Comparative Assessment of Asthma Control Test (ACT) and GINA Classification including FEV1 in predicting asthma severity

Maria Monica R. Mendoza, M.D. Bernice Ong-Dela Cruz, MD, Aileen V. Guzman-Banzon, MD; Fernando G. Ayuyao, MD and Teresita S. De Guia, MD

Background --- The gold standard in classifying severity of asthma is the GINA classification, however, the numeric cut-off values of frequency and intensity symptoms and parameters of physiologic dysfunction used to classify asthma severity are artificial and transitory. Currently, asthma questionnaires, such as the Asthma Control Test (ACT), provides a more simplified assessment of control by not requiring FEV1. It is the aim of this study to compare the Asthma Control Test (ACT) and GINA classification, including FEV1, in assessing asthma severity and validate ACT as a screening tool for asthma severity.

Methods --- This is a prospective cohort study involving adult asthmatic patients who were classified based on their ACT scores into controlled asthma (ACT>19) and uncontrolled asthma (ACT < 19). They were then classified accordingly to their GINA asthma symptom severity. After which, FEV1 and peak expiratory flow rate (PEFR) were recorded. Correlation as well as measures of validity were obtained, with level of significance set at 0.05.

Results --- Among the 86 patients included in this study, 62 have ACT scores < 20. The prevalence rate of uncontrolled asthmatics was 72% with majority classified as moderate persistent. Significant association between ACT and GINA classification (p-value 0.00), ACT and FEV1 in liter (p-value 0.013), ACT and FEV1 as % predicted (p-value 0.023) and ACT and PEFR in % predicted (p-value 0.037) were observed. There appeared to be an association between a lower ACT score and a more severe symptom severity. ACT was 92.3% sensitive and 90.5% specific with AUC of 0.972. The positive predictive value was 98% and the negative predictive value is 79%.

Conclusion --- With its high sensitivity, specificity and positive predictive value, ACT can served as an alternative diagnostic tool in assessing asthma severity even without an aid of a spirometer or a peak flow meter. An ACT score of at least 20 can classify patient as intermittent or controlled asthmatic while an ACT score < 20 can classify the patient as in persistent or uncontrolled asthmatics. ***Phil Heart Center J 2007;13(2):149-154.***

Key Words: Asthma ■ GINA ■ Severity ■ Validation Study ■ Asthma Control Test ■ FEV1

Asthma is a worldwide disease which affects all ages, sex and racial groups. In the Philippines, limited reports showed a prevalence rate of 12% in children aged 13-14 years old and 12-22% in older age groups.[2] In spite of the recent advances in the detection and treatment of the condition, asthma remains a cause of significant morbidity and economic burden.

Despite the availability of national and international guidelines, asthma management is grossly suboptimal worldwide. The Asthma Insights and Reality in Asia-Pacific (AIRIAP) survey, involving asthma subjects from eight areas including the Philippines, has demonstrated that the disease causes substantial morbidity, utilization of healthcare resources and absence from work/school, especially in those with more severe disease.[1]

Asthma severity and asthma control are distinct yet related concepts. Asthma severity describes the underlying disease in the absence of therapy and is ideally defined without concurrent treatment confounding its assessment. The in trinsic intensity of the disease, which can change, but does so only slowly over time. In the presence of the appropriate intervention, including education, environmental control, and pharmacotherapy, many of the characteristics of disease that we used to describe severity may be changed or absent.[3]

More recently, the concept of asthma control has been introduced to describe better the status of disease in the presence of intervention. Asthma control describes the clinical status of disease with medical intervention. It can rapidly change in response to triggers or therapy. However, the individual parameters by which we define asthma severity and asthma control overlap significantly.[3]

The therapeutic goal is to achieve uncontrolled

Correspondence to Maria Monica R. Mendoza, MD. Division of Adult Cardiology. Philippine Heart Center, East Avenue, Quezon City, Philippines 1100 Available at **http://www.phc.gov.ph/journal/publication** ISSN 0018-9034

asthmatics to well-controlled then ultimately total controlled. This require aggressive therapy/intervention to achieve adequate control especially in severe persistent compared to a mild disease.[2] A well-controlled asthmatic should have no or minimal symptoms or use of rescue medication, no significant limitation in activity and (near) normal lung function.[3] The gold standard in classifying severity is the GINA classification of asthma symptom severity which includes daytime and nocturnal symptoms, objective parameters using the FEV1 and PEF variability.[2]

Long term mental retention and adherence to the classification details have not been satisfactory. Because asthma is a chronic inflammatory disease, the severity of its chronic state exists in a continuum. Numeric cut-off values of frequency and intensity symptoms and parameters of physiologic dysfunction currently used to classify asthma in different levels of severity are artificial and transitory.[2] Furthermore, the availability as well as the affordability of the spirometry is not readily met by all patients.

