# The Risk Factors and Clinical Course of Asthma with Fixed Airflow Limitation

Chaicharn Pothirat MD, FCCP*, Warawut Chaiwong BS*, Chalerm Liwsrisakun MD*, Chaiwat Bumroongkit MD*, Athavudh Deesomchok MD*, Theerakorn Theerakittikul MD*, Atikun Limsukon MD*, Nittaya Phetsuk BS*

** Division of Pulmonary, Critical Care and Allergy, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand*

***Objective:*** *To identify risk factors and clinical course of asthma with fixed airflow limitation.*

***Material and Method:*** *A retrospective case-control study of asthma patients was conducted over a 15-month period. Asthma with fixed airflow limitation patients were defined as chronic asthmatics who had both post-bronchodilator (BD) and on-treatment ratio of forced expiratory in first second ($FEV_1$)/forced vital capacity (FVC) persistently less than 0.7, whereas usual chronic asthma patients had post-BD and/or on-treatment ratio of $FEV_1$/FVC more than 0.7. Serial asthma control tests (ACT), medication used, exacerbations were assessed. The risk factors were analyzed using logistic regression. Clinical characteristics between groups were compared using Student's t-test and Fisher's exact test.*

***Results:*** *One hundred twenty from 142 eligible subjects were enrolled. They had asthma with fixed airflow limitation (n = 40) and usual chronic asthma (n = 80). Potential risk factors of asthma with fixed airflow limitation included early disease onset (age <15 years) [(adjusted odd ratio (OR) = 3.9, 95% confidence interval (CI) 1.9-8.3)] with longer disease duration (adjusted OR = 8.4, 95% CI 4.6-15.4 for >30 years). Asthma with fixed airflow limitation patients had lower ACT scores (p<0.001), lower level of asthma control (p<0.001), required more asthma medications (p = 0.002), and higher rates of hospitalization (p = 0.001) than usual chronic asthma.*

***Conclusion:*** *The potential risk factors of asthma with fixed airflow limitation were earlier disease onset and longer disease duration. They had poorer asthma control, more medications needed, and higher rates of exacerbation than usual chronic asthma.*

***Keywords:*** *Asthma, Risk factor, Clinical, Airflow, Limitation*

***J Med Assoc Thai 2016; 99 (7): 777-84***
***Full text. e-Journal:*** *http://www.jmatonline.com*

Chronic obstructive pulmonary disease (COPD) is characterized by persistently fixed airflow obstruction even when being treated with optimal bronchodilator therapy[1]. The most common cause of COPD is smoking related[2]. In general, few non-smoking asthma patients have persistent airflow limitation that resembles pulmonary function pattern of smoking-related COPD, despite the optimal use of inhaled corticosteroids and/or bronchodilators[3,4]. Asthma is a common chronic disease with substantial individual morbidity as well as direct and indirect costs to society[5,6]. Achieving and maintaining optimal asthma control is a major goal of asthma management[7,8]. The asthma patient with fixed airflow obstruction often associate with more frequent exacerbations[9], increased asthma-related mortality[10], and overall mortality[11]. The causes of fixed airflow obstruction in asthma are unknown but may be related to the presence of airway wall remodeling, which is characterized by increased airway smooth muscle mass and airway wall fibrosis[12]. There are two major phenotypes of asthma patients with age greater than 40 years old attending our clinic, usual chronic asthma and asthma with fixed airflow obstruction. We intended to identify risk factors and clinical course of asthma with fixed airflow limitation compared with usual chronic asthma patients.

***Correspondence to:***
*Pothirat C, Division of Pulmonary, Critical Care and Allergy, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, 110 Inthavaroros Road, Sriphum, Maung Chiang Mai, Chiang Mai 50200, Thailand.*
*Phone: +66-53-946228, Fax: +66-53-895117*
*E-mail: chaicharn.p@cmu.ac.th*

## Material and Method

### *Study design*

A retrospective case-control study of asthma with fixed airflow limitation and usual chronic asthma patients was conducted at the outpatient chest clinic, Chiang Mai University Hospital, Chiang Mai, Thailand over a 15-month study between November 2009 and January 2011. Two hundred thirty six asthma patients routinely managed by pulmonologists were screened for the study. One hundred forty two subjects, aged between 40 and 80 years, met the inclusion criteria for

asthma diagnosis. The study was approved by the Ethics Committees of the Faculty of Medicine, Chiang Mai University [Institutional Review Board (IRB) approval number: MED-2558-02816] and filed under the Thai Clinical Trials Registry (Study ID: TCTR20150420001).

