterization of EA is needed; 2) both over- and under-diagnosis of asthma in the elderly can be reduced if the objective diagnostic tests are appropriately performed; 3) cautious prescription of ICS to selected EA patients should be encouraged, and a multifaceted approach which involves increasing medical awareness and inhaler use proficiency and adherence, seeking the assistance of caregivers, and correcting micronutrient deficiencies is required to reduce acute exacerbations in EA patients.

Keywords: Asthma; aged; immunosenescence; diagnosis; therapeutics; asthma-COPD overlap syndrome; integrative medicine

INTRODUCTION

The world is aging. According to data from the World Population Prospects 2022, one in 6 people (16%) worldwide will be aged over age 65 years by 2050.[1] The aging lung undergoes structural changes, immunosenescence, and inflammation, rendering the elderly more susceptible to developing obstructive airway disease.[2] Thus, asthma in those of chronological age ≥ 65 years (hereafter, elderly asthma [EA]) is not rare.[3] An understanding of EA is critical; it imposes considerable burdens in terms of mortality and morbidity, and expenditure.[4-7] However, clinicians lack knowledge of EA and thus often prescribe inappropriate management. In this review, we ask 3 key questions frequently encountered during EA diagnosis and treatment. We then provide tentative answers based on recent evidence. The major findings of recent studies on EA are summarized in **Table**.

QUESTION 1: IS EA DIFFERENT?

Clinical features

Age-associated changes in lung and chest wall structure and function may influence the features of EA. Senile changes, including alveolar space enlargement, weakened respiratory muscles, and/or a stiffened rib cage, may influence the physiological characteristics of elderly lungs. A reduced, static, elastic recoil pressure decreases the forced expiratory volume in 1 second (FEV1). The estimated rate of FEV1 decline is initially 25–30 mL/year at age 35–40 years but can double to 60 mL/year after the age of 70 years.[8] In addition, the immune system declines with age, and patients with EA are more prone to airway infection than younger subjects.[3] Recognition of the age of onset is the first step when distinguishing EA from non-elderly asthma (NEA). However, in some EA patients, asthma that commences in early life may persist to older age (long-standing asthma) or develop for the first time at an advanced age (late-onset asthma). In the elderly, the asthma incidence rate was reported to be 3.1 per 1,000.[3] In our previous study of a prospective cohort that sought risk factors for acute EA exacerbation,[9] about two-thirds of patients reported that their symptoms commenced within 5 years prior to enrolment (unpublished data). The clinical features of EA and NEA may differ. For example, in a study that surveyed 2,067 asthmatics (434 with EA and 1,633 with NEA), the clinical variables of EA and NEA showed distinctly different loading patterns for the first 2 principal components in principal component analysis.[10] Fixed airway obstruction, chronic

Table. Major findings of recent studies on elderly asthma

Category	Design	Reference number
Phenotype	Prospective analysis of elderly asthmatics	9
A 1-yr prospective follow-up study of elderly asthmatics (n = 628) identified the status of depression, proficiency in using inhaler devices, medication adherence measured according to self-reported questionnaires, and previous history of exacerbations at baseline as important factors predicting future exacerbations.		
Phenotype	Cross-sectional analysis of a large cohort of adult asthmatics	10
Principal component analysis of all asthmatics showed that EA (n = 434) and NEA (n = 1,633) were distinctly separated by the first and second principal component on the plot of individual asthmatics according to their scores. Clinical variables showed distinctly different patterns of loading on the first 4 principal components between the EA and the NEA group.		
Phenotype	Retrospective analysis of combined 3 cohorts of adult asthmatics	11
The exacerbation rate was 31.0% in the EA (n = 503) and 33.2% in the NEA (n = 583) group. Multivariate logistic regression analysis revealed fixed airway obstruction, chronic rhinosinusitis, and male sex as independent risk factors for exacerbation in the EA group. In the NEA group, exacerbation increased along with an increase in eosinophil count.		
Phenotype	Cluster analysis of elderly asthmatics followed up prospectively	12
K-means clustering was applied to elderly asthmatics (n = 872), and 4 clusters were identified: 1) long symptom duration and marked airway obstruction; 2) female dominance and normal lung function; 3) smoking male dominance and reduced lung function; and 4) high body mass index and borderline lung function. Cluster grouping was strongly predictive of time to first acute asthma exacerbation (log-rank $P = 0.01$). The developed decision-tree algorithm included 2 variables (percentage of predicted FEV1 and smoking pack-years), and its efficiency in proper classification was confirmed in the secondary cohort of elderly asthmatics.		
Phenotype	Cross-sectional analysis of elderly asthmatics in one tertiary center	13
In 243 elderly asthmatics, atopy was observed in 63%, mainly in those with early onset disease, and its frequency decreased as the age of asthma onset increased ($P < 0.05$). Total serum IgE was higher for allergic patients, and FEV1 values were lower for patients with long-term asthma.		
Pathogenesis	Cross-sectional analysis of elderly asthmatics in one tertiary center	15
Induced sputum samples from elderly asthmatics (n = 14) and young asthmatics (n = 15) were analyzed. Sputum cell differentials revealed a significant increase in the percentage of neutrophils in elderly asthmatics compared to younger asthmatics ($P = 0.008$). There were significant increases in MMP-9 levels ($P = 0.02$) and neutrophil elastase activity in elderly asthmatics ($P = 0.02$).		
Pathogenesis	Cross-sectional analysis of a large cohort of adult asthmatics	21
Serum SE-IgE concentrations were significantly higher in elderly asthmatics (n = 249) than in elderly controls (n = 98) ($P < 0.001$). Elderly asthmatics with high SE-IgE levels had specific characteristics of having more severe asthma, sputum eosinophilia and CRS, compared to those with lower SE-IgE levels. Multiple correspondence analyses also showed that high serum SE-IgE level had close relationships with severe asthma, CRS and sputum eosinophilia together.		
Pathogenesis	Cross-sectional analysis of elderly asthmatics in one tertiary center	23
Genome-wide gene expression on induced sputum samples from elderly asthmatics (n = 55) and elderly controls (n = 10) were analyzed. Two distinct gene clusters were found. Cluster 1 (n = 35) showed a lower eosinophil proportion in sputum and less severe airway obstruction compared to cluster 2 (n = 20). OXIDATIVE_PHOSPHORYLATION gene was significantly enriched in the cluster 1 and EPITHELIAL MESENCHYMAL TRANSITION gene set in the cluster 2. All these results were replicated in an independent data set.		