Concurrently, many asthma questionnaires were formulated to make the assessment of asthma severity and control easy. The most recent and the most simplified questionnaire done by Nathan, et al was the Asthma Control Test (ACT). As a screening tool, the overall agreement between ACT and the specialist's rating ranged from 71% to 78% and the AUC was 0.77. The ACT provides a more simplified assessment of control by not requiring FEV1 and by providing a meaningful and easy to use scoring method, which is simpler than the other previous asthma questionnaires but comprehensive enough to evaluate the range of asthma control. Still, the best measure of control would be the use of a FEV1.[10]

Objectives

General Objectives

1. To compare the Asthma Control Test (ACT) and GINA classification including FEV1 in assessing asthma severity.
2. To determine the frequency of uncontrolled asthmatics through Asthma Control Test (ACT).

Specific Objectives

1. To determine the validity of Asthma Control Test (ACT) as a screening tool in
assessing asthma severity
2. To determine if there is an association between Asthma Control Test (ACT) and GINA classification of asthma severity.
3. To determine the association of Asthma Control Test (ACT) with forced expiratory volume in 1 sec - FEV1(L and %predicted) and Peak Flow Meter Rate – PEFR (L/min and %predicted).

Methods

This was a prospective cohort study which included mainly adult asthmatic patients who have been and had been taking asthmatic medications. Patients younger than 18 years old and with concomitant lung pathology such as emphysema, bronchiectasis, bronchitis and tuberculosis were excluded.

The Asthma Control Test (ACT), a validated 5-item self-administered survey designed to assess asthma control, was administered to the subjects. ACT is scored on a scale of 5-25 with the higher scores reflective of better asthma control. An ACT score of >19 suggests controlled asthma while ACT score of less than or equal to 19 suggests uncontrolled asthma.

After the Asthma Control Test (ACT), patients had an interview wherein they were classified according to the GINA symptom severity. The GINA classification of symptom severity includes 4 categories – mild intermittent, mild persistent, moderate persistent, and severe persistent. This is based on clinical symptoms including daytime and nocturnal shortness of breath, spirometric studies with FEV1 and PEF variability.

After which, spirometric studies and peak expiratory flow rate were done. They were instructed to blow first on the Peak Flow Meter or the Mini-Wright followed by the portable ventilometer or the Microloop. The recorded FEV1 (L and % predicted) and PEFR (L/min and % predicted) were taken as the best of three satisfactory results.

Statistical Analysis: Fisher's Exact Test and Chi-squared test were used to determine association between variables. Pearson Correlation coefficient was utilized to determine correlation between FEV 1 and PEFR. ROC was used to calculate the specificity and sensitivity of ACT as a screening tool. The level of significance was set at 0.05.

Results

A total of 86 asthmatic patients were seen at the Out-Patient Department. Of these, 62 patients have ACT score of less than 20, giving a 72% prevalence rate of uncontrolled asthmatic patients or patients with persistent asthma. On the other hand, 28% of the study population showed ACT score of at least 20, which falls into the category of intermittent asthma. Table 1 shows that there was a significant difference between the mean FEV 1 in L (p: 0.013) and in % (p: 0.023) of patients with ACT score of less than 20 and patients with ACT score of at least 20. FEV1 < 2L or <80% predicted were associated with ACT score of <20 while FEV1 >2L or >80% predicted were associated with ACT score of at least 20.