***Inclusion and exclusion criteria***

The inclusion criteria were patients with asthma diagnosed based on a history episodic of wheezing, coughing, chest tightness, or dyspnea confirmed by standard of the American Thoracic Society (ATS)/European Respiratory Society (ERS), pre- and post-bronchodilator (BD) spirometry indicating reversibility of forced expiratory volume in first second ($FEV_1$) greater than 12% and 200 ml[7]. The exclusion criteria were history of irregular follow-up in the past year, poor compliance with treatment, and presence of concomitant systemic co-morbidities that could affect cardiopulmonary function. Studied patients were treated with standard asthma medications following the Global Initiative for Asthma (GINA) guidelines[7] by pulmonologists in the present study team at least a year prior to the study. However, only 120 out of 142 patients were able to enroll and repeat their pulmonary functions at one of the follow-up visit without holding their asthma medications (on-treatment spirometric test) under optimal conditions.

***Data collection***

There were 40 asthma subjects with persistently fixed airflow obstruction (post-BD and on-treatment ratio of $FEV_1$/forced vital capacity (FVC) persistently below 0.7) at both visits despite regularly receiving asthma treatment grouped under asthma with fixed airflow limitation. The other 80 asthma subjects were characterized by reversible airflow obstruction (post-BD and/or on-treatment ratio of $FEV_1$/FVC greater than 0.7), grouped under usual chronic asthma. Post-BD and on-treatment spirometric tests were performed using a standard spirometer (Vmax series 22, Sensormedics, Bilthoven, Holland) following ATS/ERS standards[13]. All tests were performed by a qualified technician and results were interpreted by a pulmonologist in the present study team. Values were calculated using the third National Health and Nutrition Examination Survey (NHANES III) reference equations[14]. However, for Asians, a correction factor of 0.88 was applied to the predicted FVC and $FEV_1$[15]. All enrolled subjects underwent face-to-face interviews to assess their baseline clinical characteristics including age, sex, smoking status, age of asthma onset, duration of asthma, concomitant chronic rhinitis, asthma control test (ACT) scores[16], details of rhinitis, and asthma medication used. All were regularly followed-up every three months for the entire 15-month study period. Serial ACT, use of rhinitis and asthma medication, compliance with inhaler use, asthma exacerbations with emergency visits, and/or hospitalizations were reviewed and recorded at every visit. Five questions of ACT, each with a maximum score of five, made the highest possible composite score of asthma control at 25. We determined that a score of 19 or less suggests that the asthma was partly controlled, and a score of 14 or less indicates that it was uncontrolled[17].

***Statistical analysis***

Data were compared between asthma with fixed airflow limitation and usual chronic asthma groups. Categorical variables were analyzed by Chi-square test. Continuous variables were compared by Student's t-test or Mann-Whitney U test as appropriate. Potential risk factors were analyzed by logistic regression in univariate and multivariate analyses and were adjusted by smoking status. Potential risk factors from univariate tests with $p$-value <0.25 were analyzed by multivariate logistic regression analysis[18]. Results were displayed as odds ratio (OR) with a 95% confidence interval (CI), $p$-value <0.05 was considered to be statistically significant. All analyses were carried out with the SPSS statistical package, version 16 for Windows (SPSS Inc. IL, USA).

**Results**

One hundred twenty patients from 142 eligible patients were enrolled, 40 patients with asthma with fixed airflow limitation, and 80 with usual chronic asthma. The schematic diagram of enrollment and reasons for exclusion at each step were shown in Fig. 1. Demographic characteristics and spirometric results were compared between groups (Table 1). There was no significant difference between the mean age of patients with asthma with fixed airflow limitation and usual chronic asthma, as well as between sex, body mass index (BMI), and smoking status between the two groups. However, age of asthma onset and asthma duration of asthma with fixed airflow limitation patients were significantly lower and longer than usual chronic asthma ($p$-value = 0.021 and $p$-value = 0.001, respectively). The prevalence of rhinitis in patients