(continued to the next page)

Table. (Continued) Major findings of recent studies on elderly asthma

Category	Design	Reference number
Diagnosis	Cross-sectional analysis of data obtained from multi-centers	26
Overall, 638 elderly cases (with asthma or COPD) and 984 elderly controls were examined. Spirometric measurements were obtained in 607 cases and 912 controls; 508 and 747 tests with at least 3 acceptable curves were obtained in cases and in controls, respectively (not significant). The average reproducibility for FEV1 was 61.6 mL in cases and 58.3 mL in controls (not significant). Male sex and age were risk factors for a poorer reproducibility of FEV1. Reproducibility tended to improve with time ($P < 0.001$). Although spirometry becomes increasingly difficult in aging patients, a rigorous quality control program can ensure that reliable data are obtained in the majority of patients.		
Diagnosis	Cross-sectional analysis of elderly asthmatics in one tertiary center	32
Xenon ventilation CT was performed in elderly asthmatics (n = 30). The severity of dyspnoea measured by the visual analogue scale showed a significant correlation with the total number of areas of XT on the xenon ventilation CT taken in the pre-BD wash-out phase (r = −0.723, $P < 0.001$). The total number of areas of XT significantly decreased after BD inhalation, and differences in the total number of areas of XT (between the pre- and post-BD wash-out phases) at baseline showed significant correlations with the per cent increases in FEV1 after subsequent anti-asthma treatment (r = −0.775, $P < 0.001$).		
Treatment	Comparative analysis of health-care database	38
In total, 6,254 consecutive elderly asthmatics were identified (in Ontario, Canada between 1992 and 1996). Sixty percent of these patients were given at least one prescription for ICSs within 90 days post-discharge from their index hospitalization for asthma. Users of ICSs post-discharge were 29% (95% CI, 20%–38%) less likely to be readmitted to hospitals for asthma and 39% (95% CI, 20%–53%) less likely to experience all-cause mortality compared to those who did not receive these drugs post-discharge over a 1-year follow-up period.		
Treatment	Prospective analysis of elderly asthmatics in one tertiary center	49
A hundred and five consecutive severe asthmatics (GINA step 4–5) treated with omalizumab for at least 1 year were divided into 3 groups according to their age at omalizumab treatment onset: 18–39, 40–64 and ≥65 yr. A similar reduction of ICSs dosage and SABA on-demand therapy was observed in all groups during omalizumab treatment; a similar increase in FEV1 was also observed. After omalizumab treatment, the risk for exacerbations was lower in subjects aged 40–64 (OR, 0.284; 95% CI, 0.098–0.826; $P = 0.021$) and 18–39 (OR, 0.133; 95% CI, 0.026–0.678; $P = 0.015$), compared to elderly asthmatics.		
Treatment	Retrospective analysis of elderly asthmatics in one tertiary center	51
Of 147 patients with severe asthma being treated with biologics, 21 patients older than 70 years were included. The median age of these patients was 76.3 year (range 71–86) and the majority were women (n = 18, 85.7%). There were 9 patients (42.9%) who experienced an AE related to biological treatment. Four (44.4%) were in treatment with omalizumab, 2 (22.2%) with mepolizumab, 2 patients (22.2%) with reslizumab and one (11.1%) with benralizumab. This study indicates that the prescription of biological therapy in elderly patients with severe asthma seems to be safe.		
Treatment	Prospective analysis of elderly asthmatics in one tertiary center	52
A total of 100 elderly asthmatics were provided multifaceted intervention for 1 year. Multifaceted interventions included repeated education on asthma and inhaler technique for patients and their caregivers, provision of an action plan to cope with acute exacerbations, short message service to prevent follow-up losses, and oral replacement of magnesium. Ninety-two subjects completed this study. Compared to the previous year, the acute asthma exacerbation rate showed a significant reduction from 67% to 50% ($P = 0.001$) and significant improvement was observed in FEV1 and FVC ($P = 0.04$, $P = 0.036$ for each). Interestingly, a subgroup analysis revealed that predicted value of FEV1 increased significantly in subjects who continued to take magnesium from 79.6% to 87.1% ($P = 0.008$).		

