

# The current state and provisions for elderly patients with asthma

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## Abstract

Demographic statistics of Japan indicate that it is moving toward a super-aging society and, accordingly, the ratio of elderly patients with asthma is also increasing. An important point in diagnosing elderly patients with asthma is that the onset of asthma in old age, along with a history of smoking, differentiation, and complications of chronic obstructive pulmonary disease must be considered. Primary care physicians must understand the characteristics of elderly patients when treating them. When conducting inhalation therapy in any asthmatic patient, especially elderly asthmatic patients, it is important to teach the patients proper technique and sustain medication adherence. We believe this effort will lead to an improvement in controlling asthma as well as a decrease in the number of asthma deaths.

## KEYWORDS

chronic obstructive pulmonary disease, education of inhalation, elderly asthma, inhaled corticosteroids, inhaler technique, medication adherence

## 1 | INTRODUCTION

There is currently no precise definition for elderly asthma. Regarding long-term disease control, in elderly patients with asthma, the first-line treatment is inhaled corticosteroids (ICS), which is similar to that used for younger patients. In principle, when treating elderly patients with asthma, primary care physicians should treat them in accordance with the Asthma Prevention and Management Guideline, Japan (JGL). However, elderly patients with asthma have various unique characteristics and it is necessary for primary care physicians to understand such characteristics when treating elderly patients.

## 2 | WITH AN AGING POPULATION IN JAPAN, THE RATIO OF ELDERLY ASTHMATIC PATIENTS INCREASES

In Japan, aging of the population has rapidly progressed. Individuals over 65 years of age accounted for 25.9% (the rate of aging) of the entire population in 2014.<sup>1</sup> It is estimated that by 2060, the rate of

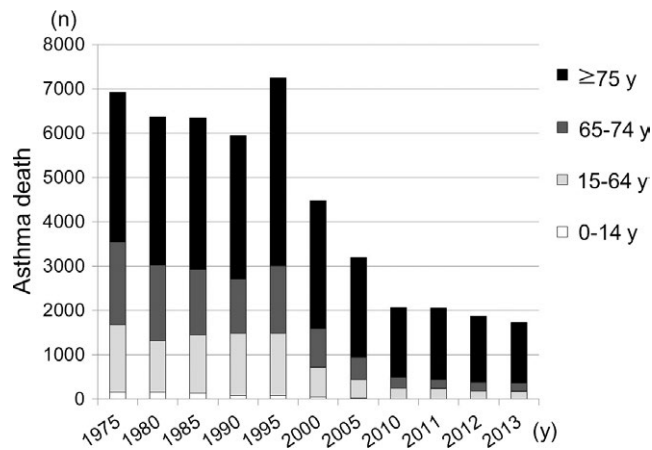
aging will increase to 39.9%.<sup>2</sup> As a result, the ratio of elderly patients with asthma has been increasing. If one were to define elderly patients with asthma as those over 65 years of age, then the percentage of elderly patients with asthma was 39.4% in patients over 15 years of age in 1995. Furthermore, this rate rose to 41.8% in 2013 according to a patient survey conducted by the Japanese Ministry of Health, Labour and Welfare in 2005<sup>3</sup> and 2011.<sup>4</sup>

## 3 | THE ASTHMA PREVALENCE RISES WITH INCREASED AGING

The percentage of patients 20-64 years of age with allergic symptoms in the respiratory organs (asthma prevalence) shifted between 4-6% according to the Ministry of Health, Labour and Welfare Survey on Public Health Welfare Trends conducted in 2003.<sup>5</sup> For those over 65 years of age, the rate increased to 8.8%, while for those over 75 years of age, it was 10.9%. Similarly, a survey conducted in 2013 by the Ministry of Health, Labour and Welfare (the Comprehensive Survey of Living Conditions' asthma outpatients rating survey by age

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**FIGURE 1** The numbers of deaths due to asthma over time (Taken from Ref. 8)

[per one thousand people)]<sup>6</sup> showed that for patients 20-64 years of age, the ratio shifted from 4.9 to 9.1% for men and 6.8-13.3% for women. For those over 65 years of age, there was an increase by 16.2% for both genders and for those over 75 years of age, 19.6% for men and 17.7% for women. It has been reported that the asthma prevalence of elderly individuals in other developed countries is between 6-10%, which is similar to that of Japan.<sup>7</sup>

#### 4 | ASTHMA DEATH HAS DECREASED, BUT REMAINS A PROBLEM FOR ELDERLY PATIENTS

The association between elderly asthma and asthma deaths is high. The rate of asthma deaths in Japan has been maintained at approximately 5.0 out of a population of 100 000 annually from 1975. Thereafter, due to the publication and spread of asthma guidelines, anti-inflammatory treatments using ICS have become routine. Thus, the number of asthma deaths has decreased and the rate of asthma deaths decreased to 1.4 by 2013 (Figure 1).<sup>8</sup> However, there is a high rate of asthma deaths among elderly patients with asthma. In 2013, elderly patients over 65 years of age accounted for 89.5% of all asthma deaths. Therefore, in order to aim for the eradication of asthma deaths, it is necessary to decrease the number of asthma deaths in the elderly patients. To achieve this, primary care physicians must appropriately diagnose and treat patients with asthma.