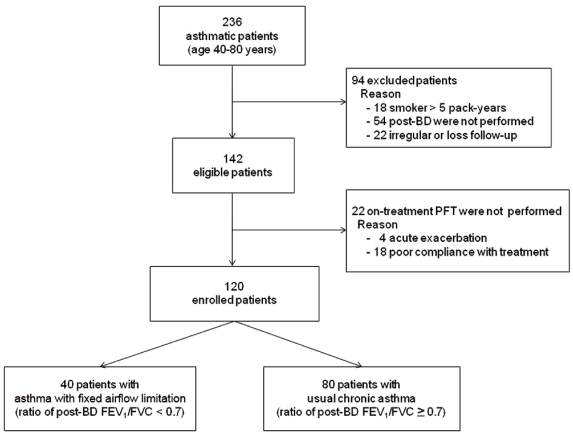


**Fig. 1** Flow-chart showing participation throughout the study.

with asthma with fixed airflow limitation was significantly higher than those with usual chronic asthma (*p*-value = 0.011). Furthermore, asthma with fixed airflow limitation patients had significantly lower pulmonary function than usual chronic asthma in terms of percentage of predicted $FEV_1$ and ratio of $FEV_1$/FVC (*p*-value <0.001 and *p*-value <0.001, respectively). The use of combination of inhaled corticosteroid (ICS) plus long-acting beta-2 agonist (LABA) in a single device and theophylline in asthma with fixed airflow limitation patients was significantly higher than patients with usual chronic asthma (*p*-value = 0.020 and *p*-value = 0.026, respectively). In contrast, the use of ICS alone in asthma with fixed airflow limitation patients was significantly lower than usual chronic asthma patients (*p*-value = 0.038). However, the use of rhinitis medication was not statistically significant between the two groups.

### *Potential risk factors of with asthma fixed airflow limitation*

In Table 2, univariate analysis showed that risk factors of asthma with fixed airflow limitation

**Table 1.** Baseline characteristics of asthma with fixed airflow limitation and usual chronic asthma

| Clinical characteristics | All patients (n = 120) | | *p*-value |
|---|---|---|---|
| | Asthma with fixed airflow limitation (n = 40) | Usual chronic asthma (n = 80) | |
| Gender | | | |
| Male | 18 (45.0) | 24 (30.0) | 0.111 |
| Female | 22 (55.0) | 56 (70.0) | |
| Age (year) | 60.3±9.9 | 58.1±10.2 | 0.262 |
| Age of asthma onset (year) | 34.6±19.6 | 43.1±16.9 | 0.021 |
| Asthma duration (year) | 25.0±17.7 | 14.0±13.6 | 0.001 |
| Body mass index (BMI) | 24.6±4.5 | 23.9±3.4 | 0.336 |
| Smoking status | | | |
| Non-smoker | 32 (80.0) | 63 (68.7) | 0.596 |
| Smoker | 8 (20.0) | 17 (21.3) | |
| Smoking pack-years | 0.5±1.1 | 2.5±7.9 | 0.763 |
| Chronic rhinitis | 39 (97.5) | 64 (80.0) | 0.011 |
| Post-BD spirometry | | | |
| Percentage of predicted $FEV_1$ | 61.6±16.8 | 80.3±14.9 | <0.001 |
| Ratio of $FEV_1$/FVC | 0.60±0.10 | 0.77±0.50 | <0.001 |
| Asthma medications | | | |
| ICS | 0 (0.0) | 8 (10.0) | 0.038 |
| ICS + LABA | 40 (100) | 70 (87.5) | 0.020 |
| Theophylline | 13 (32.5) | 12 (15.0) | 0.026 |
| Antileukotriene | 16 (40.0) | 20 (25.0) | 0.091 |
| Rhinitis medications | | | |
| Intranasal steroid | 15 (37.5) | 26 (32.5) | 0.586 |
| Antihistamine | 27 (67.5) | 4 (52.5) | 0.117 |
| Decongestant | 3 (7.5) | 2 (2.5) | 0.332 |

BD = bronchodilator; $FEV_1$ = forced expiratory volume in first second; FVC = forced vital capacity; ICS = inhaled corticosteroid; LABA = long-acting beta-2 agonists
Data were presented as mean ± SD and n (%)