EA, elderly asthma; NEA, non-elderly asthma; FEV1, forced expiratory volume in 1 second; IgE, immunoglobulin E; MMP-9, matrix metalloproteinase-9; SE, staphylococcal enterotoxin; CRS, chronic rhinosinusitis; CT, computed tomography; XT, xenon gas trapping; BD, bronchodilator; ICS, inhaled corticosteroid; CI, confidence interval; GINA, Global Initiative for Asthma; OR, odds ratio; SABA, short-acting β2 agonists; AE, adverse event.

rhinosinusitis, and male sex are independent risk factors for acute EA exacerbation, whereas the exacerbation rate increases in NEA patients as the blood eosinophil count increases.[11] In a study that subjected patients with EA (n = 872) to K-means clustering, 4 clusters were identified: 1) long symptom duration and marked airway obstruction; 2) female dominance and normal lung function; 3) smoking male dominance and reduced lung function; and 4) a high body mass index and borderline lung function.[12] Cluster grouping was strongly predictive of the time to the first acute asthma exacerbation. The decision-tree algorithm developed in that study included 2 variables (the percentage of predicted FEV1 and smoking pack-years). Its utility for appropriate classification was confirmed in the second cohort of EA patients.

Pathogenesis

As mentioned above, EA includes asthma which begins in early life. In such cases, allergic sensitization, a classic mechanism of asthma pathogenesis, may play an important role. A recent study on 243 EA patients observed atopy in 63%, mainly those with early-onset asthma (commencing in their twenties or thirties); atopy frequency decreased as the age at asthma onset increased.[13] The atopy rate declines with age, possibly reflecting immunosenescence.[13] Thus, these findings suggest that the pathogenetic mechanisms underlying late-onset EA differ from those of early-onset EA. Compared to patients with NEA, those with EA exhibit increased levels of sputum neutrophils and neutrophil-associated mediators (including matrix metalloproteinase-9, neutrophil elastase, and interleukin [IL]-8),[14,15] reminiscent of

https://doi.org/10.4168/aair.2023.15.1.8

changes seen in certain NEA patients with severe disease phenotypes.[16] In line with this, even healthy elderly individuals exhibit altered inflammatory profiles, reflecting low-grade inflammation of the lower respiratory tract.[17] The changes include significant increases in the numbers of CD4+ T cells, neutrophils, and immunoglobulins, as well as in the levels of cytokines such as IL-6 and IL-8.[17] Interestingly, epithelial cell-derived cytokines, such as IL-33 and IL-31, may contribute to less Th2 phenotype of EA, and increased levels of eotaxin-2 and transforming growth factor-β1 may determine EA severity.[18] Recent evidence suggests that staphylococcal enterotoxin (SE) plays a role in the pathophysiology of asthma.[19,20] We previously reported significant associations between SE-immunoglobulin E (IgE) sensitization and late-onset EA, particularly between the severe eosinophilic type of sensitization and chronic rhinosinusitis.[21] These findings may imply that SE is involved in the pathogenesis of severe, late-onset eosinophilic asthma in the elderly. Asthma is now recognized as a heterogeneous disease driven by different immune responses and inflammation; late-onset asthma is no exception. Cluster analyses of various cohorts identified 2 subtypes of late-onset asthma: non-allergic eosinophilic and non-allergic non-eosinophilic asthma.[22] Similarly, genome-wide gene expression profiles of sputum cells have been used to identify distinct gene clusters in EA patients.[22] In one study, the oxidative phosphorylation gene set was significantly enriched for a cluster characterized by a lower proportion of eosinophils in sputum and less severe airway obstruction. In contrast, the epithelial-mesenchymal transition gene set was significantly enriched in another cluster.[23] These findings suggest that 2 different pathogenic mechanisms underlie EA.

Tentative answer

Immunosenescence and anatomical changes associated with aging affect EA and thus could render EA different from NEA.[24] As the well-worn phrase states: "A child is not just a small adult." EA may not be simply an extension of early-onset EA. Accumulated evidence indicates that late-onset EA differs in clinical features and pathogenetic mechanisms from NEA. Further phenotypic and endotypic characterization of EA is, therefore, needed.

QUESTION 2: HOW CAN WE PROPERLY DIAGNOSE EA?

Diagnostic tests

As mentioned above, lung function decreases with age because of increased chest wall stiffness, reduced respiratory muscle function, and increased residual volume, given the loss of elastic recoil. The decline in airway elasticity is the major contributor to the increased fixed airflow obstruction and the work of breathing with age. Then the FEV1/forced vital capacity (FVC) decreases; normal elderly subjects exhibit spirometric features suggestive of obstructive lung disease.[17] To date, NEA-specific diagnostic test has considered such age-related changes. Therefore, physicians must be careful when performing and interpreting traditional diagnostic tests. Although frailty and cognitive dysfunction may render spirometry difficult in the elderly,[25,26] more than 80% can yield acceptable spirometric results after training.[3,26] Measurement of the forced expiratory volume in the first 6 seconds is more useful than the FEV1 for those who cannot perform complete expiration (and thus cannot yield an FVC value).[27] The exhaled nitric oxide fraction (FeNO) is widely used as a marker of airway eosinophilic inflammation. Of note, in healthy subjects, FeNO levels appear to plateau in adults but later linearly increase to the age of 80 years.[28] Unfortunately, the utility of FeNO levels in EA diagnosis remains unclear. The elderly show an impaired β_2-agonist bronchodilator response attributable to a decrease in the number of β_2-adrenergic

