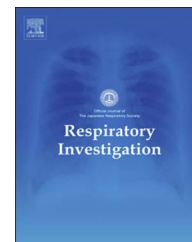




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Editorial

Obesity and severe asthma in Japan: Similarities and differences with Western countries

Several studies using data obtained from patients in Western countries have demonstrated an association between obesity and poorer asthma control, or reduced response to asthma therapy [1,2]. Obesity was defined according to the World Health Organization classification ($\text{BMI} \geq 30 \text{ kg/m}^2$). In general, obesity is fundamentally a systemic disorder of energy and metabolism. Previous studies have shown differences in the characteristics of obesity and metabolic functions between East-Asian and Western populations [3,4]. We therefore ask the question of how it is appropriate to evaluate obesity in Japanese asthma management?

On this issue, To et al. have evaluated the clinical characteristics of obesity associated severe asthma in a Japanese population and the associations between obesity and asthma control [5]. One important finding of the study is that obesity, which was defined as a $\text{BMI} \geq 25 \text{ kg/m}^2$, affected the annual exacerbation ratio. This indicates that a suitable definition of obesity should be applied when investigating or treating patients of different ethnicities or populations.

It was also found that obesity was independently associated with frequent asthma exacerbations only in the female cohort [5]. This is consistent with cluster analyses of asthma that have shown that obesity-related severe asthma is characterized by a female predominance [6]. Some factors such as sex hormones and difference in the body fat percentage between the genders may be involved, but the mechanisms underlying the influence of gender on the relationship between obesity and asthma are largely unknown.

Interestingly, the Framingham heart study have reported that females exhibited urinary creatinine-indexed 8-epi-PGF_{2α} levels (marker of systemic oxidative stress) that were 16% higher than males (regression coefficient=0.157, $p < 0.0001$) [7].

To et al. have also reported that there was no significant difference in spirometry data between the obese and non-obese patients [5]. This is not consistent however with previous reports from Europe and the United States that have shown that a loss of lung volume is associated with worsening of asthma in obese patients. These results imply that poor asthma control in Japanese patients with obesity and asthma may be associated more with metabolic factors than with the physical effects on lung function.

The percentage of body fat in East-Asian populations is higher than that in Western populations of an equal BMI [3]. To et al. speculated that adipocytokines produced from adipose tissue and obesity-related oxidative stress are thought to be higher in Japanese individuals than in Western individuals with the same BMI. The authors have previously evaluated the potential effect of systemic oxidative stress on acute exacerbations in obese asthmatic patients [8].

Serum malondialdehyde (MDA, an oxidative stress marker) levels were significantly higher in obese patients than in non-obese patients. There was a positive correlation between the frequency of severe asthma exacerbations and serum MDA in obese patients ($r = 0.542$, $p < 0.05$), but not in non-obese patients ($r = -0.017$, $p < 0.925$) [8]. Consequently decreasing oxidative stress and/or augmentation of antioxidants may be a beneficial option for the management of obesity-associated severe asthma.

Over the past decades, much effort has been focused on trying to understand the interrelationship between these syndromes by considering obesity and asthma as two separate entities. However, respiration, energy regulation and metabolism are closely integrated systems that affect every cell in the body. Obesity is characterized by chronic inflammation and oxidative stress, with an increase in the mediators of innate immunity and abnormal metabolites [9,10]. We should recognize that the lack of effective treatments for obesity-associated severe asthma remains an unresolved important clinical problem.

Kazuto Matsunaga

Department of Respiratory Medicine and Infectious Disease, Graduate School of Medicine, Yamaguchi University, Minami-kogushi, Ube, Yamaguchi 755-8505, Japan

E-mail address: kazmatsu@yamaguchi-u.ac.jp

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REFERENCES

- [1] Gibeon D, Batuwita K, Osmond M, et al. Obesity-associated severe asthma represents a distinct clinical phenotype: analysis of the British Thoracic Society Difficult Asthma Registry Patient cohort according to BMI. *Chest* 2013;143:406–14.
- [2] Anderson WJ, Lipworth BJ. Does body mass index influence responsiveness to inhaled corticosteroids in persistent asthma? *Ann Allergy Asthma Immunol* 2012;108:237–42.
- [3] WHO expert consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet* 2004;363:157–63.
- [4] McNeely MJ, Boyko EJ, Shofer JB, et al. Standard definitions of overweight and central adiposity for determining diabetes risk in Japanese Americans. *Am J Clin Nutr* 2001;74:101–7.
- [5] To M, Hitani A, Kono Y, et al. Obesity-associated severe asthma in an adult Japanese population. *Respir Investig* 2018, DOI: <https://doi.org/10.1016/j.resinv.2018.07.003>.
- [6] Dixon AE, Poynter ME. Mechanisms of asthma in obesity. Pleiotropic aspects of obesity produce distinct asthma phenotypes. *Am J Respir Cell Mol Biol* 2016;54:601–8.
- [7] Keaney JF, Larson MG, Vasan RS, et al. Obesity and systemic oxidative stress: clinical correlates of oxidative stress in The Framingham Study. *Arterioscler Thromb Vas Biol* 2003;23:434–9.
- [8] To M, Kono Y, Ogura N, et al. Obesity-related systemic oxidative stress: an important factor of poor asthma control. *Allergol Int* 2018;67:147–9.
- [9] Ghanim H, Aljada A, Hofmeyer D, et al. Circulating mononuclear cells in the obese are in a proinflammatory state. *Circulation* 2004;110:1564–71.
- [10] Hirano T, Matsunaga K. Late-onset asthma: current perspectives. *J Asthma Allergy* 2018;11:19–27.