#### 5 | PATHOPHYSIOLOGY OF ELDERLY ASTHMA

##### 5.1 | Elderly asthma presents in middle age or later, and the pathophysiology is different from early-onset asthma

One characteristic of asthma in the elderly is that over half of the patients experience asthma after middle age (late-onset asthma).<sup>9</sup> There is a pathophysiological difference between late-onset asthma and long-standing asthma, which begins in youth and continues to old

age.<sup>10</sup> Regarding early-onset asthma, the environment, genetics, and allergies, as well as Th2 inflammation, can affect the condition. As for late-onset asthma, conditions such as epigenetics (e.g, oxidative stress and telomere shortening), Th1, and neutrophilic inflammation can affect asthma more than genetics, with less involvement from allergies.<sup>10</sup>

##### 5.2 | Elderly asthma has more severe small airway disease compared with younger patients with asthma

Concerning airway lesions caused by asthma, remodeling is an important feature. Braman et al.<sup>11</sup> examined early-onset and late-onset asthma separately, according to the onset of asthma symptoms in the elderly, and found that early-onset asthma resulted in higher airway obstruction than late-onset asthma. This result suggests that if the disease duration is long, then airway remodeling will progress.

Additionally, due to old age, elderly patients experience a decrease in elastic fibers, spinal curvature, and a stiffening of the thorax caused by the decline in particular movement, all of which will cause a decrease in traction related to the bronchi of the lungs. This may result in a narrowing of the bronchioles.<sup>10</sup> Furthermore, for smokers, complications such as pulmonary emphysema or chronic bronchitis may occur, which could lead to injuries in the small airways. We previously used the forced oscillation technique to measure the R5-R20, which is the index for small airways. Our results showed that the R5-R20 was significantly higher in elderly asthma patients over 65 years of age in comparison with those younger than 65 years of age. This finding suggests that elderly asthma results in more severe small airway disease compared with younger patients with asthma.<sup>12,13</sup>

#### 6 | ELDERLY ASTHMA IS NOT DIAGNOSED APPROPRIATELY DUE TO MISUNDERSTANDING ASTHMA SYMPTOMS FOR AGING OR COMORBIDITIES

Experiencing respiratory symptoms, such as difficulties in breathing during the day and the night, wheezing, and coughing, may be indicated for asthma, and it has been reported that approximately half of all elderly asthma patients have not been adequately diagnosed.<sup>14</sup> This may be because elderly asthma patients believe that their difficulties in breathing are due to aging<sup>15</sup> or the misunderstanding that they must self-limit their activities of daily living, thus causing social isolation and/or depression, which results in coexisting symptoms such as chronic obstructive pulmonary disease (COPD) or congestive heart failure.<sup>16</sup> Moreover, many medical staff members hold the misconception that adult-onset asthma is rare or that the spirometry utilization rate is low.

#### 7 | DIFFERENTIAL DIAGNOSIS OF ELDERLY ASTHMA

Chronic obstructive pulmonary disease, congestive heart failure, lung cancer, gastroesophageal reflux disease, a previous history of

tuberculosis, bronchiectasis, upper airway obstruction, aspiration, inhaled foreign body, hyperventilation, panic disorder, and vasculitis are some of the indicating diseases where physicians may make a diagnosis of asthma in the elderly.<sup>16</sup> Representative diseases are described below.

### 7.1 | COPD

Emphysema and chronic bronchitis are components of COPD. COPD patients present with dyspnea on exertion, a chronic cough, frequent winter bronchitis, or wheezing.<sup>17</sup> Cyanosis, ankle edema, and distended neck veins indicate COPD with cor pulmonale.<sup>18</sup> A marked weight loss, spontaneous pursed-lip breathing, hyperinflation, and bullous changes on high-resolution CT, palpable liver edge without hepatomegaly, and a quiet chest on auscultation with diminished breath and heart sounds characterize emphysema.<sup>18</sup>

Recently, with regard to COPD, the potential of “overlap syndrome” of asthma and COPD has attracted a great deal of attention.<sup>19</sup> At our hospital, we examined the chief complaints at the first visit of patients newly diagnosed with overlap syndrome over 40 years of age. Those with overlap syndrome had both the symptoms of asthma and COPD (Figure 2). One of the chief complaints of patients with asthma was exertional dyspnea (Figure 2).