https://doi.org/10.4168/aair.2023.15.1.8

receptors in airway smooth muscles.[29] On the other hand, bronchial hyperresponsiveness to methacholine increases with aging.[30,31] Bronchial provocation tests may be contraindicated in certain elderly patients with low baseline lung function or cardiac comorbidities.[30,31] Computed tomography (CT) of the chest, a noninvasive modality, may be used to make inferences about lung function. Xenon ventilation CT (which assesses regional ventilation status) has revealed that dyspnea severity correlates with xenon gas-measured air trapping; reduced trapping correlates with FEV1 improvements in the elderly.[32] However, xenon ventilation CT is not readily available in clinical practice; imaging and analytical techniques are specialized.

Differentiation of EA from chronic obstructive pulmonary disease (COPD)

Physiological changes in the lung with aging may mimic airway obstruction,[33] reducing treatment effects and explaining the loss of reversibility and the persistence of airway obstruction in patients with EA. Thus, asthma and COPD may overlap or converge in the elderly.[2,3,33] Several principal clinical features distinguish between the 2 diseases. Asthma is characterized by a personal or family history of atopy or asthma with symptoms commencing in childhood and increases in the levels of biomarkers, including FeNO, peripheral and sputum eosinophils, and serum levels of total and specific IgE. Adult symptom onset renders COPD more likely.[34] Emphysema is not a feature of long-standing asthma; thus, a normal lung diffusion capacity for carbon monoxide favors asthma in the elderly.[3] CT of the chest can also help differentiate between asthma and COPD. In EA patients, CT shows increased wall thickness and air-trapping.[35] A smoking history *per se* does not afford a clear-cut distinction; a considerable proportion of EA patients are current smokers.[36] When encountering an elderly patient with a strong possibility of asthma, we recommend that physicians should actively prescribe medications including inhaled corticosteroid (ICS). In a prospective cohort of EA patients, we observed that about 11.7% of patients with FEV1/FVC values <70% at baseline showed improvements in airway obstruction (FEV1/FVC ≥ 70%) after 2 years of treatment (unpublished data).

Tentative answers

Physicians should keep in mind that both over- and under-diagnosis of asthma in the elderly would be reduced if the objective diagnostic tests were appropriately performed. We recommend that elderly patients with long-standing obstructive asthma should be treated as asthma, regardless of whether the airway obstruction is reversible. It is important to develop a uniform definition of asthma that can be used in daily practice to help physicians distinguish asthma from COPD and to detect asthma-COPD overlap in the elderly.

QUESTION 3: ARE THERE MANAGEMENT STRATEGIES SPECIFIC TO EA?

Pharmacotherapy

Patients with EA are usually excluded from randomized controlled trials associated with drug development.[37] Therefore, almost half of all EA patients are treated with drugs that have not been tested in such populations. Although no treatment guideline specific to EA is available, ICS is the mainstay of chronic asthma management in the elderly. ICS reduces hospital admissions and mortality.[38] However, as mentioned above, some patients with EA exhibit predominantly neutrophilic inflammation[15,16]; ICS may be less effective in such cases. Adverse reactions associated with high-dose ICS must be considered in the elderly. For

https://doi.org/10.4168/aair.2023.15.1.8

example, a budesonide equivalent ICS dose of ≥1,000 μg/day places EA patients (especially women) at increased fracture risk.[39] In this sense, maintenance and reliever therapy (MART) with a combination of formoterol and ICS may be useful in patients with EA. MART is as effective as maintenance therapy preventing moderate-to-severe exacerbations and reducing ICS exposure.[40] A randomized 6-month study showed that EA patients responded to MART (in terms of maintenance of asthma control and reduction of exacerbations) as well as did younger asthmatics.[41] As EA patients have been reported to show more small airway involvement,[35] ultrafine particle ICS medications may be beneficial. However, this possibility has yet to be formally tested. Another thing to be remembered is that ICS may be associated with an increased risk of pneumonia in asthmatics.[42] Clinicians need to acknowledge this possibility in treating EA patients with ICS. As discussed above, β_2-receptor density, responsiveness, and affinity may decline with aging.[29,43] Thus, a possible role for long-acting muscarinic antagonists in EA management should be tested in future studies. Previous works have found that such antagonists are effective add-on therapies in asthmatics aged up to 75 years.[44,45] The ease of use and the increased adherence render leukotriene receptor antagonists attractive in oral EA control. Only a few studies have examined the effects of such antagonists in EA patients, and the overall efficacy was thought to be less than that of ICS.[46,47] However, a recent study using health insurance claim data showed that leukotriene receptor antagonists could be considered first-line therapy for mild EA patients with a similar risk of acute exacerbation but better compliance compared to low-dose ICS.[48] Some EA patients show clinical improvement after anti-IgE therapy, although the response may be less than in younger patients.[49,50] In real-world settings, mepolizumab may be effective in elderly patients with severe eosinophilic asthma.[51] In addition, a recent study found that biological therapy seems to be safe in elderly patients with severe asthma.[52] However, the real-world data on other biologics (in terms of how the effects vary with age) are limited; we cannot offer any helpful information.