**Table 2.** Univariable and multivariable logistic regression analysis for potential risk factors of asthma with fixed airflow limitation

| Clinical characteristics | Crude odds ratio (95% CI) | *p*-value | Adjusted odds ratio* (95% CI) | *p*-value |
|---|---|---|---|---|
| Gender | | | | |
| Female (ref. male) | 0.5 (0.2-1.2) | 0.107 | 0.4 (0.1-1.5) | 0.198 |
| Age of asthma onset (year) | | | | |
| <15 | 5.2 (1.7-16.5) | 0.003 | 3.9 (1.9-8.3) | <0.001 |
| 16-30 (ref.) | 1 | | 1 | |
| >30 | 1.0 (0.3-3.2) | 0.985 | 0.7 (0.2-2.6) | 0.585 |
| Asthma duration (year) | | | | |
| <10 (ref.) | 1 | | 1 | |
| 10-20 | 1.9 (0.6-5.6) | 0.261 | 2.4 (0.6-9.3) | 0.195 |
| 20-30 | 3.7 (1.0-14.2) | 0.052 | 8.4 (4.5-15.4) | <0.001 |
| >30 | 6.3 (2.0-19.9) | 0.002 | 8.4 (4.6-15.4) | <0.001 |
| BMI ($kg/m^2$) | | | | |
| Low (<18.50) | 1.8 (0.4-8.6) | 0.484 | | |
| Normal (18.50-24.99) (ref.) | 1 | | NA | |
| Overweight (25.00-29.99) | 1.1 (0.5-2.7) | 0.875 | | |
| Obesity (30.00-34.99) | 2.9 (0.7-12.1) | 0.136 | | |
| Smoking status | | | | |
| Smoker (ref. non-smoker) | 0.9 (0.4-2.4) | 0.874 | NA | |
| Chronic rhinitis | 9.8 (1.2-76.4) | 0.030 | 7.5 (0.8-83.1) | 0.057 |

ref. = reference; BMI = body mass index; CI = confidence interval; NA = not available
* Adjusted by smoking status

were younger age onset of disease (age <15 years). Disease duration of more than 10 year was an independent risk factor and the risk was increasing every decade of the disease duration. Co-morbidity with chronic rhinitis was also the risk factors. Multivariate analysis revealed that the only two risk factors of asthma with fixed airflow limitation were younger age of disease onset and longer disease duration.

***Level of asthma control***

During the 15-month treatment period, the percentage of patients with asthma with fixed airflow limitation had significantly lower ACT scores and level of asthma control (every 3-month visit between November 2009 and January 2011, *p*-value <0.05, Table 3, 4). Patients with asthma with fixed airflow limitation had higher usage of chronic rhinitis and asthma medications (every 3-month visit between November 2009 and January 2011, *p*-value <0.05, Table 4), except rhinitis medication only in one trimester (May to July 2010, *p*-value = 0.075). Patients with asthma with fixed airflow limitation revealed statistically significant higher numbers of exacerbation, emergency visits, and hospitalization per patient-year (Table 5).

**Discussion**

Our study demonstrated that younger age of onset and disease duration were potential risk factors for asthma remodeling. A disease duration of more than 10 year is one of the independent risk factors and the risk is higher every decade of the disease duration. Asthma with fixed airflow limitation associated with a younger age of onset and longer disease duration was previously reported to correlate with ongoing inflammation and sputum eosinophilia and neutrophilia despite high doses of inhaled/oral corticosteroids[19]. Airway smooth muscle mass is known to be increased in asthmatic subjects with longer disease duration[20], and in subjects with fatal asthma[21] or persistent severe asthma[22]. Chronic rhinitis is usually found in asthma with fixed airflow limitation. However, in our study it was determined to be a potential risk factor only by univariate analysis. Both lung function ($FEV_1$) and clinical course in asthma with fixed airflow limitation were significantly more impaired than usual chronic asthma at baseline during the 15-month treatment period. Outcomes were generally less favorable in asthma with fixed airflow limitation than usual chronic asthma in several major clinical aspects, poorer level of asthma control, and higher rates of exacerbation, emergency visits, and hospitalization despite more