### 7.2 | Congestive heart failure

It is occasionally difficult to differentiate congestive heart failure (CHF) from asthma in older individuals. Airway obstruction and bronchial hyperreactivity can be present in both asthma and CHF.<sup>20</sup> Episodic and nocturnal dyspnea may also be present in both.<sup>17</sup> Crackles and gallop on auscultation, an acutely ischemic ECG and a chest radiograph showing pulmonary edema or other signs of pulmonary congestion all help to make the diagnosis of left ventricular failure.<sup>17</sup> Furthermore, the levels of B-type natriuretic peptide (BNP) are elevated in heart failure. The negative predictive value of the BNP levels is <100 pg/mL for the diagnosis of CHF.<sup>21</sup> Most patients with significant CHF as a cause of their dyspnea will have levels of >400 pg/mL.<sup>21</sup> In patients

presenting with levels between 100 and 400 pg/mL, one needs to exclude baseline left ventricular dysfunction without exacerbation, pulmonary embolism, and cor pulmonale.<sup>21</sup>

### 7.3 | Lung cancer

Patients with bronchogenic carcinoma may also present with a cough, dyspnea, and wheezing that are focal, but with symptoms that are less likely to be intermittent, as is characteristic in asthma.<sup>17,18</sup> A chest X-ray is especially indicated due to the likelihood of carcinoma in elderly patients with significant smoking histories.<sup>18</sup>

### 7.4 | Gastroesophageal reflux disease (GERD)

The incidence of GERD increases with asthma and age<sup>22</sup> and leads to bronchoconstriction via microaspiration and vagal stimulation.<sup>17</sup> For elderly asthma patients who are unusually resistant to routine therapy and have heartburn, a cough, and nocturnal symptoms, GERD should be considered.<sup>22</sup>

### 7.5 | Bronchiectasis

Acute exacerbations of bronchiectasis are frequently associated with dyspnea, a cough, and wheezing.<sup>18</sup> The presence of clubbing, chronic purulent sputum, increased marking on the chest X-ray, and hemoptysis are diagnostic features of bronchiectasis.<sup>18</sup>

### 7.6 | Upper airway obstruction

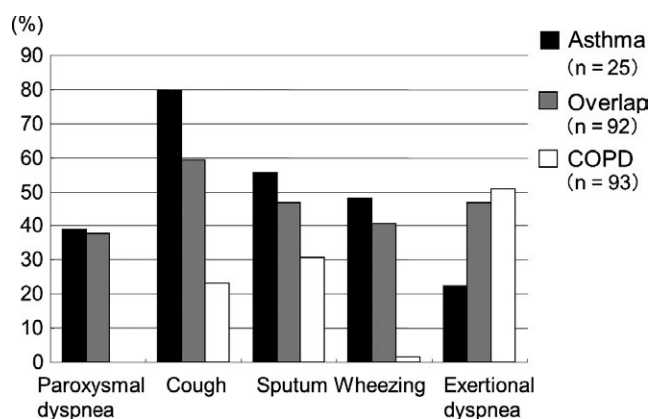
Tumors of the larynx and upper trachea, benign tracheal stenosis, vocal cord dysfunction, thyroid enlargement, and compressing thoracic aorta aneurysm can all produce wheezing sounds mimicking asthma except that stridor (inspiratory wheezing) is predominant.<sup>17</sup> An inspiratory/expiratory flow volume loop can be used to assist in the identification of an extrathoracic airflow obstruction as opposed to the lower airflow obstruction of asthma.<sup>17,18</sup>

### 7.7 | Aspiration

In elderly individuals, aspiration can cause or exacerbate a cough and wheezing, symptoms of asthma.<sup>18</sup> Various diseases make elderly patients particularly prone to aspiration including dementia, Parkinson's disease, and stroke, as well as the use of medications such as sedatives, alcohol, and antipsychotics.<sup>18</sup>

## 8 | INFLUENCE OF DRUGS FOR COMORBIDITIES ON ASTHMA TREATMENT

Comparing elderly patients with asthma and those without, the incidence rates of chronic sinusitis, rhinitis, COPD, diabetes, cardiovascular disease, stroke, arthritis, and osteoporosis tended to be higher among elderly patients with asthma.<sup>7</sup> Accordingly, the number of



**FIGURE 2** Chief complaints from patients (over 40 years of age) who were diagnosed with asthma, COPD, and overlap

prescription drugs also increased. As a decline in medication adherence is predicted as a result of having to take a greater number of prescription drugs, physicians must be aware of this fact and be cautious.