Special considerations

A multidimensional approach based on a comprehensive assessment of physical, psychological, cognitive, and social factors is required to manage EA appropriately. For example, we found a significant reduction in the acute exacerbation rate in 100 EA patients who received multifaceted interventions for 1 year. These included several educational sessions on asthma, and inhaler techniques, for both patients and caregivers; creating action plans to cope with acute exacerbations; using a short message service to prevent follow-up loss; and using an oral supplement of magnesium.[53] The American Thoracic Society has recommended that a multidimensional approach should include: a standardized evaluation of comorbidities and screening for frailty and psychosocial impediments to care using geriatric-specific tools, assessment of barriers to inhaled therapy adherence, individualization of treatment incorporating age- and disease-specific factors, and multiple points of care and evaluation including social workers, pharmacists, nurses, certified asthma educators, and physicians.[24] In this context, appropriate management of depression is necessary; the condition is relatively common in the elderly, affecting up to 20% of older adults in Western countries.[54] Depression assessed by the Korean version of the Geriatric Depression Scale Short Form is a factor predicting acute exacerbations of EA.[8] Similarly, EA patients with depression are almost twice as likely to show poor asthma outcomes (asthma-related emergency department and urgent care visits) compared to those without.[55] Thus, we recommend that physicians screen EA patients for depression and treat them appropriately. Inadequate nutrition is common in the elderly, attributable to tooth loss, impaired digestive function, decreased physical activity, and low income.[56] Lower serum levels of magnesium

https://doi.org/10.4168/aair.2023.15.1.8

are significantly associated with a history of asthma exacerbation.[57] Moreover, magnesium supplementation (as part of a multidimensional approach) significantly decreases the asthma exacerbation rate and increases lung function in EA patients.[53] Nutritional education of caregivers or patients improves the nutritional status of elderly patients.[58,59] The role of nutritional support in EA management should be evaluated in a future study.

Tentative answers

Despite the associated adverse reactions, ICS therapy remains the preferred medication for EA. However, ICS appears to be underused in EA patients.[60,61] Cautious prescription of ICS to selected EA patients should be encouraged. To facilitate this, specific EA phenotypes that respond well to ICS must be identified, as has been achieved in younger patients with asthma. Apart from asthma management issues, comorbid conditions may pose significant burdens for the elderly. These include upper airway diseases, obesity, smoking, and depression. To reduce acute exacerbations in EA patients, a multifaceted approach is required; it should involve increasing medical awareness and inhaler use proficiency and adherence, seeking the assistance of caregivers, and correcting micronutrient deficiencies. Such an approach is likely to be effective.

CONCLUSIONS

EA is a common disease. It is associated with unique features in terms of symptoms, pathogenesis, diagnosis, and treatment (**Figure**). These must be identified and appropriately managed to provide optimal care. In addition, EA management must be based on a multidimensional assessment that considers the frequent presence of comorbid conditions and associated polypharmacotherapy.

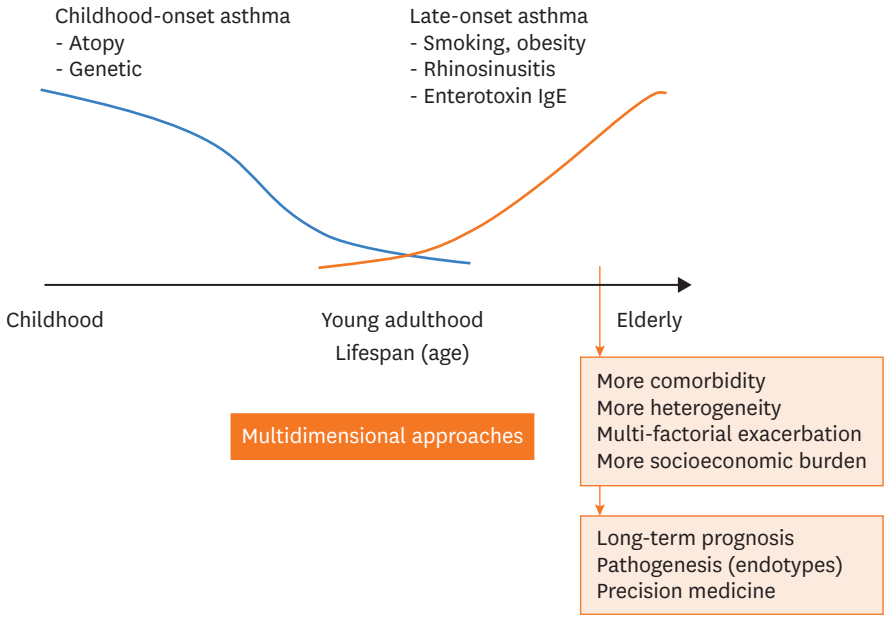

Figure. Characteristics of elderly asthma requiring a multidimensional approach.
IgE, immunoglobulin E.