There was also an association between GINA classification of asthma symptom severity and ACT score

Table 1. Characteristics of eligible patients grouped based on their ACT scores

Clinical and Demographic Characteristics	ACT Score (≤ 19) N=62	ACT Score (>19) N=24	p-value
Age, y (mean, SD)	40.0 (10.5)	38.5 (10.6)	0.540
Sex			
male, n(%)	14 (23)	9 (38)	0.130
female, n(%)	48 (77)	15 (62)	
Smoking History			
Smoker, n(%)	3 (5)	3 (12)	0.211
Non smoker, n(%)	59 (95)	21 (88)	
Presence of Allergic Rhinitis			
With, n(%)	9 (14)	7 (29)	0.106
Without, n(%)	53 (86)	17 (71)	
GINA classification (n,%)			
Mild Intermittent	2 (3)	19 (79)	
Mild Persistent	15 (24)	1 (4)	0.000*
Moderate Persistent	32 (52)	2 (8)	
Severe Persistent	13 (21)	2 (8)	
FEV 1, L (mean, SD)	1.9 (0.6)	2.2 (0.6)	0.013*
% (mean, SD)	76.0 (18.0)	83.9 (12.4)	0.023*
PEFR , L/min (mean, SD)	344.5 (95.8)	382.3 (93.5)	0.102

*significant

Table 2. Derived Asthma Control Test (ACT) scores and asthma symptom severity using the GINA classification

GINA Classification of Asthma Severity	ACT Score (5-14)	ACT Score (15-19)	ACT Score (20-25)	Total
Mild Intermittent	0 (0.0)	2 (4.5)	19 (79.2)	21(25)
Mild Persistent	0 (0.0)	15 (34.1)	1 (4.2)	16(18)
Moderate Persistent	8 (44)	24 (54.5)	2 (8.3)	34(40)
Severe Persistent	10 (56)	3 (6.8)	2 (8.3)	15(17)
TOTAL	18(21%)	44(51%)	24(28%)	86

(p value: 0.00). However, no association were noted with sex, smoking history and allergic rhinitis and the ACT score. Both group exhibited almost the same population characteristics; the age ranged between 30 -40 y/o, > 50% of the subject population were females, majority were non-smoker(>70%) and a small proportion of asthmatics has concomitant allergic rhinitis (7%).

In Table 2, we could see the breakdown of the different ACT Score in conjunction with the GINA classification of asthma severity. The derived ACT scores were based on the AIRIAP study by Lai, et.al.[9]

In our study, 51% of the patient had ACT score of 15-19, which signifies not controlled asthmatic and 21% had scores below ACT 15 or classified as poorly controlled asthmatics. Based on the GINA classification of asthma symptom severity, majority of the asthmatics were moderate persistent(40%), followed by mild persistent(18%) and severe persistent(17%) and lastly, the mild intermittent(25%). There appeared to be an association between a lower derived ACT score and a more severe symptom severity. Although, there was an overlapping of ACT score for moderate persistent from

Table 3. Comparison of the derived ACT score level with GINA Classification of Asthma Symptom Severity, FEV1, PEFR (% predicted)

	ACT Score (5-14)	ACT Score (15-19)	ACT Score (20-25)	p-value
GINA Classification of Asthma Severity (n,%)				0.000*
Intermittent	0 (0.0)	2 (4)	19 (79)	
Persistent	18 (100.0)	42 (96)	5 (21)	
FEV1, L (mean, SD)	1.7 (0.6)	1.9 (0.6)	2.2 (0.6)	0.022*
FEV1, % (mean, SD)	71.4 (17.6)	77.8 (18.0)	83.9 (12.4)	0.057
PEFR (n,%)				0.037*
> 80% predicted	7 (38.9)	28 (63.6)	19 (79.2)	
60 – 80% predicted	7 (38.9)	14 (31.8)	4 (16.7)	
< 60% predicted	4 (22.2)	2 (4.5)	1 (4.2)	

Table 4. Sensitivity and Specificity of ACT as a screening tool in assessing asthma severity

ACT Score	GINA Classification Persistent	GINA Classification Intermittent	SN	SP	PPV	NPV	Area Under the Curve
≤ 19	60	2	92.3%	90.5%	98%	79%	0.972
> 19	5	19					

ACT 5 to 19, again, it can be classified generally as not controlled asthmatics..