**Table 3.** Level of asthma control between asthma with fixed airflow limitation and usual chronic asthma

| Follow-up time | Group of patients | Level of asthma control (%) | | | *p*-value |
|---|---|---|---|---|---|
| | | Well controlled | Partially controlled | Un-controlled | |
| Nov 2009 to Jan 2010 | Asthma with fixed airflow limitation | 57.5 | 30.0 | 12.5 | 0.001 |
| | Usual chronic asthma | 83.8 | 16.2 | 0.0 | |
| Feb 2010 to Apr 2010 | Asthma with fixed airflow limitation | 66.7 | 15.4 | 17.9 | 0.012 |
| | Usual chronic asthma | 86.3 | 7.6 | 6.3 | |
| May 2010 to Jul 2010 | Asthma with fixed airflow limitation | 67.6 | 18.9 | 13.5 | 0.001 |
| | Usual chronic asthma | 91.3 | 7.5 | 1.2 | |
| Aug 2010 to Oct 2010 | Asthma with fixed airflow limitation | 66.5 | 31.6 | 7.9 | <0.001 |
| | Usual chronic asthma | 92.5 | 7.5 | 0.0 | |
| Nov 2010 to Jan 2011 | Asthma with fixed airflow limitation | 67.6 | 11.6 | 10.8 | <0.001 |
| | Usual chronic asthma | 97.3 | 2.7 | 0.0 | |
| Total 15 months | Asthma with fixed airflow limitation | 67.6 | 11.6 | 10.8 | <0.001 |
| | Usual chronic asthma | 97.3 | 2.7 | 0.0 | |

**Table 4.** Asthma control test score, number of asthma and rhinitis medications between asthma with fixed airflow limitation and usual chronic asthma

| Follow-up time | Group of patients | ACT score | No. of asthma medication | No. of AR medication |
|---|---|---|---|---|
| Nov 2009 to Jan 2010 | Asthma with fixed airflow limitation | 19.4±4.2*** | 1.8±0.9* | 1.6±1.2* |
| | Usual chronic asthma | 22.1±3.3 | 1.4±0.6 | 1.2±1.1 |
| Feb 2010 to Apr 2010 | Asthma with fixed airflow limitation | 19.7±5.3** | 1.9±0.9* | 1.7±1.0* |
| | Usual chronic asthma | 22.1±3.3 | 1.4±0.6 | 1.2±1.1 |
| May 2010 to Jul 2010 | Asthma with fixed airflow limitation | 20.1±4.5*** | 1.9±1.1* | 1.7±1.1 |
| | Usual chronic asthma | 22.9±2.6 | 1.4±0.7 | 1.3±1.1 |
| Aug 2010 to Oct 2010 | Asthma with fixed airflow limitation | 19.9±4.3*** | 2.1±1.6* | 1.9±1.1* |
| | Usual chronic asthma | 23.1±2.1 | 1.5±0.7 | 1.4±1.2 |
| Nov 2010 to Jan 2011 | Asthma with fixed airflow limitation | 20.1±4.4*** | 2.0±1.1** | 2.1±1.1** |
| | Usual chronic asthma | 23.4±1.6 | 1.4±0.7 | 1.5±1.3 |
| Total 15 months | Asthma with fixed airflow limitation | 20.1±4.5*** | 10.1±5.6** | 8.7±5.3* |
| | Usual chronic asthma | 22.9±2.6 | 7.0±3.1 | 6.4±5.4 |

ACT = asthma control test; AR = allergic rhinitis
Data were presented as mean ± SD, comparison between groups; * $p<0.05$, ** $p<0.01$, and *** $p<0.001$

**Table 5.** Number of asthma exacerbations, emergency visits, and hospitalization between asthma with fixed airflow limitation and usual chronic asthma

| Times (per patient-year) | Asthma with fixed airflow limitation | Usual chronic asthma | *p*-value |
|---|---|---|---|
| Exacerbation | 1.8±0.8 | 0.2±0.5 | 0.008 |
| Emergency visit | 0.8±1.3 | 0.1±0.4 | 0.025 |
| Hospitalization | 0.3±0.8 | 0.0±0.0 | 0.001 |

Data were presented as mean ± SD

vigorous rhinitis and asthma medications. Recent studies have reported that specific genetic variants are associated with childhood-onset asthma and poor asthma control[23,24]. Physicians caring for usual chronic asthma should be aware of these potential risks (age onset <15 years old, disease duration >20 years, and presence of chronic rhinitis) for long-term remodeling of asthma with fixed airflow limitation and should consider that asthma with fixed airflow limitation patients are more difficult to control despite aggressive treatment with asthma and rhinitis medications.