https://doi.org/10.4168/aair.2023.15.1.8

REFERENCES

1. United Nations. World population prospects 2022 [Internet]. New York (NY): United Nations; 2022 [cited 2022 Sep 24]. Available from: https://population.un.org/wpp/.
2. Brandsma CA, de Vries M, Costa R, Woldhuis RR, Königshoff M, Timens W. Lung ageing and COPD: is there a role for ageing in abnormal tissue repair? Eur Respir Rev 2017;26:170073.
PUBMED | CROSSREF
3. Baptist AP, Busse PJ. Asthma over the age of 65: all's well that ends well. J Allergy Clin Immunol Pract 2018;6:764-73.
PUBMED | CROSSREF
4. American Lung Association. Asthma trends and burden [Internet]. Chicago (IL): American Lung Association; 2022 [cited 2022 Sep 14]. Available from: https://www.lung.org/research/trends-in-lung-disease/asthma-trends-brief/trends-and-burden.
5. Sato K, Ishii T, Kaise T. Burden of asthma in elderly Japanese patients: using hospital-based administrative claims data. Pulm Ther 2020;6:247-60.
PUBMED | CROSSREF
6. Lee E, Kim A, Ye YM, Choi SE, Park HS. Increasing prevalence and mortality of asthma with age in Korea, 2002–2015: a nationwide, population-based study. Allergy Asthma Immunol Res 2020;12:467-84.
PUBMED | CROSSREF
7. Plaza V, Serra-Batlles J, Ferrer M, Morejón E. Quality of life and economic features in elderly asthmatics. Respiration 2000;67:65-70.
PUBMED | CROSSREF
8. Sharma G, Goodwin J. Effect of aging on respiratory system physiology and immunology. Clin Interv Aging 2006;1:253-60.
PUBMED | CROSSREF
9. Park HW, Kim TW, Song WJ, Kim SH, Park HK, Kim SH, et al. Prediction of asthma exacerbations in elderly adults: results of a 1-year prospective study. J Am Geriatr Soc 2013;61:1631-2.
PUBMED | CROSSREF
10. Park HW, Kwon HS, Kim TB, Kim SH, Chang YS, Jang AS, et al.; COREA Study Group. Differences between asthma in young and elderly: results from the COREA study. Respir Med 2013;107:1509-14.
PUBMED | CROSSREF
11. Sohn KH, Song WJ, Park JS, Park HW, Kim TB, Park CS, et al. Risk factors for acute exacerbations in elderly asthma: what makes asthma in older adults distinctive? Allergy Asthma Immunol Res 2020;12:443-53.
PUBMED | CROSSREF
12. Park HW, Song WJ, Kim SH, Park HK, Kim SH, Kwon YE, et al. Classification and implementation of asthma phenotypes in elderly patients. Ann Allergy Asthma Immunol 2015;114:18-22.
PUBMED | CROSSREF
13. Agondi RC, Andrade MC, Takejima P, Aun MV, Kalil J, Giavina-Bianchi P. Atopy is associated with age at asthma onset in elderly patients. J Allergy Clin Immunol Pract 2018;6:865-71.
PUBMED | CROSSREF
14. Brooks CR, Gibson PG, Douwes J, Van Dalen CJ, Simpson JL. Relationship between airway neutrophilia and ageing in asthmatics and non-asthmatics. Respirology 2013;18:857-65.
PUBMED | CROSSREF
15. Nyenhuis SM, Schwantes EA, Evans MD, Mathur SK. Airway neutrophil inflammatory phenotype in older subjects with asthma. J Allergy Clin Immunol 2010;125:1163-5.
PUBMED | CROSSREF
16. Moore WC, Hastie AT, Li X, Li H, Busse WW, Jarjour NN, et al. Sputum neutrophil counts are associated with more severe asthma phenotypes using cluster analysis. J Allergy Clin Immunol 2014;133:1557-1563.e5.
PUBMED | CROSSREF
17. Yáñez A, Cho SH, Soriano JB, Rosenwasser LJ, Rodrigo GJ, Rabe KF, et al. Asthma in the elderly: what we know and what we have yet to know. World Allergy Organ J 2014;7:8.
PUBMED | CROSSREF
18. Ulambayar B, Lee SH, Yang EM, Ye YM, Park HS. Association between epithelial cytokines and clinical phenotypes of elderly asthma. Allergy Asthma Immunol Res 2019;11:79-89.
PUBMED | CROSSREF
19. Song WJ, Jo EJ, Lee JW, Kang HR, Cho SH, Min KU, et al. Staphylococcal enterotoxin specific IgE and asthma: a systematic review and meta-analysis. Asia Pac Allergy 2013;3:120-6.
PUBMED | CROSSREF

20. Bachert C, Humbert M, Hanania NA, Zhang N, Holgate S, Buhl R, et al. *Staphylococcus aureus* and its IgE-inducing enterotoxins in asthma: current knowledge. Eur Respir J 2020;55:1901592.
PUBMED | CROSSREF

21. Song WJ, Sintobin I, Sohn KH, Kang MG, Park HK, Jo EJ, et al. Staphylococcal enterotoxin IgE sensitization in late-onset severe eosinophilic asthma in the elderly. Clin Exp Allergy 2016;46:411-21.
PUBMED | CROSSREF