As we compared the derived ACT score with the GINA classification and the FEV1, it almost showed the same association as in Table 1.; ACT scores of 5-14 and 15-19 falls in persistent asthma with a FEV1 <2L while ACT scores above 20 falls in intermittent asthma with a FEV1 >2L(Table 3) except for the FEV1(%).

In our study, PEFR (% predicted) was shown to be associated with the derived ACT scores but not the actual value of PEFR(L/min). As the ACT scores fall, the PEFR (% predicted) also fall <60% (Table 3). ACT score is 92.3% sensitive and 90.5% specific with area under the curve of 0.972 (97.2%). The positive predictive value is 98% and the negative predictive value is 79%. In consequence, ACT score is an excellent diagnostic tool for screening asthma severity with its high sensitivity and positive predictive value.

Discussion

Based on NIH(1997), Asthma is now considered as a disease of airway inflammation. The incessant release of the inflammatory mediators from eosinophils and mast cells results in persistent bronchial inflammation of the airways. Obviously, the airways undergo structural abnormalities resulting in the following: fibrosis, increase in mass of the smooth muscle and mucus glands, epithelial shedding, thickening of the reticular basement membrane and fibronectin deposition in the subepithelial layer. Histological sections show thickening of the airways by 50-300% of normal.

Airway remodeling results in the following physiologic consequences: 1) increase in airway hyperre

sponsiveness 2) non-reversibility of airway obstruction and residual obstruction after bronchodilator and anti-inflammatory therapy and 3) accelerated decline in the FEV1 in a subset of asthmatic patients.[2]

Asthma is diagnosed by a combination of history (positive family history), clinical findings: 1)cough which worsens at night, 2) wheeze, 3) dif ficulty of breathing, 4) chest tightness. In addition, objective measurements of variable airflow obstruction using spirometry(FEV1) and peak flow meter(PEFR). However, in some cases, the medical history and PE may not be reliable in diagnosing asthma. Furthermore, the physical examination maybe normal as asthma symptoms are characteristically episodic especially in children. An objective measure is needed to diagnose asthma accurately(GRADE A).[2]

Asthma can be classified according to: 1) etiology 2) severity (clinical condition on presentation whether the patient is in acute or in a chronic state). The first classification is limited as no environmental cause can be identified. For identification of the specific etiology will guide both the physician and the patient on the use of avoidance strategies in management.[2]

The second classification is based on the severity of the disease. It is important to put emphasis on patient who are in acute exacerbation such could be fatal if not treated appropriately.

Even patient with chronic asthma, however mild, may have an acute exacerbation. Any patient, even with mild symptoms, should be considered as having asthma exacerbation if there is: 1) history of life threatening acute attacks, 2) hospitalization within previous year, 3) psychosocial problem, 4) history of intubation for asthma, 5) recent reductions or cessation of glucocorticoid therapy, and 6) noncompliance with recommended medical therapy. These clinical conditions are associated with a higher risk of asthma mortality. Since acute exacerbation demands an urgent need to intervene and modify existing treatment.[2]

Crockcroft and Swystun have suggested that the only measure that can distinguish asthma severity and asthma control is the minimal amount of controller medication required to achieve adequate control. However, this measure is an accurate reflection of disease severity only when optimal control has been achieved. Unfortunately, optimal control is not routinely achieved among the general population which limits the usefulness of such measure. Therefore, efforts are made to develop measures that accurately classify asthma severity and asthma control.[3]

Fuhlbrigge, et.al. assessed asthma burden in the US using 3 components: Short-term symptom burden(4-week recall), Long-term symptom burden(past year) and Functional impact(activity limitation). In this study, there is a discordance in the pattern of the asthma symptoms by individuals. Also seen by Colice, et.al., evaluation of the asthma severity utilizing individual component of disease may lead to inadequate treatment of asthma . Hence, no single variable can give a complete picture of the clinical status of disease. Accurate assessment requires a combination of parameters.[4]

Eventually, validated instruments such as questionnaire has developed to evaluate asthma control. The Asthma Therapy Assessment Questionnaire (ATAQ) by Vollmer, et.al. showed a significant association between the level of control and healthcare utilization5. The Asthma Control Questionnaire (ACQ) by Juniper, et.al. has demonstrated high evaluative and discriminative properties. Recent evidence showed ACQ compared to the composite measure based by GINA/NIH criteria showed significant association with the ACQ score and the severity of the disease.[6]

The Asthma Control Test, a five item self administered survey which scored from 0 -5; Recent analysis compared it with the specialist assessment showed a specificity of 76.2% and a sensitivity of 68.4%7. Nathan, et al . studied the overall agreement between ACT and the specialist's rating ranged from 71% to 78% and the AUC was 0.77.[10]

All questionnaires focus on patient-oriented features of the disease.[4] All 3 describe the impact of asthma on daily activities, sleep disrupted by asthma and the need for rescue medication.