Although lung function measurement is considered an indirect measurement of airway remodeling, a low post-BD $FEV_1$/FVC ratio was

proven to be a useful marker[9]. Bronchial biopsy to verify airway remodeling and oral corticosteroid trials to assess reversibility would have been preferable, however, for obvious reasons these measurements were not possible in an epidemiologic study. Our observations supported previous findings that progressive loss of lung function through childhood with less reversible airway narrowing progressed toward irreversible damage[25]. The present study had been conducted to evaluate the efficacy of pulmonary function test as an airway remodeling assessment method. A longitudinal population study of asthma from childhood to adulthood demonstrated that a low post-BD ratio of $FEV_1$/FVC was useful as an airway remodeling marker, which, in turn, was associated with an accelerated decline in lung function and reversibility[25].

Our study was limited as it was conducted at a single academic center and the risks identified in the present study might not be generalized to other centers. However, every asthma clinic, whether supervised by a pulmonologist or general practitioner, should raise awareness on asthma with fixed airflow limitation and improving quality of care. Furthermore, the number of hospitalizations due to asthma exacerbation in the present study was rather low, probably due to the strict study inclusion criteria, which only enrolled patients that complied with every scheduled visit. Finally, other potential risk factors that could impair lung function were not explored in the present study, including exposure to air pollution, inflammatory biomarkers, level of education, socioeconomic status, and personal psychosocial factors.

## Conclusion

Our study identified two major potential risk factors of asthma with fixed airflow limitation phenotype: younger disease onset and longer disease duration. This asthma phenotype had a higher prevalence of chronic rhinitis and poorer asthma control, higher use of asthma and rhinitis medications, and higher rates of exacerbation and hospitalization than usual chronic asthma.

## What is already known on this topic?

The asthma patient with fixed airflow obstruction often associated with more frequent exacerbations[9], increased asthma-related mortality[10], and overall mortality[11]. The causes of fixed airflow obstruction in asthma are unknown but may be related to the presence of airway wall remodeling, which is characterized by increased airway smooth muscle mass and airway wall fibrosis[12].

## What this study adds?

This study adds the information that two major potential risk factors of asthma with fixed airflow limitation phenotype: younger disease onset and longer disease duration. This asthma phenotype had a higher prevalence of chronic rhinitis and poorer asthma control, higher use of asthma and rhinitis medications, and higher rates of exacerbation and hospitalization than usual chronic asthma.

## Acknowledgments

The authors wish to thank the staff members of the Division of Pulmonary Critical Care and Allergy, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University for their contribution to the present trial.

## Potential conflicts of interest

None.

## References

1. Rabe KF, Hurd S, Anzueto A, Barnes PJ, Buist SA, Calverley P, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2007; 176: 532-55.
2. U.S. Surgeon General. The health consequences of smoking: chronic obstructive pulmonary disease. Washington, DC: U.S. Department of Health and Human Services; 1984.
3. Boulet LP, Turcotte H, Brochu A. Persistence of airway obstruction and hyperresponsiveness in subjects with asthma remission. Chest 1994; 105: 1024-31.
4. Brown PJ, Greville HW, Finucane KE. Asthma and irreversible airflow obstruction. Thorax 1984; 39: 131-6.
5. Mannino DM, Homa DM, Akinbami LJ, Moorman JE, Gwynn C, Redd SC. Surveillance for asthma--United States, 1980-1999. MMWR Surveill Summ 2002; 51: 1-13.
6. Weiss KB, Sullivan SD. The health economics of asthma and rhinitis. I. Assessing the economic impact. J Allergy Clin Immunol 2001; 107: 3-8.
7. Global Initiative for Asthma. Global strategy for asthma management and prevention [Internet]. NIH publication no. 95-3659. Bethesda, MD: National Heart, Lung, and Blood Institute,