22. Kaur R, Chupp G. Phenotypes and endotypes of adult asthma: moving toward precision medicine. J Allergy Clin Immunol 2019;144:1-12.
PUBMED | CROSSREF

23. Kim BK, Lee HS, Sohn KH, Lee SY, Cho SH, Park HW. Different biological pathways are up-regulated in the elderly with asthma: sputum transcriptomic analysis. Allergy Asthma Immunol Res 2019;11:104-15.
PUBMED | CROSSREF

24. Skloot GS, Busse PJ, Braman SS, Kovacs EJ, Dixon AE, Vaz Fragoso CA, et al. ATS ad hoc Committee on Asthma in the Elderly. An official American Thoracic Society workshop report: evaluation and management of asthma in the elderly. Ann Am Thorac Soc 2016;13:2064-77.
PUBMED | CROSSREF

25. Sherman CB, Kern D, Richardson ER, Hubert M, Fogel BS. Cognitive function and spirometry performance in the elderly. Am Rev Respir Dis 1993;148:123-6.
PUBMED | CROSSREF

26. Bellia V, Pistelli R, Catalano F, Antonelli-Incalzi R, Grassi V, Melillo G, et al. Quality control of spirometry in the elderly. The SA.R.A. study. SAlute Respiration nell'Anziano = Respiratory Health in the Elderly. Am J Respir Crit Care Med 2000;161:1094-100.
PUBMED | CROSSREF

27. Sorino C, Sherrill D, Guerra S, Enright P, Pedone C, Augugliaro G, et al. Prognostic value of FEV1/FEV6 in elderly people. Clin Physiol Funct Imaging 2011;31:101-7.
PUBMED | CROSSREF

28. Jacinto T, Malinovschi A, Janson C, Fonseca J, Alving K. Evolution of exhaled nitric oxide levels throughout development and aging of healthy humans. J Breath Res 2015;9:036005.
PUBMED | CROSSREF

29. Pfeifer MA, Weinberg CR, Cook D, Best JD, Reenan A, Halter JB. Differential changes of autonomic nervous system function with age in man. Am J Med 1983;75:249-58.
PUBMED | CROSSREF

30. Cuttitta G, Cibella F, Bellia V, Grassi V, Cossi S, Bucchieri S, et al. Changes in FVC during methacholine-induced bronchoconstriction in elderly patients with asthma: bronchial hyperresponsiveness and aging. Chest 2001;119:1685-90.
PUBMED | CROSSREF

31. Scichilone N, Messina M, Battaglia S, Catalano F, Bellia V. Airway hyperresponsiveness in the elderly: prevalence and clinical implications. Eur Respir J 2005;25:364-75.
PUBMED | CROSSREF

32. Park HW, Jung JW, Kim KM, Kim TW, Lee SH, Lee CH, et al. Xenon ventilation computed tomography and the management of asthma in the elderly. Respirology 2014;19:389-95.
PUBMED | CROSSREF

33. Battaglia S, Benfante A, Spatafora M, Scichilone N. Asthma in the elderly: a different disease? Breathe (Sheff) 2016;12:18-28.
PUBMED | CROSSREF

34. Busse PJ, Lurslurchachai L, Sampson HA, Halm EA, Wisnivesky J. Perennial allergen-specific immunoglobulin E levels among inner-city elderly asthmatics. J Asthma 2010;47:781-5.
PUBMED | CROSSREF

35. Inoue H, Niimi A, Takeda T, Matsumoto H, Ito I, Matsuoka H, et al. Pathophysiological characteristics of asthma in the elderly: a comprehensive study. Ann Allergy Asthma Immunol 2014;113:527-33.
PUBMED | CROSSREF

36. de Marco R, Cappa V, Accordini S, Rava M, Antonicelli L, Bortolami O, et al. Trends in the prevalence of asthma and allergic rhinitis in Italy between 1991 and 2010. Eur Respir J 2012;39:883-92.
PUBMED | CROSSREF

37. Battaglia S, Basile M, Spatafora M, Scichilone N. Are asthmatics enrolled in randomized trials representative of real-life outpatients? Respiration 2015;89:383-9.
PUBMED | CROSSREF

38. Sin DD, Tu JV. Inhaled corticosteroid therapy reduces the risk of rehospitalization and all-cause mortality in elderly asthmatics. Eur Respir J 2001;17:380-5.
PUBMED | CROSSREF

39. Battaglia S, Cardillo I, Lavorini F, Spatafora M, Scichilone N. Safety considerations of inhaled corticosteroids in the elderly. Drugs Aging 2014;31:787-96.
PUBMED | CROSSREF

40. Di Marco F. Today's improvement in asthma treatment: role of MART and Easyhaler. Multidiscip Respir Med 2020;15:649.
PUBMED | CROSSREF

41. Haughney J, Aubier M, Jørgensen L, Ostinelli J, Selroos O, van Schayck CP, et al. Comparing asthma treatment in elderly versus younger patients. Respir Med 2011;105:838-45.
PUBMED | CROSSREF

42. Kim MH, Rhee CK, Shim JS, Park SY, Yoo KH, Kim BY, et al. Inhaled corticosteroids in asthma and the risk of pneumonia. Allergy Asthma Immunol Res 2019;11:795-805.
PUBMED | CROSSREF