Physicians must also be careful when prescribing medicine for treating comorbidities. Medicines such as beta blockers for hypertension, ACE inhibitors, topical beta blockers for glaucoma, and nonsteroidal anti-inflammatory drugs (NSAIDs) for arthritis could worsen the condition of asthma.

## 9 | INFLUENCE OF ASTHMA MEDICATIONS ON COMORBIDITIES

Decisions regarding the management of elderly asthma patients must take into account both the general goals of symptom control and risk minimization and the impact of comorbidities.<sup>23</sup> Inhaled corticosteroids (ICS) are the mainstay of elderly asthma treatment. For poorly controlled patients on ICS, adding long-acting beta<sub>2</sub>-agonists (LABA) are recommended.<sup>23</sup> However, there have been instances where anti-asthma drugs could worsen the comorbidity.

### 9.1 | Beta<sub>2</sub>-agonists

Cardiovascular disease is common in older patients. Beta<sub>2</sub>-agonists have inotropic and chronotropic effects that can produce resting sinus tachycardia and precipitate cardiac rhythm disturbances in susceptible patients.<sup>24,25</sup> Elderly patients have been grossly underrepresented in trials of LABA, and many trials having excluded those  $\geq 65$  years of age.<sup>17</sup>

The Cochrane review showed that no significant difference in all-cause nonfatal serious adverse events was noted with regular formoterol or salmeterol with ICS in comparison with ICS alone.<sup>26,27</sup> This finding seems to have remarkably few clinical implications.<sup>24</sup> In some patients, the doses of LABA should be reduced if cardiovascular adverse events are troublesome.<sup>28</sup>

### 9.2 | Anticholinergics

Tiotropium by soft-mist inhaler, a long-acting muscarinic antagonist (LAMA), has become used for not only COPD, but also moderate to severe asthma as add-on therapy for adult patients with a history of exacerbations.<sup>29</sup> It is consistently noted that the use of anticholinergic drugs has been associated with acute urinary retention (AUR).<sup>30</sup> AUR is a highly prevalent disease in elderly men.<sup>31</sup> In contrast, no significant increase in the incidence of AUR was reported in COPD patients treated with tiotropium, compared to those taking placebo, in several randomized-controlled trials and a pilot study.<sup>32-34</sup> No data have suggested a true causal relationship between anticholinergics and prostatic symptoms.<sup>24</sup> In patients with benign prostate hypertrophy (BPH), 5 $\alpha$ -reductase inhibitors combined with an  $\alpha$ -blocker may reduce the risk of AUR and BPH surgery.<sup>35,36</sup> When tiotropium is used in elderly asthma complicated with BPH, it is thought that medication for BPH may be required.

### 9.3 | Others

Physicians must pay careful attention to GERD caused by theophylline, insomnia, and a worsening of osteoporosis caused by steroid medications.<sup>37</sup>

## 10 | MEDICATION ADHERENCE DECLINES IN ELDERLY ASTHMA

Regarding the JGL, the objective of treating asthma is to favorably control the disease using ICS as a first-line treatment for controller medications, although it is highly important to retain medication adherence in the treatment of elderly asthma. Several reports have demonstrated that medication adherence significantly declines in patients with elderly asthma over 65 years of age.<sup>38</sup> Several reasons for the decline in adherence include little knowledge concerning the treatment and the disease itself and/or worrying about potential side effects of the medicine. Due to such reasons, the treatment may be interrupted and, in turn, could cause complications for the treatment regimens. Moreover, due to the deterioration of eyesight, muscular strength, movements, and depression, elderly patients with asthma may not be able to follow the advice given by the medical staff. Another potential reason could be a lack of communication due to cognitive decline, which would result in elderly patients incorrectly remembering the prescription contents.<sup>7</sup>

## 11 | COGNITIVE FUNCTION, MANUAL DEXTERITY, AND FINGER STRENGTH MAY INFLUENCE INHALATION TECHNIQUE FOR ELDERLY ASTHMA

To maintain and improve the medication adherence of ICS, devices must be chosen in accordance with the conditions of each patient. The cognitive function, manual dexterity, finger strength, synchronization of spray, and inhalation (when using a pressurized metered-dose inhaler, pMDI) have been shown to be important indicators when considering which device is suitable for each patient. The use of training tools for inhalation manufactured by each dry powder inhaler (DPI) is useful for judging whether or not patients can obtain the maximal inspiratory flow rates. The training tools for inhalation are designed to produce sounds when patients inhale them and when the inspiratory flow rates are sufficient for the DPI inhalation formulation. If a proper inspiratory capacity cannot be obtained, then the use of a pMDI is recommended. In such cases, if the spray and inhalation are not synchronized, then a spacer is prescribed.