National Institutes of Health; 1995 [updated 2006; cited 2009 Dec 15]. Available from: http://www.ginasthma.org
8. National Asthma Education and Prevention Program. Expert panel report 3: guidelines for the diagnosis and management of asthma [Internet]. NIH publication no. 07-4051. July 1997 [updated August 2007; cited 2009 Dec 15]. Available from: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm
9. Contoli M, Baraldo S, Marku B, Casolari P, Marwick JA, Turato G, et al. Fixed airflow obstruction due to asthma or chronic obstructive pulmonary disease: 5-year follow-up. J Allergy Clin Immunol 2010; 125: 830-7.
10. Panizza JA, James AL, Ryan G, de Klerk N, Finucane KE. Mortality and airflow obstruction in asthma: a 17-year follow-up study. Intern Med J 2006; 36: 773-80.
11. Hansen EF, Phanareth K, Laursen LC, Kok-Jensen A, Dirksen A. Reversible and irreversible airflow obstruction as predictor of overall mortality in asthma and chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1999; 159: 1267-71.
12. James AL, Wenzel S. Clinical relevance of airway remodelling in airway diseases. Eur Respir J 2007; 30: 134-55.
13. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. Eur Respir J 2005; 26: 319-38.
14. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. Am J Respir Crit Care Med 1999; 159: 179-87.
15. Hankinson JL, Kawut SM, Shahar E, Smith LJ, Stukovsky KH, Barr RG. Performance of American Thoracic Society-recommended spirometry reference values in a multiethnic sample of adults: the multi-ethnic study of atherosclerosis (MESA) lung study. Chest 2010; 137: 138-45.
16. Nathan RA, Sorkness CA, Kosinski M, Schatz M, Li JT, Marcus P, et al. Development of the asthma control test: a survey for assessing asthma control. J Allergy Clin Immunol 2004; 113: 59-65.
17. Thomas M, Kay S, Pike J, Williams A, Rosenzweig JR, Hillyer EV, et al. The Asthma Control Test (ACT) as a predictor of GINA guideline-defined asthma control: analysis of a multinational cross-sectional survey. Prim Care Respir J 2009; 18: 41-9.
18. Hosmer D, Lemeshow S. Applied logistic regression. 2nd ed. New York: John Wiley & Sons; 2000.
19. Kaminska M, Foley S, Maghni K, Storness-Bliss C, Coxson H, Ghezzo H, et al. Airway remodeling in subjects with severe asthma with or without chronic persistent airflow obstruction. J Allergy Clin Immunol 2009; 124: 45-51.
20. Bai TR, Cooper J, Koelmeyer T, Pare PD, Weir TD. The effect of age and duration of disease on airway structure in fatal asthma. Am J Respir Crit Care Med 2000; 162: 663-9.
21. Carroll N, Elliot J, Morton A, James A. The structure of large and small airways in nonfatal and fatal asthma. Am Rev Respir Dis 1993; 147: 405-10.
22. Benayoun L, Druilhe A, Dombret MC, Aubier M, Pretolani M. Airway structural alterations selectively associated with severe asthma. Am J Respir Crit Care Med 2003; 167: 1360-8.
23. Moffatt MF, Kabesch M, Liang L, Dixon AL, Strachan D, Heath S, et al. Genetic variants regulating ORMDL3 expression contribute to the risk of childhood asthma. Nature 2007; 448: 470-3.
24. Tavendale R, Macgregor DF, Mukhopadhyay S, Palmer CN. A polymorphism controlling ORMDL3 expression is associated with asthma that is poorly controlled by current medications. J Allergy Clin Immunol 2008; 121: 860-3.
25. Rasmussen F, Taylor DR, Flannery EM, Cowan JO, Greene JM, Herbison GP, et al. Risk factors for airway remodeling in asthma manifested by a low postbronchodilator FEV1/vital capacity ratio: a longitudinal population study from childhood to adulthood. Am J Respir Crit Care Med 2002; 165: 1480-8.

## ปัจจัยความเสี่ยงและสาเหตุทางคลินิกของโรคหอบหืดที่มีผลการตรวจสมรรถภาพปอดแบบอุดกั้นเรื้อรัง

**ชายชาญ โพธิรัตน์, วราวุฒิ ไชยวงค์, เฉลิม ลิ่วศรีสกุล, ชัยวัฒน์ บำรุงกิจ, อรรถวุฒิ ดีสมโชค, ธีรกร ธีรกิตติกุล, อติคุณ ลิ้มสุคนธ์, นิตยา เพชรสุข**