43. Connolly MJ, Crowley JJ, Charan NB, Nielson CP, Vestal RE. Impaired bronchodilator response to albuterol in healthy elderly men and women. Chest 1995;108:401-6.
PUBMED | CROSSREF

44. Kerstjens HA, Engel M, Dahl R, Paggiaro P, Beck E, Vandewalker M, et al. Tiotropium in asthma poorly controlled with standard combination therapy. N Engl J Med 2012;367:1198-207.
PUBMED | CROSSREF

45. Kerstjens HA, Casale TB, Bleecker ER, Meltzer EO, Pizzichini E, Schmidt O, et al. Tiotropium or salmeterol as add-on therapy to inhaled corticosteroids for patients with moderate symptomatic asthma: two replicate, double-blind, placebo-controlled, parallel-group, active-comparator, randomised trials. Lancet Respir Med 2015;3:367-76.
PUBMED | CROSSREF

46. Creticos P, Knobil K, Edwards LD, Rickard KA, Dorinsky P. Loss of response to treatment with leukotriene receptor antagonists but not inhaled corticosteroids in patients over 50 years of age. Ann Allergy Asthma Immunol 2002;88:401-9.
PUBMED | CROSSREF

47. Bozek A, Warkocka-Szoltysek B, Filipowska-Gronska A, Jarzab J. Montelukast as an add-on therapy to inhaled corticosteroids in the treatment of severe asthma in elderly patients. J Asthma 2012;49:530-4.
PUBMED | CROSSREF

48. Hong SH, Kang HR, Nam JH, Park SK, Kim TB, Lee EK. A comparison of leukotriene receptor antagonists to low-dose inhaled corticosteroids in the elderly with mild asthma. J Allergy Clin Immunol Pract 2019;7:2642-2652.e3.
PUBMED | CROSSREF

49. Korn S, Schumann C, Kropf C, Stoiber K, Thielen A, Taube C, et al. Effectiveness of omalizumab in patients 50 years and older with severe persistent allergic asthma. Ann Allergy Asthma Immunol 2010;105:313-9.
PUBMED | CROSSREF

50. Sposato B, Scalese M, Latorre M, Scichilone N, Matucci A, Milanese M, et al. Effects of omalizumab in severe asthmatics across ages: a real life Italian experience. Respir Med 2016;119:141-9.
PUBMED | CROSSREF

51. Isoyama S, Ishikawa N, Hamai K, Matsumura M, Kobayashi H, Nomura A, et al. Efficacy of mepolizumab in elderly patients with severe asthma and overlapping COPD in real-world settings: a retrospective observational study. Respir Investig 2021;59:478-86.
PUBMED | CROSSREF

52. Mir-Ihara P, Narváez-Fernández E, Domínguez-Ortega J, Entrala A, Barranco P, Luna-Porta JA, et al. Safety of biological therapy in elderly patients with severe asthma. J Asthma 2022;59:2218-22.
PUBMED | CROSSREF

53. Lee SH, Song WJ, Park HW, Kang MG, Kim SH, Park HK, et al. Multifaceted interventions to reduce acute exacerbations in elderly asthmatics. Asia Pac Allergy 2018;8:e1.
PUBMED | CROSSREF

54. Volkert J, Schulz H, Härter M, Wlodarczyk O, Andreas S. The prevalence of mental disorders in older people in Western countries - a meta-analysis. Ageing Res Rev 2013;12:339-53.
PUBMED | CROSSREF

55. Patel PO, Patel MR, Baptist AP. Depression and asthma outcomes in older adults: results from the National Health and Nutrition Examination Survey. J Allergy Clin Immunol Pract 2017;5:1691-1697.e1.
PUBMED | CROSSREF

56. Norman K, Haß U, Pirlich M. Malnutrition in older adults—Recent advances and remaining challenges. Nutrients 2021;13:2764.
PUBMED | CROSSREF

57. Lee SH, Song WJ, Park HW, Kim SH, Park HK, Kim SH, et al. Serum micronutrients levels and clinical features of elderly asthmatics. Allergy Asthma Respir Dis 2017;5:223-7.
CROSSREF

58. Fernández-Barrés S, García-Barco M, Basora J, Martínez T, Pedret R, Arija V, et al. The efficacy of a nutrition education intervention to prevent risk of malnutrition for dependent elderly patients receiving Home Care: a randomized controlled trial. Int J Nurs Stud 2017;70:131-41.
PUBMED | CROSSREF

59. Kim BH, Kim MJ, Lee Y. The effect of a nutritional education program on the nutritional status of elderly patients in a long-term care hospital in Jeollanamdo province: health behavior, dietary behavior, nutrition risk level and nutrient intake. Nutr Res Pract 2012;6:35-44.
PUBMED | CROSSREF

60. Hartert TV, Togias A, Mellen BG, Mitchel EF, Snowden MS, Griffin MR. Underutilization of controller and rescue medications among older adults with asthma requiring hospital care. J Am Geriatr Soc 2000;48:651-7.
PUBMED | CROSSREF

61. Sin DD, Tu JV. Underuse of inhaled steroid therapy in elderly patients with asthma. Chest 2001;119:720-5.
PUBMED | CROSSREF