For patients whose cognitive function has declined, it may be difficult to use either the DPI or pMDI, which is similar to patients who do not have good control over their hands and fingers. If the patient's finger strength is declined, then it would not be possible to push the pMDI canister because it is too firm. In such cases, a DPI is recommended; however, some pMDI may be beneficial because a special

auxiliary tool has been created which makes spraying possible with little finger strength. In cases of difficulties using both the DPI and pMDI, it is possible to choose an inhaled budesonide suspension using a nebulizer under the caregivers' supervision.

## 12 | COOPERATION WITH PHARMACISTS IS EFFECTIVE FOR INHALATION EDUCATION FOR ELDERLY ASTHMA

To control elderly asthma properly, the medical staff must educate the patients on the correct inhalation technique of ICS and make sure that the patients continue to use the inhaler. In many cases, it is difficult for physicians themselves to educate the patients due to time constraints. Therefore, cooperation with the medical staff (e.g. pharmacists and/or nurses) is important.

For asthma patients who go to primary care physicians, many of them receive their prescriptions from health insurance pharmacies. A useful tool to advance team-based medical practice between the physicians and pharmacists is the written request for inhalation education from the physicians to the pharmacists and an evaluation checklist for inhalation education (medication information referral document)<sup>39</sup> from the pharmacists to the physicians. According to this written request for inhalation education, the pharmacists then conduct inhalation education, record the results on the evaluation checklist for inhalation education (medication information referral document), and give the physician's feedback. These evaluation checklists should improve communication between the physicians and the pharmacists, thereby leading to a better practice of inhalation education in elderly asthma patients and improvements in asthma control.

In elderly asthma patients, it is possible to maintain medication adherence by repeatedly conducting inhalation education. It has been reported that when inhalation education was conducted every 6 months, for a total of 2 years, in a group of patients with asthma aged between 50-90 years of age, the pMDI inhalation technique improved and was successfully maintained.<sup>40</sup>

## 13 | CONCLUSION

We recommend that primary care physicians refer the patients to medical specialists in order to receive an appropriate diagnosis, if the diagnosis and/or control of the condition of elderly asthma are found to be difficult. During routine medical care for asthma, physicians can instruct individual elderly asthma patients according to his/her conditions by increasing/decreasing the ICS dosage or simultaneously using other medicines, such as bronchodilators and leukotriene antagonists. However, if an inhalant cannot be used, then the physicians may have no choice but to choose oral medication or medicated patches, taking into account the potential side effects. In medical care for elderly asthma, patient education and observation is necessary. We hope that such efforts will lead to improvements in the treatment outcomes, as well as a decrease in elderly asthma deaths.

## 14 | RECOMMENDED GUIDELINES

1. Asthma Prevention and Management Guideline 2015, Japan. Japanese Society of Allergology. Kyowa Kikaku, Tokyo, 2015. The asthma guidelines from the Japanese Society of Allergology. It is the only asthma guidelines in Japanese (the asthma guideline is not published by the Japanese Respiratory Society). It provides detailed information regarding elderly asthma.
2. Global Initiative for Asthma. Global Strategy for Asthma Management, and Prevention. Updated 2017 [online]. This provides international guidelines for asthma. This guideline is available at: <http://ginasthma.org/2017-gina-report-global-strategy-for-asthma-management-and-prevention/>.

## 15 | CLINICAL SIGNIFICANCE

1. Clinical features of elderly asthma (Table 1).

**TABLE 1** Clinical features of elderly asthma

- The prevalence is increasing
- High death rate
- Coexists with more severe small airway disease
- Prone to misdiagnosis due to aging and/or comorbidities
- Differential diagnosis: COPD, Congestive heart failure, Lung cancer, GERD, Bronchiectasis, Upper airway obstruction, Aspiration
- Influence of drugs for comorbidities: beta blockers, ACE inhibitors, NSAIDs

2. Points of inhalation education for elderly asthma (Table 2).

**TABLE 2** Points of inhalation education for elderly asthma

- Regarding influence: Cognitive function, Manual dexterity, Finger strength for inhalation education
- Effectiveness of cooperation with medical staff for disease and inhalation education using tools to advance team-based medical practice between the physicians and pharmacists
- Necessity of physician's confirmation for patient's inhalation technique as well as indicated dosage and administrations

## CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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