***วัตถุประสงค์:*** *เพื่อหาปัจจัยและสาเหตุทางคลินิกของโรคหอบหืดที่มีผลการตรวจสมรรถภาพปอดแบบอุดกั้นเรื้อรัง*

***วัสดุและวิธีการ:*** *การศึกษาย้อนหลังในผู้ป่วยโรคหอบหืด คำจำกัดความของโรคหอบหืดที่มีผลการตรวจสมรรถภาพปอดแบบอุดกั้นเรื้อรังคือ ผู้ป่วยที่มีผลการตรวจสมรรถภาพปอดแบบอุดกั้นเรื้อรังซึ่งค่าร้อยละระหว่างค่าปริมาตรของอากาศที่วัดได้ในวินาทีแรกของการหายใจออกอย่างเร็วและแรงเต็มที่จากตำแหน่งหายใจเข้าเต็มที่ต่อค่าปริมาตรสูงสุดของอากาศที่หายใจออกอย่างเร็วและแรงเต็มที่จนสุดจากตำแหน่งที่หายใจเข้าเต็มที่ (FEV /FVC) ทั้งหลังพ่นยาขยายหลอดลมและหลังจากที่ได้รับการรักษาอย่างเต็มที่แล้วน้อยกว่าร้อยละ 70 ในขณะที่ผู้ป่วยโรคหอบหืดเรื้อรังทั่วไปนั้นค่า FEV /FVC ทั้งหลังพ่นยาขยายหลอดลมและหลังจากที่ได้รับการรักษาอย่างเต็มที่แล้วมากกว่าหรือเท่ากับร้อยละ 70 โดยมีการเก็บข้อมูลย้อนหลังทั้งคะแนนจากแบบสอบถามควบคุมโรคหอบหืด ยาที่ใช้และการกำเริบของโรคเป็นระยะเวลา 15 เดือน ปัจจัยที่ทำให้เกิดโรคหอบหืดที่มีผลการตรวจสมรรถภาพปอดแบบอุดกั้นเรื้อรังนั้นวิเคราะห์ด้วยการวิเคราะห์การถดถอยโลจิสติก ลักษณะทางคลินิกระหว่างกลุ่มใช้สถิติ Student's t-test หรือ Fisher's exact test ตามความเหมาะสมของข้อมูล*

***ผลการศึกษา:*** *ผู้ป่วย 120 ราย จาก 142 ราย ถูกคัดเลือกเข้าร่วมในการศึกษา โดยแบ่งเป็นผู้ป่วยโรคหอบหืดที่มีผลการตรวจสมรรถภาพปอดแบบอุดกั้นเรื้อรัง 40 ราย และโรคหอบหืดเรื้อรังทั่วไป 80 ราย ปัจจัยเสี่ยงที่ทำให้เกิดโรคหอบหืดที่มีผลการตรวจสมรรถภาพปอดแบบอุดกั้นเรื้อรังคือ ผู้ป่วยเริ่มมีอาการของโรคในช่วงก่อนวัยรุ่น (อายุ <15 ปี) (odds ratio (OR) = 3.9, 95% confidence interval (CI) 1.9-8.3) และมีระยะเวลาที่เป็นโรคยาวนานกว่า 30 ปี (adjusted OR 8.4 = 95% CI 4.6-15.4) นอกจากนี้ยังพบว่าผู้ป่วยหอบหืดที่มีผลการตรวจสมรรถภาพปอดแบบอุดกั้นเรื้อรังมีคะแนนจากแบบสอบถามควบคุมโรคหอบหืดและระดับการควบคุมโรคหอบหืดต่ำกว่าผู้ป่วยโรคหอบหืดเรื้อรังทั่วไปอย่างมีนัยสำคัญทางสถิติ อีกทั้งยังพบว่าผู้ป่วยโรคหอบหืดที่มีผลการตรวจสมรรถภาพปอดแบบอุดกั้นเรื้อรังยังมีการใช้ยารักษาโรคหอบหืดและอัตราการกำเริบของโรคสูงกว่าผู้ป่วยโรคหอบหืดเรื้อรังทั่วไปอย่างมีนัยสำคัญทางสถิติด้วย*

***สรุป:*** *ปัจจัยที่ทำให้เกิดเป็นโรคหอบหืดที่มีผลการตรวจสมรรถภาพปอดแบบอุดกั้นเรื้อรังคือผู้ป่วยเริ่มมีอาการของโรคในช่วงก่อนวัยรุ่นและมีระยะเวลาที่เป็นโรคยาวนาน ซึ่งส่งผลให้ผู้ป่วยกลุ่มนี้มีการควบคุมโรคหอบหืดได้ไม่ดี ใช้ยารักษาโรคมากขึ้น และมีอัตราการกำเริบของโรคสูงกว่าผู้ป่วยโรคหอบหืดเรื้อรังทั่วไปด้วย*