Disease severity is not a patient-focused measures, limited by the requirement that it should be assessed prior to use of medication and includes measures of lung function. Unfortunately, these are not performed regularly. In contrast, these 3-survey tools can be assessed in the presence of controller medications, are not dependent on the availability of spirometer and report on asthma control over a longer period of time (1-4wks) depending on the questionnaire used. Disease severity and control have the inherent disconnect of the patient with mild disease that is not well controlled or severe disease who has good contro.[l8]

There is still a continued debate on how to assess asthma control in a way supports management and is easy to use in practice. The ACT questionnaire ask patient to report for the previous 4-weeks(short term recall) regarding: limitations to activities, shortness of breath, night-time awakening, use of rescue medication, perception of control. Completion of the ACT results in a potential score of between 5-25: > or = 20 indicates well controlled and a score < or = 15 suggests poor controlled asthma.[9]

Lai, et al, showed that poorer asthma control, as measured by the derived ACT, was associated with a higher requirement for hospitalization and unscheduled healthcare over the previous year and elevated healthcost based on the questionnaires used in the AIRIAP study.[9]

For ACT of <15, the mean per-patient annual cost

of asthma management was US $861, US $319 for patients with a derived ACT score 15-19 and US $193 for patients with derived ACT score of at least 209. As the ACT scores went down, the expenditure for asthma care went up which connotes an inverse relationship. As asthma is not controlled, the more expenses the patient would incurred.[9]

In our study, only 24 patients(28%) has controlled asthma and the rest were uncontrolled(72%). This substantiates the AIRIAP study which showed that in our part of the world, the Asia-Pacific region, still asthma is not totally contained. This should alert us, the physician, to educate our patient with the nature of the disease that they have incurred. Still, patient education plays an important role in the control of a disease entity.

According to Nathan, et.al., ACT score of < 19 shows that most patients are uncontrolled. ACT is a simple, inexpensive test that has been already been validated10.

Stempel, et al, in his study of 522 subjects showe d that ACT may serve as a useful screening tool in the community to determine whether patients have controlled or uncontrolled asthma.[12]

In our study, there was an association noted between the asthma control test (ACT) and the GINA classification of asthma symptom severity, FEV1(L and %) as well as peak expiratory flow rate (% predicted). The ACT score was able to give a 92.3% sensitive and 90.5% specific with area under the curve of 0.972 (97.2%). Likewise, the positive predictive value is 98% and the negative predictive value is 79%. Consequently, this makes it an excellent diagnostic tool for screening asthma severity. Our findings has corroborated with the above studies.

An ACT score of at least 20 can classify patient as in intermittent or controlled asthmatics with an of FEV1 and PEFR of >80% predicted while an ACT score of less than 20 can classify the patient as in persistent or uncontrolled asthmatics with an FEV1 and PEFR of < 80% predicted.

In the GOAL study, it was designed to assess whether total control or well control status was achievable. This study demonstrated that well or total control of asthma could be attained in the majority of the patients treated with a salmeterol/fluticasone combination. Although control was established at a high threshold, majority of the patients were able to achieve and sustain well or total asthma control. This allows for the establishment of a new goal for assessing asthma outcomes.[13]

In our study, majority of the patients interviewed do not have any controller medication. Only 32 asthmatics(37%) of the study population has used combination beta-agonist and steroids. Not all of them are maintained on a regular basis, some have stopped due to financial constraint, some are still using on a p.r.n. basis and luckily, a few are able sustain its use. Hence, majority of them falls into the category of moderate persistent. Using the patient-oriented concept thru asthma control test (ACT), we hope that detecting uncontrolled asthmatics would be easier, leading to a better adherence to the controller medication and ultimately, a better or total control of asthmatic patients in our country.

Limitations

This study is limited by the relatively small sample size and could lead to variations in values that may not be reflective of the larger, general population specifically the asthmatics. Another is the objectivity analysis of the investigator assessment as the gold standard which is to classify the patients according to the GINA asthma symptom severity. Nonetheless, the magnitude of association flow meter are not readily available. Despite its limitation, this study has demonstrated asthma control test (ACT) with a high positive predictive value as well as high sensitivity and specificity making it a good screening tool in asthmatics. between the asthma control test and GINA classification asthma symptom severity as well as FEV1(L and %) and PEFR(%) indicates that asthma control test (ACT) can be used as a surrogate test in assessing asthma severity especially in places where spirometry as well as peak

Conclusion

With its high sensitivity, specificity and positive predictive value, asthma control test (ACT) can served as an alternative diagnostic tool in assessing asthma severity even with out an aid of a spirometer or a peak flow meter in an out-patient basis or as home based. An ACT score of at least 20 can classify patient as intermittent or controlled asthmatics with an of FEV1 and PEFR of >80% predicted while an ACT score of less than 20 can classify the patient as persistent or uncontrolled asthmatics with an FEV1 and PEFR of < 80% predicted. It can serve as a guide in the case management of asthmatic patients. Therefore, asthma control test (ACT) is a simple, inexpensive tool that can be used especially in our country where financial resources are limited, disabling our patient to do the standard diagnostic test such as the spirometry.

References

1. Lai CKW, De Guia TS, Kim YY, et.al. Asthma Control in the Asia-Pacific Region: the Asthma Insights and Reality in Asia-Pacific Study. *J Allergy Clin Immunol 2003;111:263-268.*
2. PCCP. *Evidence-based Guidelines in the diagnosis of Asthma. 2005.*
3. Cockcroft DW, Swystun VA, Asthma Control versus asthma severity. *J Allergy Clin Immunol* 1996;98:1016-1018.
4. Fuhlbrigge AL. Asthma Severity and Asthma Control: symptoms, pulmonary function and inflammatory markers. *Curr Opin Pulm Med 2004;10:1-6.*
5. Vollmer W, Markson L, O'Conner E, et.al. Associatioan of Asthma Control with Health Care utilization and Quality of life. *Am J Respir Crit Care Med 1999;160:1647-1652.*

6. Juniper EF, O'Bryne PM, Guyatt GH, Ferrie PJ, King DR. Development and validation of a questionnaire to measure asthma control. *Eur Respir J 1999;14:902-907*
7. Schatz M, Li JT, Sorkness CA, et.al. Responsiveness of the Asthma Control Test (ACT) to changes in specialist ratings of asthma control and FEV1. *Am J Respir Crit Care Med 2004;169:A319*
8. Stempel,A. et.al. Improving Asthma Diagnosis and Assessment. *J Allergy Clin Immunol* 2005.
9. Lai CKW, De Guia TS, Kuo,SH, Spencer,MD, et.al. Asthma Control and its Direct Healthcare Costs : findings using derived Asthma Control Test Score in Eight Asia-Pacific areas. *Eur Resp Rev 2006;15:98,24-29.*
10. Nathan,RA, Sorkness CA, et.al. Development of Asthma Control Test: a survey for assessing asthma control. *J Allergy Clin Immunol 2004;113:59-65*
11. Schatz M, Sorkness CA, Li JT, Marcus P, Murray JJ, Nathan RA, Kosinski M, Pendergraft TB, Jhingran P. Asthma Control Test: reliability, validity, and responsiveness in patients not previously followed by asthma specialists. *J Allergy Clin Immunol. 2006 Mar;117(3):549-56.*
12. Stemple D, Williamson A, Stanford R. Comparative assessment of asthma control with both ACT and Spirometry in subjects attending community events. *J Allergy Clin Immunol 2005;115:S216*
13. Bateman ED, Boushey HA, Bousquet J, et. al. GOAL Investigators Group. Can guideline-defined asthma control be achieved? The Gaining Optimal Asthma Control Study. *Am J Respir Crit Care Med 2004; 170: 836-844.*